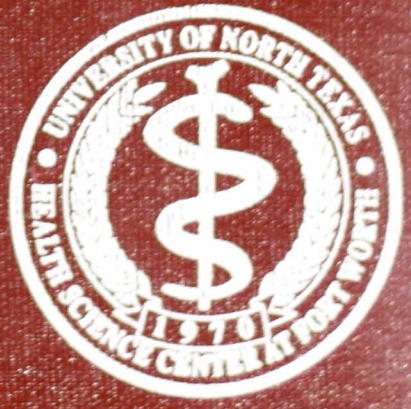

UNIVERSITY OF NORTH TEXAS
HEALTH SCIENCE CENTER AT FORT WORTH
1970

Segars, Larry W., Differences in Risk of Injury between Stimulant-Treated and Untreated ADHD Patients. Doctor of Public Health (Epidemiology), August 2006, 63 pp, 7 tables, 0 illustrations, references, 78 titles.

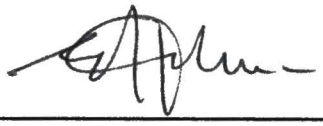
ADHD is a common psychiatric disorder of childhood and adolescence that also occurs in adults and spans the life of the patient. ADHD is characterized by lack of focus, distractibility, and poor concentration. Limited data have been generated focusing on ADHD patients and the association with an increased risk of injury. Unfortunately, no study has been published evaluating the effect of stimulant treatment for ADHD on the risk of injury requiring ambulatory medical care. This research utilized four concatenated years, specifically 1998-2001, of the National Ambulatory Medical Care Survey (NAMCS). This dissertation is comprised of five chapters beginning with a description of ADHD, its characteristics, diagnosis, and treatment. This overview chapter is followed by a complete review of the literature describing the publication's which assessed the association between ADHD and the risk of injury. The next chapter is a thorough review of the NAMCS and its methodology. The concatenated dataset captured 889 office visits associated with a diagnosis of ADHD, 666 of which were also related to the prescription of a stimulant for the management of ADHD. Using NAMCS's weight variable these values produced a national estimate of 21,223,391 office visits associated with the ADHD diagnosis and 15,604,329 office visits associated with the prescription of a stimulant for ADHD.

This research determined that there was a borderline statistically significant increased association with the prescription of a stimulant for the treatment of ADHD and the risk of injury requiring treatment in an ambulatory medical care setting. Interestingly, compared to patient's who recorded their race as Caucasian, patients who recorded their race as "Other"; representing the races of Asian, Native Hawaiian/Other Pacific Islander, or American Indian/Alaska Native, and individuals indicating more than one race, had a statistically significant increased risk of injury necessitating treatment in an ambulatory medical care setting. Potential theories for this unique finding, along with the limitations of this research, are provided in the final discussion chapter.

DIFFERENCES IN RISK OF INJURY BETWEEN STIMULANT-TREATED AND UNTREATED ADHD PATIENTS

Larry W. Segars, PharmD, FCCP, BCPS

APPROVED:



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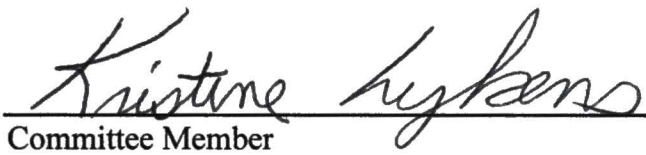

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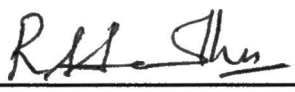

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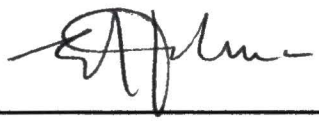

Department Chair

Dean, School of Public Health

DIFFERENCES IN RISK OF INJURY BETWEEN STIMULANT-TREATED AND UNTREATED ADHD PATIENTS

DISSERTATION

Presented to the School of Public Health

University of North Texas Health Science Center at Fort Worth

in Partial Fulfillment of the Requirements

for the Degree of

Doctor of Public Health

By

Larry W. Segars, PharmD, FCCP, BCPS

Fort Worth, Texas

August 2006

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Table 1

Select Information on the Four NAMCS Study Years

NAMCS Study Component	1998	1999	2000	2001
Number of physicians randomly selected to participate	2,500	2,499	3,000	2,744
M.D./D.O. ratio of physicians randomly selected to participate	2,324/176	2,262/237	2,763/237	2,566/178
Number of physicians deemed in-scope for participation (%)†	1,806 (72%)	1,728 (69%)	2,049 (68%)	1,910 (70%)
Number of physicians participating from in-scope group (%)	1,226 (68%)	1,087 (63%)	1,388 (68%)	1,230 (64%)
Number of office visits captured by in-scope participating physicians	23,339	20,760	27,369	24,281
Weighted number of representative office visits in the U.S.	829,280,407	756,733,854	823,541,999	880,486,669

†Common reasons physicians were deemed out of scope (i.e., ineligible for survey participation) included: retired, no patients seen during the selected survey week, or employed in teaching, research, or administration and having no direct patient-care responsibilities (http://www.cdc.gov/nchs/about/major/ahcd/ahcd1.htm, Accessed November, 18, 2005).

Table 2

Unweighted and Weighted ADHD Patient Demographics[†]

Patient Demographic	Unweighted ADHD Diagnosis *N* (%)	Weighted ADHD Diagnosis *N* (%)
Sex		
Female	282 (31.7%)	6,369,237 (30.0%)
Male	607 (68.3%)	14,854,154 (70.0%)
Recoded Age Groups		
Under 15 years	547 (61.5%)	14,302,959 (67.4%)
15-24 years	165 (18.6%)	3,493,297 (16.5%)
25-44 years	94 (10.6%)	1,746,862 (8.2%)
≥45 years	83 (9.3%)	1,680,273 (7.9%)
Recoded Races		
White	796 (89.6%)	19,106,838 (90.0%)
Black	74 (8.3%)	1,723,559 (8.1%)
Other	19 (2.1%)	392,994 (1.9%)
Recoded Ethnicities		
Blank	174 (19.6%)	4,531,742 (21.4%)
Hispanic or Latino	60 (6.7%)	1,233,311 (5.8%)
Not Hispanic or Latino	655 (73.7%)	15,458,338 (72.8%)
Recoded Payment Sources		
Private Insurance	448 (50.4%)	10,902,157 (51.4%)
Medicare/Medicaid	198 (22.3%)	4,877,058 (23.0%)
Self-Pay	168 (18.9%)	3,654,740 (17.2%)
Other Forms of Payment	60 (6.7%)	1,499,732 (7.0%)
Blank	15 (1.7%)	289,704 (1.4%)
Recoded Physician Specialties		
General/Family/Internal Medicine	76 (8.6%)	4,158,003 (19.6%)
Pediatrics	161 (18.1%)	6,558,086 (30.9%)
Psychiatry	548 (61.6%)	9,726,718 (45.8%)
Neurology	104 (11.7%)	780,584 (3.7%)
All Others Specialties	0 (0.0%)	0 (0.0%)
Region		
Northeast	170 (19.1%)	4,178,046 (19.7%)
Midwest	178 (20.0%)	4,810,722 (22.7%)
South	275 (30.9%)	7,348,683 (34.6%)
West	266 (30.0%)	4,885,940 (23.0%)
Prescription of Stimulant for ADHD		
Yes	666 (74.9%)	15,604,329 (73.5%)
No	223 (25.1%)	5,619,062 (26.5%)
Office Visit for Injury		
No Injury	864 (97.2%)	20,495,133 (96.6%)
Injury	25 (2.8%)	728,258 (3.4%)
Presence of Comorbidities with ADHD		
Yes	194 (21.8%)	3,685,662 (17.4%)
No	695 (78.2%)	17,537,729 (82.6%)
Total Unweighted & Weighted	**889**	**21,223,391**

[†]No missing cases occurred within any of the above selected or created variables.

Table 3

E-Codes (Cause of Injury), Reason for Visit Codes & Summary Of Verbatim Text for ADHD Study Population

Codes/Variable	*N*
E-Codes (800-999)	
Open wound to upper limb	1
Injury to blood vessels of lower extremity	2
Late effects of injury to skin and subcutaneous tissue	1
Superficial injury to foot or toe	1
Crushing injury to trunk	1
Burn to internal organs	1
Poisoning by other CNS depressants or anesthetics	7
Poisoning by sedatives or hypnotics	7
Reason for Visit (5000-5999)	
Sunburn	1
Rape	2
Medication adverse event	1
Injury NOS to foot or finger	1
Bite; Animal/Snake/Human	1
Violence NOS	4
Sexual abuse	2
Verbatim Text Entry	
Alcohol abuse	1
Basketball injury	1
Dog bite	1
Drug reaction	1
Neglect and/or physical abuse	3
Sexual abuse	4
Skiing injury	1
Sunburn	1

Table 4

Stratified and Adjusted Analyses for Associations between all Selected Independent Variables†

Patient Demographic	OR (95% CI)	*p* value
Sex		
Age groups	1.09 (0.80, 1.49)	0.562
<15 years	0.29 (0.15, 0.58)	0.001
15-24 years	0.39 (0.18, 0.85	0.019
25-44 years	0.75 (0.34, 1.69)	0.479
≥45 years	1.0 Reference	
Races	0.82 (0.57, 1.17)	0.259
White	1.0 Reference	
Black/African American	0.56 (0.22, 1.46	0.228
Other Races	0.86 (0.28, 2.61)	0.780
Ethnicities	0.96 (0.76, 1.21)	0.743
Not Hispanic/Latino	1.0 Reference	
Hispanic/Latino	0.47 (0.21, 1.06)	0.069
Payment Sources	0.97 (0.87, 1.09)	0.613
Private Insurance	1.0 Reference	
Medicare/Medicaid	0.65 (0.38, 1.10)	0.106
Self-pay	0.95 (0.60, 1.51)	0.822
Other payment sources	0.86 (0.42, 1.77)	0.683
Physician Specialties	1.03 (0.99, 1.07)	0.206
General/Family/Internal med.	1.0 Reference	
Pediatrics	0.51 (0.18, 1.44)	0.195
Psychiatry	0.99 (0.65, 1.53)	0.981
Neurology	1.15 (0.66, 1.98)	0.617

Table 4 Continued

Stratified and Adjusted Analyses for Associations between all Selected Independent Variables†

Patient Demographic	OR (95% CI)	*p* value
Regions	0.86 (0.74, 1.01)	0.064
Northeast	1.0 Reference	
Midwest	0.84 (0.47, 1.51)	0.548
South	0.70 (0.41, 1.19)	0.182
West	0.54 (0.23, 1.26)	0.149
Comorbidities	1.78 (1.20, 2.65)	0.005
No	1.0 Reference	
Yes	1.78 (1.20, 2.65)	0.005
Age groups		
Races	2.28 (0.73, 5.34)	0.057
White	1.0 Reference	
Black/African American	4.51 (0.73, 27.83)	0.103
Other Races	1.45 (0.74, 2.85)	0.274
Ethnicities	1.04 (0.63, 1.71)	0.890
Not Hispanic/Latino	1.0 Reference	
Hispanic/Latino	0.67 (0.14, 3.25)	0.609
Payment Sources	1.03 0.84, 1.26)	0.768
Private Insurance	1.0 Reference	
Medicare/Medicaid	4.29 (1.41, 13.05)	0.011
Self-pay	0.67 (0.31, 1.48)	0.315
Other payment sources	2.53 (0.78, 8.20)	0.120

†Logistic regression using selected independent variable as dependent variable.

Table 4 Continued

Stratified and Adjusted Analyses for Associations between all Selected Independent Variables†

Patient Demographic	OR (95% CI)	*p* value
Physician Specialties	0.92 (0.83, 1.03)	0.144
General/Family/Internal med.	1.0 Reference	
Pediatrics	29.99 (6.13, 146.79)	<0.001
Psychiatry	0.83 (0.32, 2.18)	0.705
Neurology	1.39 (0.36, 5.42)	0.630
Regions	1.16 (0.90, 1.49)	0.257
Northeast	1.0 Reference	
Midwest	13.68 (4.89, 38.30)	<0.001
South	1.74 (0.68, 4.42)	0.241
West	1.85 (1.00, 3.42)	0.049
Comorbidities	0.67 (0.30, 1.50)	0.324
No	1.0 Reference	
Yes	0.67 (0.30, 1.50)	0.324
Races		
Ethnicities	0.98 (0.58, 1.67)	0.939
Not Hispanic/Latino	1.0 Reference	
Hispanic/Latino	0.43 (0.15, 1.21)	0.106
Payment Sources	1.10 (0.96, 1.26)	0.178
Private Insurance	1.0 Reference	
Medicare/Medicaid	3.51 (2.09, 5.90)	<0.001
Self-pay	0.82 (0.23, 2.86)	0.747
Other payment sources	2.43 (1.15, 5.15)	0.022

†Logistic regression using selected independent variable as dependent variable.

Table 4 Continued

Stratified and Adjusted Analyses for Associations between all Selected Independent Variables†

Patient Demographic	OR (95% CI)	*p* value
Physician Specialties	0.98 (0.91, 1.04)	0.464
General/Family/Internal med.	1.0 Reference	
Pediatrics	1.92 (0.81, 4.57	0.137
Psychiatry	1.01 (0.41, 2.45)	0.987
Neurology	1.74 (0.73, 4.17	0.209
Regions	1.26 (0.97, 1.64)	0.078
Northeast	1.0 Reference	
Midwest	25.08 (10.08, 62.38)	<0.001
South	19.90 (6.92, 57.20)	<0.001
West	10.74 (3.92, 29.44)	<0.001
Comorbidities	0.92 (0.47, 1.80)	0.807
No	1.0 Reference	
Yes	0.92 (0.47, 1.80)	0.807
Ethnicities		
Payment Sources	0.99 (0.86, 1.14)	0.913
Private Insurance	1.0 Reference	
Medicare/Medicaid	1.14 (0.60, 2.16)	0.692
Self-pay	1.49 (0.60, 3.69)	0.377
Other payment sources	0.58 (0.25, 1.37)	0.208

†Logistic regression using selected independent variable as dependent variable.

Table 4 Continued

Stratified and Adjusted Analyses for Associations between all Selected Independent Variables†

Patient Demographic	OR (95% CI)	*p* value
Physician Specialties	1.04 (0.94, 1.15)	0.430
General/Family/Internal med.	1.0 Reference	
Pediatrics	1.62 (0.73, 3.62)	0.233
Psychiatry	1.92 (0.69, 5.35)	0.204
Neurology	0.67 (0.16, 2.78)	0.578
Regions	0.83 (0.70, 0.99)	0.046
Northeast	1.0 Reference	
Midwest	0.47 (0.24, 0.89)	0.022
South	0.57 (0.19, 1.69)	0.301
West	0.42 (0.21, 0.84)	0.015
Comorbidities	0.98 (0.44, 2.16)	0.957
No	1.0 Reference	
Yes	0.98 (0.44, 2.16)	0.957
Payment Sources		
Physician Specialties	0.94 (0.80, 1.10)	0.411
General/Family/Internal med.	1.0 Reference	
Pediatrics	0.84 (0.08, 9.12)	0.882
Psychiatry	0.56 (0.06, 5.74)	0.620
Neurology	0.27 (0.04, 1.84)	0.176

†Logistic regression using selected independent variable as dependent variable.

Table 4 Continued

Stratified and Adjusted Analyses for Associations between all Selected Independent Variables†

Patient Demographic	OR (95% CI)	*p* value
Regions	1.10 (0.80, 1.52)	0.541
Northeast	1.0 Reference	
Midwest	1.52 (0.49, 4.69)	0.461
South	2.71 (0.51, 14.46)	0.236
West	1.10 (0.49, 2.47)	0.806
Comorbidities	0.49 (0.14, 1.71)	0.254
No	1.0 Reference	
Yes	0.49 (0.14, 1.71)	0.254
Physician Specialties		
Regions	1.14 (0.87, 1.49)	0.332
Northeast	1.0 Reference	
Midwest	1.07 (0.42, 2.74)	0.879
South	1.28 (0.47, 3.51)	0.625
West	1.80 (0.68, 4.77)	0.228
Comorbidities	4.58 (1.27, 16.50	0.021
No	1.0 Reference	
Yes	4.58 (1.27, 16.50)	0.021
Regions		
Comorbidities	1.37 (0.87, 2.17)	0.168
No	1.0 Reference	
Yes	1.37 (0.87, 2.17)	0.168

†Logistic regression using selected independent variable as dependent variable.

Table 5

Unadjusted and Adjusted Odds Ratios for Selected Independent Variables Using Injury as Dependent Variable[†]

Patient Demographic	Unadjusted OR (95% CI)	*p* value	Adjusted OR[/] (95% CI)	*p* value
Sex	0.36 (0.10, 1.24)	0.103	0.32 (0.09, 1.18)	0.086
Males	1.0 Reference		1.0 Reference	
Female	0.36 (0.10, 1.24)	0.103	0.32 (0.09, 1.18)	0.086
Age Groups	1.02 (0.53, 1.96)	0.946	1.22 (0.63, 2.35)	0.544
<15 years	1.32 (0.38, 4.62)	0.656	0.50 (0.10, 2.43)	0.380
15-24 years	0.31 (0.09, 1.16)	0.080	0.20 (0.03, 1.42)	0.105
25-44 years	1.32 (0.15, 11.68)	0.802	0.88 (0.06, 13.33)	0.923
≥45 years	1.0 Reference		1.0 Reference	
Races	2.38 (1.15, 4.92)	0.020	2.74 (1.26, 5.99)	0.012
White	1.0 Reference		1.0 Reference	
Black/African American	1.56 (0.37-6.60)	0.539	1.52 (0.37-6.27)	0.556
Other Races[£]	6.79 (2.35-19.65)	0.001	13.20 (4.24-41.09)	<0.001
Ethnicities	0.77 (0.39, 1.52)	0.437	0.74 (0.36, 1.51)	0.400
Not Hispanic/Latino	1.0 Reference		1.0 Reference	
Hispanic/Latino	0.98 (0.22, 4.43)	0.973	1.00 (0.20, 5.05)	0.999
Payment Sources	1.07 (0.84, 1.35)	0.599	1.08 (0.86, 1.35)	0.491
Private Insurance	1.0 Reference		1.0 Reference	
Medicare/Medicaid	2.83 (0.93, 8.63)	0.066	2.95 (0.86, 10.06)	0.083
Self Pay	0.43 (0.09, 2.07)	0.285	0.77 (0.13, 4.45)	0.764
Other Payment Sources[¥]	0.1.52 (0.26, 8.91)	0.634	2.25 (0.41, 12.24)	0.340

[†]Logistic regression using dichotomous injury variable as dependent variable.
[/]Full model included all independent variables listed.
[£]Includes Asian, Native Hawaiian/Other Pacific Islander, American Indian/Alaska Native, and those individuals indicating more than one race.
[¥]Includes Worker's Compensation, No Charge/Charity, and Unknown.

Table 5 Continued

Unadjusted and Adjusted Odds Ratios for Selected Independent Variables Using Injury as Dependent Variable[†]

Patient Demographic	Unadjusted OR (95% CI)	*p* value	Adjusted OR[ƒ] (95% CI)	*p* value
Physician Specialties	0.97 (0.84, 1.12)	0.645	0.95 (0.81, 1.11)	0.486
General/Family/Internal Med.	1.0 Reference		1.0 Reference	
Pediatrics	0.46 (0.11, 1.99)	0.288	0.26 (0.04, 1.60)	0.143
Psychiatry	1.00 (0.33, 3.04)	0.999	0.46 (0.11, 1.93)	0.283
Neurology	0.55 (0.06, 5.45)	0.599	0.34 (0.03, 3.29)	0.339
Region	0.92 (0.51, 1.67)	0.780	0.78 (0.41, 1.48)	0.435
Northeast	1.0 Reference		1.0 Reference	
Midwest	0.90 (0.31, 2.62)	0.848	0.58 (0.06, 5.20)	0.614
South	1.54 (0.45, 5.22)	0.481	0.80 (0.08, 7.78)	0.841
West	0.54 (0.24, 1.22)	0.133	0.32 (0.04, 2.53)	0.274
Presence of Comorbidities	1.17 (0.43, 3.13)	0.756	1.53 (0.53, 4.44)	0.424
No	1.0 Reference		1.0 Reference	
Yes	1.17 (0.43, 3.13)	0.756	1.53 (0.53, 4.44)	0.424
Prescription of Stimulant	2.68 (0.92, 7.82)	0.070	2.90 (0.98, 8.58)	0.055
No	1.0 Reference		1.0 Reference	
Yes	2.68 (0.92, 7.82)	0.070	2.90 (0.98, 8.58)	0.055

[†]Logistic regression using dichotomous injury variable as dependent variable.
[ƒ]Full model included all independent variables listed.

Table 6

Partial Model Logistic Regression Analysis Including Stimulant & All Other Selected Independent Variables And Injury Dependent Variable

Patient Demographic	OR (95% CI)	*p* value
Stimulant	2.63 (0.90, 7.69)	0.075
Sex	0.36 (0.10, 1.26)	0.108
Stimulant	2.66 (0.90, 7.83)	0.075
Age groups	0.84 (0.32, 2.20)	0.719
Stimulant	2.75 (0.94, 7.99)	0.063
Races	1.64 (1.03, 2.62)	0.037
Stimulant	2.73 (0.91, 8.16)	0.071
Ethnicities	0.76 (0.38, 1.52)	0.422
Stimulant	2.68 (0.92, 7.83)	0.071
Payment Sources	1.06 (0.84, 1.35)	0.602
Stimulant	2.72 (0.91, 8.19)	0.073
Physician Specialties	0.96 (0.84, 1.10)	0.567
Stimulant	2.71 (0.90, 8.15)	0.074
Regions	0.94 (0.56, 1.56)	0.794
Stimulant	2.69 (0.93, 7.77)	0.067
Comorbidities	1.18 (0.44, 3.14)	0.735

Table 7

Partial Model Logistic Regression Stratified Analysis Including Stimulant & All Other Selected Independent Variables And Injury Dependent Variable

Patient Demographic	OR (95% CI)	*p* value
Stimulant	2.63 (0.90, 7.69)	0.075
Males	1.0 Reference	
Female	0.36 (0.10, 1.26)	0.108
Stimulant	2.74 (0.92, 8.16)	0.070
<15 years	0.86 (0.16, 4.72)	0.854
15-24 years	0.27 (0.04, 1.84)	0.176
25-44 years	1.04 (0.08, 13.25)	0.973
≥45 years	1.0 Reference	
Stimulant	2.86 (0.97, 8.39)	0.056
White	1.0 Reference	
Black/African American	1.70 (0.40, 7.17)	0.460
Other Races[£]	8.12 (3.71, 17.76)	<0.001
Stimulant	2.69 (0.94, 7.67)	0.064
Not Hispanic/Latino	1.0 Reference	
Hispanic/Latino	1.06 (0.24, 4.64)	0.934
Stimulant	2.94 (0.99, 8.70)	0.051
Private Insurance	1.0 Reference	
Medicare/Medicaid	3.09 (0.85, 11.26)	0.086
Self Pay	0.68 (0.11, 4.06)	0.666
Other Payment Sources[¥]	2.15 (0.33, 13.92)	0.413

[£]Includes Asian, Native Hawaiian/Other Pacific Islander, American Indian/Alaska Native and those individuals indicating more than one race.
[¥]Includes Worker's Compensation, No Charge/Charity, and Unknown.

Table 7 Continued

Partial Model, Univariable Logistic Regression Stratified Analysis Including Stimulant & All Other Selected Independent Variables And Injury Dependent Variable

Patient Demographic	OR (95% CI)	*p* value
Stimulant	2.68 (0.89, 8.09)	0.079
General/Family/Internal Med.	1.0 Reference	
Pediatrics	0.30 (0.05, 1.75)	0.176
Psychiatry	0.53 (0.14, 2.03)	0.346
Neurology	0.31 (0.03, 3.50)	0.331
Stimulant	2.68 (0.87, 8.29)	0.085
Northeast	1.0 Reference	
Midwest	0.82 (0.10, 6.53)	0.847
South	1.16 (0.13, 10.12)	0.888
West	0.55 (0.08, 3.93)	0.541
Stimulant	2.69 (0.93, 7.77)	0.067
Comorbidities – No	1.0 Reference	
Comorbidities – Yes	1.18 (0.44, 3.14)	0.735

CHAPTER 1

INTRODUCTION

Introduction to Attention-Deficit/Hyperactivity Disorder

Attention-deficit/hyperactivity disorder (ADHD) is a neurobehavioral disorder recognized mostly in children and adolescents but that continues into adulthood, thereby spanning the life of the patient (American Psychiatric Association [APA], 1994; Brown, 2001). Authorities in ADHD believe the disorder results from a clinically significant neurochemical imbalance involving neurotransmitters within the brain, specifically dopamine and norepinephrine, with the imbalance producing the clinical characteristics that can include impulsivity, inattention and/or hyperactivity (American Academy of Pediatrics [AAP], 2000; APA, 1994). Due to the neurotransmitter dysregulation, and given the broad clinical characteristics, individuals with ADHD have difficulty focusing on tasks and assignments which can lead to academic underachievement or poor job performance. Patients may also exhibit aggression or other disruptive behavior and often have relationship problems with family members, friends, classmates, and workplace associates. ADHD patients may also be socially withdrawn, a circumstance that often culminates in low self-esteem (AAP, 2000; Dulcan, 1997).

Epidemiology of Attention-Deficit/Hyperactivity Disorder

A variety of studies indicate that the prevalence of ADHD in children and adolescents varies between 4% to 12%, with a median prevalence rate of 5%, depending

on the age group studied, the diagnostic criteria utilized, and the study population being evaluated, such as community sample or clinic-referred sample (August, 1989, 1992; Bird, 1988; Brown, 2001; Cohen, 1993; Costello, 1996; Dulcan, 1997; Green, 1999; King, 1982; Kuperman, 1996; Pelham, 1992; Shaffer, 1996; Shekim, 1985; Wolraich, 1996, 1998). The American Academy of Pediatrics, the American Psychiatric Association, and the American Academy of Child and Adolescent Psychiatry (AACAP) calls ADHD "the most common neurobehavioral disorder of childhood" (AAP, 2000; Brown, 2001; Dulcan, 1997). Research indicates that males are more likely than females to be diagnosed with ADHD and to exhibit hyperactivity and impulsive characteristics. However, other research has found limited or no relationship between gender and ADHD (APA, 1994; Breen, 1989; Brown, 2001; Dulcan, 1997; Horn, 1989; McGee, 1987; Wolraich, 1996, 1998).

Diagnosis of Attention-Deficit/Hyperactivity Disorder

The current diagnostic criteria for ADHD, as defined by the APA, includes specific symptomatology, characteristics of the disorder, the age of onset, the duration of symptoms, the impact on the patient's life and the settings where symptoms occur. The diagnostic criteria are used by clinicians to diagnose the three main sub-types of ADHD: (1) *predominantly inattentive*, (2) *predominantly hyperactive/impulsive*, and (3) *combined*, where characteristics of both inattentive and hyperactive/impulsive subtypes are exhibited (APA, 1994). A fourth subtype, *not otherwise specified (NOS)*, is a diagnosis utilized for patients exhibiting clinically significant ADHD-like symptoms not fully meeting the diagnostic criteria of the other sub-types. Symptoms must have been

present prior to the age of seven years and have a clinically significant impact upon two key settings with which the patient is involved, for example, academic and non-academic settings, and have a clinically significant impairment in academic, occupational or social functioning. The Appendix lists the official diagnostic criteria for the medical diagnosis of ADHD for children and adolescents (APA, 1994). Assessments of symptomatology, impact, and severity are derived from standardized and validated assessment questionnaires, or rating scales, completed by the clinician during patient testing. Disease impact is also obtained from family member interviews as well as parent and teacher questionnaires and measures of academic performance (Dulcan, 1997).

Comorbidity with Attention-Deficit/Hyperactivity Disorder

Other psychiatric and behavioral disorders can occur concomitantly with ADHD, including bipolar disorder (BP), oppositional defiant disorder (ODD), anxiety and depressive disorders, conduct disorder (CD) and developmental disorders, such as learning disabilities and language or speech delays (AAP, 2000; August, 1989, 1996; Bird, 1988; Green, 1999; Pelham, 1992; Shekim, 1985; Wolraich, 1996). Comorbidity prevalence rates range from 9% to 50%, depending on the study population, the study design, and the selected comorbidities (Anderson, 1987; Biederman, 1996; Costello, 1988, 1988; Szatmari, 1989).

Treatment of Attention-Deficit/Hyperactivity Disorder

A variety of treatment modalities can be employed for the management of ADHD, including pharmacotherapy – both psychostimulants and non-psychostimulants – and non-pharmacotherapies, such as psychosocial, educational, and behavioral

interventions for patients and their families. The psychostimulants are the most commonly utilized therapy and are considered by clinicians and researchers as the most effective first line therapy due to their long history of use, safety parameters, and large effect size compared to the non-stimulants and the non-pharmacotherapies (AAP, 2001; Dulcan, 1997; Wilens, 2002).

Specific Research Problem Pertaining to Attention-Deficit/Hyperactivity Disorder

Numerous studies have investigated the health, social, and financial impact of behavior problems on patients, their families, and the health care system (Barkley, 1993, 1996; Bijur, 1986, 1988; Brehaut, 2003; Bussing, 1996; Chan, 2002; Davidson, 1988, 1992; DiScala, 1998; Farmer, 1995; Gayton, 1986; Guevara, 2001; Jaquess, 1994; Langley, 1983; Leibson, 2001; Mandell, 2003; Mangus, 2004; McDonald, 1996; Rowe, 2004; Schwebel, 2002; Swensen, 2004; Thomas, 2004; Wozniak, 1999). Some of these studies did not specifically include patients diagnosed with ADHD yet included subjects with general behavioral problems, as suggested by rating scale assessments by teachers, or surrogate markers substituting for an official diagnosis (Bijur, 1986, 1988; Brehaut, 2003; Bussing, 1996; Davidson, 1988, 1992; Jaquess, 1994; Langley, 1983; McDonald, 1996). The studies that did evaluate patients with a diagnosis of ADHD evaluated the risk of serious injuries requiring hospitalization or treatment in an emergency room setting (Bijur, 1988; Davidson, 1988; Pless, 1995). Some of the studies limited the subjects included to males (Davidson, 1988; Schwebel, 2002), Caucasians (Dal Santo, 2004) or preschool or school-age children (Bijur, 1988; Davidson, 1988; Langley, 1983; Pless, 1995; Rowe, 2004; Schwebel, 2002). Several studies have evaluated the risk factors for

injury associated specifically with ADHD or the differences in serious injury rates from a variety of causes (e.g., trauma, burns, dental, pedestrian, motor vehicle accidents) in those patients with and without ADHD (Bussing, 1996; DiScala, 1998; Mangus, 2004; Petridou, 1998; Rowe, 2004; Sabuncuoglu, 2005; Thomas, 2004). However, none of the studies have evaluated the impact of pharmacotherapy on the risk of injuries requiring only ambulatory-based medical care. The premise of this research project is that patients with ADHD may also be at increased risk for minor injury secondary to the disorders' impact on their level of distractibility and lack of focus and attention during the activities of life.

Most of the studies to date have limited study participants to select genders, races, or age groups, or only included patients from individual physician practices or institutions, or to those who resided in a single state, or were conducted over a short duration, 1 year or less. Studies which utilized a national database, such as Medicaid, often did not include pharmacotherapy as a group variable or only evaluated injuries serious enough to require hospitalization. Finally, a detailed meta-analysis of many of the studies cited above found significant limitations, flaws, and biases (Davidson, 1987).

The limitations of previous studies significantly reduce the generalizability and hinder the proper interpretation of the impact of ADHD on the risk of various types of severe injuries. A recent study even found no association between the presence of ADHD and the risk of severe injury, which questions the true association between ADHD and risk of injury (Christoffel, 1996). Despite the noted limitations of past studies, an extensive literature search found no study that utilized the National Ambulatory Medical

Care Survey (NAMCS) dataset to evaluate the differences in risk of injuries receiving treatment in the ambulatory medical care setting. Furthermore, no study has evaluated the presence of any differences in injury risk between psychostimulant-treated versus non-psychostimulant-treated ADHD patients.

CHAPTER 2

REVIEW OF THE LITERATURE

Behavioral Characteristics and Injuries

Most of the studies published to date have not uniformly focused on specific patient psychiatric diagnoses, such as ADHD, yet have sought to determine the psychosocial and behavioral characteristics patients exhibit that are associated with various types and causes of accidents and injuries. Most of the behavioral characteristics noted to be associated with injuries and accidents are similar to those experienced by patients with the current day medical diagnosis of ADHD.

Studies initially sought to evaluate injury risk or injury proneness and a variety of patient behavioral characteristics. Investigators began by assessing children who had experienced accidents or injuries or due to the number or frequency of injuries were categorized as either accident repeaters, accident-prone or having a high accident rate or liability. These children then had their behavioral characteristics assessed by a variety of means, mostly by psychological rating scales, personal observation, or behavioral characteristic identifiers listed on questionnaires completed by parents or teachers. An early, small study was comprised of nine children defined as accident-prone and an equal number of children defined as not accident-prone (Langford, 1953). The study concluded that the children denoted as accident-prone were more bold and daring in their behavior. Several other investigators have also investigated this topic and found accident-prone

children to be more active, aggressive and disobedient, and to have a greater likelihood of displaying behavioral characteristics similar to those associated with ADHD, such as being impulsive and inattentive, having deficits in vigilance, being fearless and daring, having poor discipline, liking exploring and being adventurous, being extraverted and overly active (hyperactive), being argumentative, careless, and unreliable, lacking self control, defying authority, having lower social adjustment scores, and even seeking attention (Christoffel, 1996; Dal Santo, 2004; Grossman, 1992; Husband, 1972; Krall, 1953; Langford, 1953; Langley, 1983; Matheny, 1971; Pless, 1995).

In 1987, Dr. Davidson challenged the validity of these findings after determining the presence of flaws in the methodology of these studies since many were retrospective, did not include adequate controls, were associated with recall biased from being based on parent assessment of past behaviors of the child which were acquired after the accident, and some studies even included behavioral variables not consistently and uniformly validated (Davidson, 1987). However, other studies that utilized more appropriate controls were population-based, or utilized more appropriate validated behavioral variables, have also found that those children injured or classified as accident repeaters were more likely to display aggressive behavioral characteristics and be overly active compared to non-accident repeaters (Bijur, 1986; Langley, 1983; Manheimer, 1967). Based on the critical analysis of the literature, and in an attempt to overcome some of the methodological issues plaguing previous studies, Dr. Davidson subsequently published a study utilizing the hospital emergency room records of 951 children previously enrolled in a five-year prospective, consecutive birth cohort study developed to investigate milk

supplementation but that also captured detailed behavioral data (Davidson, 1988). Children included in this cohort study were born in one of two community hospitals in South Wales. Hospital records were reviewed within one month of the child's fifth birthday for injuries requiring emergency room medical care. Behavior was assessed by an interview using the Behavior Screening Questionnaire (BSQ). Boys were found to have 1.52 times the relative risk of injury compared to girls (95% CI, 1.23, 1.88; $p<0.001$). Those children classified as having discipline issues were found to have an increased relative risk of injury (RR=1.29; 95% CI, 1.04, 1.60; $p<0.03$). Only those children specifically found to be labeled by their parents as fearful were significantly more likely to sustain injuries (RR=1.95; 95% CI, 1.35, 2.83; $p<0.01$). The overall BSQ score was not associated with a significant increase in the risk of injury. Furthermore, the behavioral characteristics associated with the primary study hypothesis, specifically being over active and lacking concentration, both of which are aspects associated with ADHD, did not demonstrate a statistically significant increase in injury risk (RR of 1.06 and 1.01, respectively; $p>0.05$). A subsequent study in 1988 by Bijur, prospectively evaluated the behavior of 10,394 British children aged five to ten years acquired in a Great Britain birth cohort (Bijur, 1988). The study utilized the Rutter Child Behavior Questionnaire that was completed by a parent of the child. Dr. Bijur found that compared to control boys with low scores, and after controlling for social and family factors, those boys with high aggression and over activity scores were found to be more likely to sustain severe injuries requiring hospital medical care and more likely to sustain less severe injuries necessitating ambulatory treatment. Girls with high scores were only found to have

significantly greater injuries requiring ambulatory medical care compared to girls with low scores. There was no difference in severe injuries requiring hospital-based medical care and aggression or activity scores in girls.

More recent studies have found conflicting results, with some studies finding no association with hyperactivity and aggression behavioral characteristics and injury risk or burns, and other studies finding an association with oppositional or defiant behavior reported by the child's parents, and increased risk of injury (Jaquess, 1994; Petridou, 1998). One of the largest behavioral studies conducted was by Bussing in 1996, and utilized the National Center for Health Statistic's 1988 National Health Interview Study (NHIS) to assess the relationship between unintentional injuries in U.S. children and their behavioral problems (Bussing, 1996). The study was a cross sectional analysis of 11,630 children, aged five to seventeen years. As part of NHIS, the survey asked parents if their child had experienced an injury, accident, or poisoning that required medical care or treatment in the past twelve months. Parents were also asked about the number of such events during the same time period. Emotional and behavioral components were captured by the NHIS survey with use of the Behavior Problems Index (BPI), which is based on the Child Behavior Checklist (CBC). These emotional and behavioral components captured by the survey were assessed during the previous three months. No official psychiatric diagnoses were utilized in this study. Results of the study determined that Caucasian children had a higher rate of injuries than African American and Hispanic children ($p<0.01$). Compared to females, males of all ethnic groups, both individually and combined, had higher rates of injuries. Finally, all three ethnicities, that had a history of

behavioral or emotional problems, had higher rates of unintentional injuries. However, when evaluating specific behavioral and psychiatric characteristics individually and by ethnicity, only hyperactivity (OR=1.25; 95% CI 1.02, 1.48) and antisocial behavior (OR=1.27; 95% CI 1.04, 1.51) were reported to be statistically significant for Caucasian children. No significant findings were noted in the remaining two ethnicities. However, similar to previous studies, recall bias could have impacted the findings of this study. In their concluding discussion the authors commented that, "Future research should also investigate the role of treatment of mental health conditions in reducing the incidence of unintentional injuries".

Psychiatric Disorders and Risk of Injury and Accidents

Several studies have assessed specific psychiatric disorders and their association with the risk of injury. Some investigators have looked at the association between a patient's psychiatric disorder and the risk of traffic and general accidents or injuries, including burns, and the patient's tendency for fighting (Brehaut, 2003; Davidson, 1985; Halperin, 1995; MacArthur, 1975; Noyes, 1979; Rockwell, 1988; Rowe, 2004; Steiner, 1977; Ward, 1987). Factors found to be associated with burns have included alcoholism, drug overuse, and "chronic mental illness". Traffic accidents and fractures have been found to occur at a greater frequency in those with schizophrenia, ADHD, and social and general personality disorders (Crancer, 1969; Eelkema, 1970; Kuhn, 1989; Rowe, 2004). Children classified as frequent fighters or fight initiators were found to be associated with increased impulsivity, a behavioral characteristic commonly seen in those formally diagnosed with ADHD, CD, and ODD (Halperin, 1995). However, some of these studies

did not use specific psychiatric diagnoses or they used general terms such as "psychiatric disorder" or "psychosis", thereby making specific disease interpretation difficult. One of the largest studies conducted used the 1999 British Child and Adolescent Mental Health Survey (Rowe, 2004). The study included 10,438 children aged five to fifteen years who were from England, Scotland and Wales, each having their psychiatric diagnosis captured with the use of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) diagnostic codes (APA, 1994). Injuries were captured from parental interviews which assessed the child's injury occurrences, and the types of injuries they sustained which required admission to a hospital for medical care. The study findings indicated that gender played a role in the rates of unintentional injuries, with boys having more injuries of all types compared to girls. Burns occurred more frequently in those children with a psychiatric diagnosis. The increased frequency of burns was statistically significant in the univariate analysis only for those children with a diagnosis of ADHD, anxiety, and ODD. The multivariate analysis for burns resulted in only ODD remaining significant. The increased frequency of poisonings was statistically significant in both the univariate and multivariate analyses only for those children with a diagnosis of ODD and anxiety. An association between increased risk of head injuries and anxiety was only significant in the multivariate full model. Depression and ADHD were the only psychiatric diagnoses statistically associated with an increased risk of fractures in the full model. In summary, Rowe determined by use of a national cohort study that various psychiatric diagnoses, including ADHD, are significantly associated with an increased risk of various types of injuries.

Risk of Injury and Attention-Deficit/Hyperactivity Disorder

There have been limited studies evaluating the risk of injury in children with ADHD. One of the early studies conducted in 1970 by Stewart evaluated what was then termed Hyperactive Child Syndrome (HCS) (Stewart, 1970). This study supported previous research evaluating general psychosocial, psychiatric, and behavioral conditions that reported an association between behavioral characteristics of HCS and injuries and accidents. The study randomly sampled 179 pediatric poisoning cases treated in the emergency room of St. Louis Children's Hospital. Families of 98 of these poisoning cases were located for interview, and 88 of these families agreed to participate in the study. The authors interviewed the parents of the poisoned children, along with the children's teachers, to assess their grade school-age behavioral characteristics and related HCS symptoms, such as hyperactivity, distractibility, or both. Those children determined to fit the diagnostic criteria of Hyperactive Child Syndrome made up the cases included in the study. The controls of these poisoned, hyperactive children were obtained from poisoning-related questionnaires sent to all parents of hyperactive children aged seven to fourteen years attending a local psychiatric clinic. This poisoning-related questionnaire was also sent to all parents of second grade children attending a large local public school. The poisoning questionnaire assessed if a poisoning had occurred, and if so the number of poisoning episodes, the description of the poisonings, the circumstances surrounding each event and any treatments required for the poisonings. The HCS-poisoned children were found to have behavioral characteristics that allowed them to be classified as overly active, hyper, daring and impulsive, all symptoms associated with the current day

medical diagnosis of ADHD. Furthermore, compared to controls, boys with HCS were more likely to have a history of accidental poisonings. Therefore, the findings of this study supported previous psychological studies reporting that ADHD-like behaviors and characteristics are associated with an increased rate of poisonings.

A subsequent study was published in 1992 by Dr. Davidson who also evaluated the behavioral characteristic of hyperactivity and its association with the risk of injury (Davidson, 1992). This study was a prospective, cohort study conducted in a systematically drawn sample of boys, aged six to eight years, in a single borough of London, England. Boys, born in 1974 and 1975, were selected from every other school in the borough. Control subjects were matched to cases by gender. The boys selected for this study were measured at the start and end of the study by use of questionnaires that were completed by the boy's teachers. The parents of each boy also completed a behavior questionnaire at the beginning of the study. Injuries were captured during a period spanning 16 months by reviewing the emergency room medical records of five local hospitals. The study found that the behavioral characteristic of hyperactivity was not associated with an increased risk of injuries requiring medical care in an emergency room. However, the study did report an association between the risk of serious injuries and the psychiatric diagnosis of conduct disorder (RR=1.79; 95% CI, 1.20, 2.67; $p<0.011$).

In 1995, Dr. Farmer conducted a psychological study in children with ADHD to assess possible risk factors associated with an increased risk of injury (Farmer, 1995). Using videotaped scenarios of risky and dangerous activities and situations, two groups

of seven to eleven year old boys were questioned about the scenes they were asked to witness. The boys' thoughts were acquired regarding the actions or non-actions they might take if they were in similar situations. Study participants included fourteen consecutively referred boys with ADHD. Sixteen non-ADHD boys, serving as controls, were selected from local community groups. The methodology of the study allowed capture, using a computer, of the participant's responses when risky or potentially harmful situations were viewed on the videotape. A detailed interview of each study participant was also completed to gain further insight into the perception of the level of risk and injury the participants determined could have occurred following the viewing of the videotape. Dr. Farmer determined that young boys with ADHD differed in their ability to detect risky scenarios and in their responses to these situations. The boys with ADHD were found to have lower expectations of the potential consequences of certain risky behaviors they had viewed. They also had developed fewer rule-governed alternatives to actions associated with risk. The boys with ADHD were less likely to develop acceptable preventive strategies or alternative behaviors seen as safer. In conclusion, Dr. Farmer noted that boys with ADHD in this study appeared to be less likely to assess their own risk in certain situations and less likely to develop, conceive, or implement preventive strategies to reduce the risk of harm and injury.

In 1988, Dr. Jensen evaluated the medical records of 38 stimulant-treated ADHD children for injuries sustained from birth until the time of ADHD diagnosis (Jensen, 1988). Subjects included all patients being treated with a stimulant during a three-month study period at a single general military hospital clinic. Cases were matched by gender

with control subjects from the same clinic. The variables that were assessed included injuries necessitating hospitalization and psychosocial conditions, chronic medical illnesses, family turmoil, and abuse or neglect. The author reported that compared to controls, the stimulant-treated ADHD patients had more events in each variable category.

Also in 1998, Dr. DiScala published a study using the National Pediatric Trauma Registry (NPTR) (DiScala, 1998). This study assessed hospital admission for injuries in children with ADHD aged five to fourteen years. The NPTR includes over 70 hospitals, mostly pediatric trauma centers or children's hospitals. Dr. DiScala captured all consecutively registered children between October 1988 and April 1996. Children captured in the registry were divided into those with a pre-injury diagnosis of ADHD and those without the diagnosis. A total of 240 ADHD cases and 21,902 non-ADHD controls were captured by the registry. The study resulted in the discovery that the ADHD children injured a greater number of body regions than their non-ADHD counterparts. It was noted that the ADHD group had more head injuries, were more severely injured, had a greater proportion admitted to the intensive care unit, were more likely to develop post-injury physical limitations, and were more likely to result in a disability necessitating post-discharge rehabilitation. The study found no statistically significant difference between in total length of hospital stay between groups. The ADHD group had an increased risk of being injured as a pedestrian and while riding a bicycle, even though the ADHD group was more likely to wear a helmet at the time of injury. The authors commented that future research should assess the risk of ambulatory or outpatient injuries.

In contradiction to Dr. DiScala's findings, Dr. Wozniak reported in 1999 that in 140 Caucasian children with ADHD between the ages of six and seventeen years, there was not an increased risk of trauma exposure or developing post-traumatic stress disorder (PTSD) (Wozniak, 1999). It was also reported that children with bipolar mania were at increased risk of injury from trauma.

In 2002, Dr. Schwebel evaluated 79 consecutive clinic-referred preschool-age boys and 76 demographically matched controls (Schwebel, 2002). The boys were evaluated in a longitudinal fashion for two years to determine if there was an increased risk of unintentional injury in those with disruptive behavior. The classification of disruptive behavior was given to children with ODD or concomitant ODD and ADHD. Injuries requiring medical care by a medical professional, such as a nurse, physician, or dentist, were captured by use of a parental questionnaire administered at the beginning of the study and at years one and two. The study determined that compared to the control boys, boys with ODD had two times greater risk of injury ($p<0.01$). The study also found that comorbidity of ADHD with ODD did not significantly increase the risk of injury compared to boys with ODD alone ($p=0.46$), but still had a significantly increased risk of injury compared to controls. The authors commented that since many factors contribute to unintentional injuries in children, all interventions that could possibly reduce injuries, including pharmacotherapy, would be worth investigating.

One investigator utilized the British Columbia Health and the British Columbia Triplicate Prescription Program datasets to evaluate childhood behavior disorders and the risk of injuries (Brehaut, 2003). The investigator included all children in the dataset 19

years of age or younger as of December 31st, 1996. The cases included 16,806 children who were assumed to have a childhood behavior disorder, such as ADHD, due to the fact they were being treated with methylphenidate (MPH), a psychostimulant used to treat ADHD. The study also included 1,010,067 subjects who were deemed not to have a childhood behavioral disorder from their lack of use of MPH. Injuries, occurring between 1990 and 1996, were captured from the datasets by use of the *International Classification of Diseases* (ICD-9-CM) N and E codes. While controlling for age, gender, socioeconomic status, and the region of the country the subject resided in, Dr. Brehaut determined that compared to non-MPH consuming controls, children taking MPH and with a presumed childhood behavior disorder had a greater odds of sustaining an injury, both by type (OR=1.67; 99% CI 1.54, 1.81) and cause (OR=1.52; 99% CI 1.40, 1.66). Similar to previous studies, this study was limited in the fact that it did not assess injuries necessitating only ambulatory medical care.

A few authors have sought to investigate the costs associated with the utilization of medical care services in children with ADHD. These studies report an increased utilization of medical care, including emergency room visits and hospitalizations, and a higher cost of care for patients with ADHD (Chan, 2002; Guevara, 2001; Leibson, 2001). An additional study analyzed the incidence of accident and injury claims to an administrative medical, pharmacy, and disability database. The study also evaluated the program costs for the injuries in patients with ADHD (Swensen, 2004). Dr. Swensen found that ADHD was significantly associated with an accident claim being made to the administrative system (OR=1.7; $p<0.05$). The study determined that there was an equal

program cost related to the accident claims for both ADHD and non-ADHD subjects, regardless of age. One aspect for consideration is the fact that stimulant-treated ADHD patients do incur additional office care costs since these stimulant-treated patients must see their physician on a monthly basis for a new prescription. Stimulants are rated by the U.S. Food and Drug Administration (FDA) as a Schedule II medication, due to the high abuse potential for these agents. Most insurers will only pay for a one month supply thereby requiring the stimulant-treated ADHD patient to return to the office of their physician in order to receive an additional prescription for therapy. Irrespective of injuries or accidents sustained requiring medical care, the need for monthly follow up visits to assess the appropriateness of treatment and the need for monthly prescription renewals may in part add to greater medical care utilization and cost associated with a diagnosis of ADHD.

Two recent studies published in a 2004 issue of the journal *Burns* evaluated the risk of traumatic burn-related injuries in children with ADHD. The first, in 2004 by Dr. Mangus, involved the evaluation of all medical charts of ADHD children aged five to eighteen years presenting to a single regional pediatric burn center over a seven year period (N=278) (Mangus, 2004). Children with a pre-injury diagnosis of ADHD (N=35) were compared to those without this pre-injury diagnosis. Those with the pre-burn diagnosis of ADHD were found to have a greater risk of thermal burns compared to flame-related burns (83% thermal versus 58% flame; $p<0.01$) and more likely to have more extensive burns (10% body surface area versus 5% body surface area; $p=0.03$). The ADHD children also had a longer duration of stay within the burn center (11 days versus

7 days; p=0.05). The authors reported that the common ADHD-characteristics of lack of vigilance and impulsivity were directly related to the finding of increased injury risk. The other article, by Thomas, and also published in 2004, utilized a retrospective chart review procedure to evaluate all of the youth admitted to a single burn care unit during the previous 20 years who did and did not have a pre-burn psychiatric diagnosis of ADHD (Thomas, 2004). A total of 39 patients with a diagnosis of ADHD were admitted to the burn unit during the study period. Based on the situational attributes related to the burns of the ADHD patients, the author concluded that the behavioral characteristic of impulsivity could have played a significant role in 54% of cases. The author concluded that ADHD is an important psychiatric diagnosis to consider when evaluating the risk of serious burn injuries in the pediatric population.

No study has evaluated the effect of treatment, versus non-treatment, on the risk of injury, specifically injuries requiring ambulatory care in those with a medical diagnosis of ADHD. In the Thomas study mentioned above, it was noted that of the ADHD burn patients admitted to the pediatric specialty burn center, nine of the 39 ADHD-associated cases had not taken their stimulant medication the day of the accident. Although no statistics were performed on this finding, it suggests that proper treatment with stimulant therapy may impart some protective effect on risk. One other study, reviewed in this section, evaluated stimulant therapy for ADHD (Swensen, 2004). However, this study was from the perspective of medication claims to an administrative claims database and not related to injuries. ADHD patients did not have more medication claims to the administrative database than those who did not have ADHD. Again, the

authors evaluated all medication claims and did not specifically evaluate stimulant medication claims and risk of injury. Finally, in 2005 Dr. Sabuncuoglu conducted a study in Istanbul, Turkey evaluating the risk of traumatic dental injury in patients with ADHD (Sabuncuoglu, 2005). Dr. Sabuncuoglu enrolled 475 consecutive patients, between the ages of eight and seventeen years, being seen at a local child psychiatry clinic. Children were diagnosed with ADHD based on DSM-IV criteria. Those without a diagnosis of ADHD served as controls. Parents of the children were interviewed regarding the occurrence of traumatic dental injuries, the cause of the injury, and the timing of the injury, and the injury's required treatment. The study found that 32 of the ADHD children had a traumatic dental injury and that these ADHD children had a significantly greater odds of injury occurrence than those without ADHD (OR=17.41; 95% CI, 4.11, 73.55; $p<0.0001$). The authors commented that, "psychostimulants are the drug of first choice in ADHD with a well established therapeutic efficacy" and "preventive efforts should focus into treating the underlying condition (ADHD)." Furthermore, the author summarized his publication by stating, "...to what extent psychostimulants may produce a preventive effect needs to be investigated."

In conclusion, numerous studies have noted that ADHD, or its associated behavioral characteristics, are associated with an increased risk of injury. Most of the studies have evaluated the association between ADHD and injuries necessitating medical care in an emergency room or hospital. Limited data have been generated specifically focusing on those patients with a formal medical diagnosis of ADHD and an associated risk of injury requiring ambulatory-based medical care. However, no study within the

published literature could be found that evaluated the effect of stimulant treatment for ADHD on the risk of injury requiring ambulatory medical care. This void in the literature led to the development of this dissertation research project focusing on patients with ADHD who are treated with a psychostimulant and differences in rates of injuries requiring ambulatory medical care.

CHAPTER 3

METHODOLOGY

The NAMCS Sampling, Instrumentation, and Data Collection

The National Ambulatory Medical Care Survey (NAMCS) is one of several surveys conducted annually by the National Center for Health Statistics (NCHS), a component of the Centers for Disease Control and Prevention (CDC). The NAMCS is a national multi-stage, clustered, probability sample survey of patient visits to U.S. office-based physician practices. Office visits are subsequently weighted by the NCHS based on the probability of selection for the survey in order to create national estimates describing the annual utilization of ambulatory medical care services in the U.S. (NCHS, 2005).

The NAMCS utilizes a three-stage, clustered, probability survey design with the first stage consisting of the selection of the primary sampling units (PSU's). The PSU's are drawn from the set of PSU's sampled for the 1985-1994 National Health Interview Survey (NHIS). The NHIS PSU's are sampled from 1,900 PSU's defined by geographical variables, stratified by demographic and socioeconomic variables, and encompassing all 50 states and the District of Columbia. The PSU's utilized for the NHIS are probabilistically selected proportional to the size of the PSU's. These PSU's are created to include a county or group of counties or their equivalents, such as parishes, towns or townships, minor civil divisions, or a metropolitan statistical area (MSA) as defined by

the U.S. Office of Management and Budget based on the 1980 Census. The NAMCS initially samples the 26 NHIS PSU's with the largest populations. The NAMCS continues with the PSU selection by randomly selecting one-half of the next 26 largest NHIS PSU's and culminating with the random selection of one PSU from each of the remaining NHIS 73 PSU strata (NCHS, 2005).

The second stage utilized by the NAMCS is a probability sample of clustered office-based physician's practices obtained from the databases of the American Medical Association (AMA) and American Osteopathic Association (AOA) as of the 31st of December two years prior to the annual NAMCS study year. Physician practices may be selected if they are classified as office-based, as defined by the AMA and AOA. The physician practices could also be selected if they are non-federally funded and are principally involved in the provision of patient medical care and not the medical specialties of pathology, radiology and anesthesiology. Each physician's practice is then stratified within each selected PSU based on 15 pre-defined medical specialty groupings and includes internal medicine, pediatrics, general and family practice, psychiatry, urology, obstetrics and gynecology, dermatology, ophthalmology, neurology, otolaryngology, general surgery, orthopedic surgery, cardiovascular diseases, osteopathy, and "all other" medical specialties. All probabilistically selected physician practices are then divided into 52 random sub-samples, each approximately equal in size. These sub-samples are randomly assigned to one of the 52 weeks of the study year and represent the week of the year the physician's practice is surveyed (NCHS, 2005).

The NAMCS's final sampling stage is a probabilistic selection of office-based encounters between physician and patients. A systematic random sampling process is utilized for the selection of encounters within each physician's practice and their selected study week. This probability selection process occurs from the office's generated listing of all patient visits that occurred during the assigned study week, including scheduled and previously unscheduled patient visits. Patient office visits are randomly selected from the complete office-generated patient visit list utilizing a random start time and pre-determined sampling interval as derived from estimates of the physician's number of visits for the study week and the number of office practice days during the same time frame. This random sampling technique is designed such that approximately 30 study forms are completed during the selected study week, thereby minimizing office staff and physician workload and to provide approximately equal reporting among practice sites. This probability sampling process results in the selection of patient visits ranging from 100 percent to 20 percent of the patient office visits occurring during the study week. The range is generated based on whether or not the physician's practice is defined by NCHS to be very small or very large. It is not the intent of the NAMCS to capture multiple office visits from the same patient and is not considered a panel or repeated measures survey. Each physician's practice is contacted prior to the actual assigned survey week and provided instruction on the survey design and educated on completing the survey patient record forms (NCHS, 2005).

Specific types of physician and patient interactions are excluded from the NAMCS. These exclusions include contacts between patient and physician by way of the

telephone, interactions occurring outside the physicians office, such as house calls, contacts made in an institutional or hospital setting, such as nursing homes or non-office-based in-patient settings, and contacts made in offices primarily utilized for administrative purposes, such as centers for insurance processing or medical services payment, biomarker or anatomical specimen collection centers (NCHS, 2005).

The physicians, or their office staff, capture the vital patient office visit information. Information from each randomly selected patient office visit is recorded on the NAMCS's Patient Record form. All patient identifying information is subsequently removed prior to submission to the NCHS (NCHS, 2005).

Data Analysis

The NAMCS datasets for each of the four individual NAMCS years included in this research project, spanning the years of 1998 through 2001, were acquired from the NAMCS portion of the NCHS website (NCHS, 2005). These datasets are readily available to the general public and are de-identified thereby preventing identification of individual patients included in the NAMCS. The datasets for each of the four study years were concatenated using SAS statistical software (SAS, Inc., Cary, NC) and renamed with the file name "NAMCS4". The file was subsequently converted into an SPSS format (SPSS, Inc., Chicago, IL) with use of the statistical management program, Stat/Transfer (Circle Systems, Inc., Seattle, WA). The newly converted file was given the file name "NAMCS4.2full". The file was then thoroughly reviewed using SPSS software and assessed for accuracy and completeness of the concatenation and conversion process.

Complete descriptive and frequency statistical analysis was performed on this newly converted dataset to fully assess the data.

Using the SPSS software, a new dichotomous dummy variable, labeled "DIAGADHD", was then created and consisted of all NAMCS patient office visits from the concatenated "NAMCS4.2full" dataset associated with a diagnosis of ADHD. Capture of these records was accomplished by recoding each of the NAMCS's three diagnosis-related variables using the ICD-9-CM diagnostic codes for ADHD, specifically codes 314.00, 314.01, and 314.90 (U.S.DHHS, 1999). An additional dichotomous dummy variable was then created, labeled "ADHDSTIM", consisting of those NAMCS subjects with ADHD and who were prescribed treatment with a stimulant medication for their ADHD. This new variable was created by selecting out those patients with a diagnosis of ADHD and prescribed a stimulant medication by recoding each of the NAMCS's six drug classification variables associated with a stimulant therapy, using the FDA's National Drug Code for the stimulant drug class, specifically 0631, and those with the ICD-9-CM diagnosis code for ADHD (FDA, 1995). This step was deemed acceptable due to the fact that there are no other FDA-approved indications for the stimulant medications. Furthermore, it was the intent of this research project to only evaluate the effect of stimulant therapy, used specifically for treatment of ADHD, on the risk of injuries necessitating medical care in an ambulatory setting.

The dependent variable for this research project consisted of all office visits occurring for the purpose of ambulatory medical care and treatment of an injury, including poisonings. The information was captured by the dichotomous NAMCS

variable "INJURY". The dichotomous response was generated from the question on the NAMCS data record form in which the physician was asked if the office visit was related to an injury or poisoning. E-codes, verbatim text entry describing the type of injury, and reason for the office visit were also requested on the data record form for visits associated with an injury. These E-codes, text entries, and reasons for the office visit were assessed for potential use as individual dependent variables with the goal being to additionally ascertain if there were any differences in specific types of injuries requiring ambulatory medical care in ADHD patients being treated with a stimulant medication. Detailed descriptive statistics were performed on the NAMCS E-code and reason for the office visit variables to determine which codes were recorded and their frequencies and were compared with verbatim text entries for each injury type, if provided by the treating physician.

Independent variables used in this research project began with the following NAMCS variables; gender (variable "SEX"), ethnicity (variable "ETHNIC"), age group (recoded by NAMCS staff; variable "AGER"), race (recoded by NAMCS staff, variable "RACER"), payment source for the office visit (variable "PAYTYPE"), region of the country the office visit took place (variable "REGION"), and the specialty of the treating physician (recoded by NAMCS staff, variable "SPECR"). Detailed descriptive statistics were performed on each of these variables to determine the frequency of their occurrence in the selected ADHD subpopulation. It was determined that some of these variables captured very few, if any, patients associated with a diagnosis of ADHD. Those variable categories with few to no patient visits associated with the ADHD study population were

collapsed with other variable categories to reduce their lack of interpretability during subsequent advanced statistical evaluation. This procedure is supported by the NCHS staff to assure that no cell within a variable category has fewer than 30 unweighted patient records to ensure stability and reliability of standard error determinations and subsequent statistical analyses. Specifically, the NAMCS variable "ETHNIC" was recoded into a new variable labeled "ETHNICF" permitting the combination of the two category codes of "0" and "3", used in different survey years and totaling 174 office visits, representing the response on the patients' data record form was left blank for this variable. The remaining two category codes for this variable were left as originally coded and included "1", representing Hispanic or Latino, and "2", representing Not Hispanic or Latino. The NAMCS variable "AGER" was recoded into a new variable labeled "AGERF" allowing the two category codes of "5" (*N*=3) and "6" (N=1), representing the two oldest age groups (≥65 to ≤74 years, and ≥75 years, respectively), to be collapsed into and combined with the variable category code "4", originally representing the age group of ≥45 years to ≤64 years (*N*=79). The new variable category code "4" now represented the age group of ≥45 years and totaled 83 office visits. The remaining three variable category codes were left as originally coded by the NCHS staff and included "1" representing ages <15 years, "2" representing ages ≥15 to ≤24 years, and "3" representing ages ≥25 to ≤44 years.

The next NAMCS variable to be recoded was "PAYTYPE". Following the performance of detailed descriptive statistics on this NAMCS variable, it was determined that several variable codes captured fewer than 30 office visits that were associated with

the diagnosis of ADHD. A new recoded variable, labeled "PAYTYPEF", was created permitting the two variable category codes of "0" and "9", totaling 15 office visits and used in different survey years and representing the response on the patients' data record form for this variable was left blank, to be combined. Additionally, the category codes for Medicare ("2"; *N*=18) and Medicaid ("3"; *N*=180) were combined into one category code ("3") representing the joint payment sources of both Medicare/Medicaid. Lastly, four additional variable category codes were combined into a collapsed new code representing "All Other" payment sources ("7"). The combined original codes were "4", representing "Worker's Compensation" (*N*=1), "6" representing "No Charge/Charity" (*N*=3), "7" representing "Other" (*N*=40), and "8" representing an "Unknown" form of payment (*N*=16). Each of these four payment source codes were collapsed into a new category code of "7" representing "All Other" payment sources. The remaining variable category codes, "1" representing Private Insurance and "5", representing "Self-Pay", were left as originally coded.

The final NAMCS variable to be recoded was the "SPECR" variable. Again, following the performance of detailed descriptive statistics on this variable it was determined that several of the physician specialties captured far fewer than 30 office visits associated with the medical diagnosis of ADHD. Some captured no office visits associated with ADHD. Like the variables described above, for statistical appropriateness some of the category codes for this variable were combined. Specifically, category code "01", representing the specialty of "General/Family Medicine" (*N*=66), and category code "03", representing "Internal Medicine" (*N*=10) were combined into a new category

code "01" representing the specialties of "General/Family/Internal Medicine". Lastly, numerous other physician specialty codes were combined into a new category code labeled "15" representing the "Other" physician specialty designation. However, each of these codes contained no patient visit associated with a medical diagnosis of ADHD so the newly combined variable resulted in a total count of zero office visits. The original category codes of the combined codes were "05", representing "General Surgery", "06", representing "Obstetrics and Gynecology", "07" representing "Orthopedic Surgery", "08" representing "Cardiovascular Diseases", "09" representing "Dermatology", "10" representing "Urology", "13" representing "Ophthalmology", "14" representing "Otolaryngology", and "15" representing an "All Other" types of physician specialties. The remaining three variable category codes were left as originally coded and included "04" representing Pediatrics, "11" representing Psychiatry, and "12" representing Neurology. There was no category originally labeled by the NCHS as "02" for this NAMCS recoded variable.

Several new dichotomous dummy variables were created to be utilized as additional independent variables. A new dichotomous dummy variable was created, labeled "COMORB_A", describing the presence or absence of a psychiatric comorbidity in those patients with ADHD. The comorbid conditions were captured in a fashion similar to that utilized in capturing patients diagnosed with ADHD described above, by using specific ICD-9 codes for the various common comorbidities and searching each of NAMCS's three diagnostic variables. The only psychiatric comorbidities found to exist in conjunction with the medical diagnosis of ADHD in this concatenated dataset were;

schizophrenia (ICD-9-CM code 295.00 through 295.99, labeled "SCHIZOPH"; *N*=1); episodic mood disorders, which includes bipolar disorder types I and II, major depressive disorder, and mania (ICD-9-CM codes 296.00 through 296.99, labeled "MOOD"; *N*=95); pervasive developmental disorders (ICD-9-CM codes 299.00 through 299.99, labeled "PERVASDE"; *N*=7); anxiety, dissociative, and somatoform disorders (ICD-9-CM codes 300.00 through 300.99, labeled "ANXIETY"; *N*=27); personality disorders (ICD-9-CM codes 301.00 through 301.99, labeled "PERSON_C"; *N*=6); adjustment reaction disorders (ICD-9-CM codes 309.00 through 309.99, labeled "ADJUSTMN"; *N*=20); disturbances in conduct not elsewhere specified (ICD-9-CM codes 312.00 through 312.99, labeled "CONDUCTN"; *N*=10); and disturbances of emotions specific to childhood and adolescence (ICD-9-CM codes 313.00 through 313.99, labeled CHILDE_C"; *N*=46). No other psychiatric ICD-9-CM-defined conditions were included in the new dummy variable creation process due to the fact that they are either not commonly co-occurring with ADHD or no patients (zero) with these diagnoses were captured by the NAMCS in patients who also had ADHD. Due to the majority of comorbidities having less than 30 office visits associated with them and the extreme subjectivity involved with the possible combination of select comorbidities (those with less than 30 office visits), it was decided it more appropriate to utilize only the dichotomous dummy variable, representing all comorbidities. It was decided that the following reference, or comparator, independent variable categories would be selected for the logistic regression modeling procedures and would include; "males" for the variable "SEX", and "no" for the variable "ADHDSTIM" representing patients who were not

prescribed a stimulant to treat their ADHD. It was also determined that the ethnicity category of "not Hispanic/Latino" would be selected as the reference group for the variable "ETHNICF". Additionally the category of "≥45 years of age" was selected as the reference for the variable "AGERF", "private insurance" would be used as the reference for the variable "PAYTYPEF", "general/family/internal medicine" would be the comparator for the physician specialty variable "SPECRF", "Caucasian" would be selected reference for the race variable "RACER", the category designation of "no" would be utilized for the variable "COMORB_A" representing the absence of comorbidities with ADHD, and the region category of "Northeast" would be selected as the comparator for the variable "REGION".

The "NAMCS4.2full" dataset was then converted into a readable Stata/SE 8.0 format (Stata Corp., Inc., College Station, TX) using the statistical management software program, Stat/Transfer (Circle Systems, Inc., Seattle, WA). The converted dataset was subsequently reviewed for the presence of PSU's with single strata. Four PSU's were found to have single strata and all were joined with other regionally similar stratum, as recommended by the NCHS. All statistical analyses were performed utilizing the NAMCS's weight variable and the multi-stage survey-appropriate survey set (svyset) process within the Stata/SE program on the ADHD subpopulation.

Statistical analyses were conducted on the dataset and included the performance of multiple individual and stratified descriptive analyses, Chi square test and logistic regression procedures. It is important to note that it was the desire within this research project to also conduct multinomial logistic regression modeling by utilizing the available

E-codes (specific injury type), reason for the office visit, and possibly the verbatim text entries for those office visits associated with an injury and ADHD. However, due to the limited number of patient office visits captured with the various individual E-codes and verbatim text entries, use of this statistical procedure was deemed inappropriate. Each independent variable was assessed for confounding, effect modification, and significance for final model development. Statistically significant independent variables were included in the final logistic regression model and stratified, as appropriate. Unadjusted and adjusted odds ratios, with 95% confidence intervals, were computed for each independent variable included in the study and an *a priori* level of 0.05 ($p \leq 0.05$) was utilized for all analyses.

CHAPTER 4

RESULTS

Concatenation of the 1998 through 2001 NAMCS datasets produced a total of 95,749 patient records detailing the patient office visits sampled during these four study years. Use of the NAMCS weighting variable resulted in a national estimate of 3,290,042,929 representing the estimated patient office visits occurring in the U.S. for these four study years. Table 1 provides additional select data for each of the four NAMCS study years.

From this concatenated four-year dataset, it was determined that a total of 889 patient office visits were associated with a diagnosis of ADHD. This became the study population for this research project and included stimulant-treated and un-treated ADHD patients. Six hundred and sixty six of these 889 ADHD-related office visits were found to also be associated with the prescription of a stimulant medication for the treatment of ADHD, with 27 of these 666 office visits associated with the prescribing of two stimulant medications. The number of stimulants prescribed was not considered a factor necessary for this analysis, especially due to the small number of patients on more than one stimulant. No patients were prescribed three stimulants. Therefore, these two-stimulant ADHD office visits were managed in a dichotomous fashion for the treatment variable. This resulted in a total of approximately 75% of the original 889 patients with a diagnosis of ADHD who were prescribed a stimulant medication for the pharmacotherapy of their

disorder. Use of the NAMCS weighting variable allowed the 889 patients associated with a diagnosis of ADHD to represent a national estimate of 21,223,391 office visits occurring during the four selected study years. The 666 stimulant-treated ADHD patient office visits were weighted to a national estimate of 15,604,329 patient office visits occurring during the same time frame. Table 2 provides complete information on the unweighted and weighted frequencies for the surveyed ADHD patients and the selected independent variables. Graphical and detailed descriptive analysis of each of the independent variables, including the NAMCS original and investigator recoded variables, indicated that essentially all of the variables were either normally distributed or had a distribution that would allow them to be considered near normal. There were no missing cases for any of the variables studied. The independent variable demonstrating the largest amount of non-normality was the patient's reported race, with most patients reporting their race as being Caucasian (White). The injury dependent variable was also negatively skewed indicating that the vast majority of office visits were not associated with an injury. A detailed descriptive analysis was also conducted on several other NAMCS-acquired variables relating to the type of injury, called E-codes, the reason for the office visit, and verbatim text entries used for description of the injury necessitating ambulatory medical care. This descriptive process was undertaken to confirm those office visits dichotomously listed as being associated with an injury, along with the desire to attempt to ascertain if any specific or broad injury categories were commonly occurring and associated with the use of stimulants for treatment of ADHD. After a detailed and exhaustive review of each of the NAMCS's variables relating to injury (E-codes, reason

for the office visit, and verbatim text entries), it was determined that each of these variables approximated those few office visits also captured dichotomously as being related to an injury. There were a total of 25 office visits dichotomously captured as being related to an injury in patients with ADHD. Table 3 includes a listing of the various E-codes (causes of injury), reasons for the office visit, and verbatim text entries related to the injuries which were captured on the NAMCS patient record forms specifically for the ADHD study population. The minor differences between the dichotomous injury variable and the frequencies of the E-codes (cause of injury), reasons for the office visit, and the verbatim text entries associated with the injury most likely represent the situation in which the recording physician more consistently checked the dichotomous injury survey item of whether or not the office visit was associated with an injury and not universally also completing the E-code variable or taking the time to provide a detailed verbatim text entry describing the injury. For those physicians who also took the time to complete the E-code and verbatim text entry survey items, both were found to be consistent. Unfortunately, each of the types of injuries sustained by the ADHD study population occurred infrequently. This finding resulted in the realization that using individual E-codes, the reason for the visit, or the available verbatim text entries describing the specific types of injuries for a multinomial logistic regression analysis would be statistically inappropriate. In the end it was decided to refrain from additionally evaluating these variables for possible multinomial logistic regression analysis as these variables did not add any additional specificity to this evaluation and in fact provided a greater statistical limitation had they been used. Therefore, all analyses were conducted

using the NAMCS's weight variable and the 889 ADHD-related office visits with the NAMCS dichotomous injury variable as the only dependent variable.

Initial statistical analyses were conducted using each selected independent variable as the ad-hoc dependent variable and conducting unadjusted, adjusted and stratified analyses on the remaining independent variable to assess for possible association by confounding and affect modification. All variables were eventually selected as the outcome variable for assessment against all remaining independent variables. Table 4 includes the output for these analyses.

Individual and stratified statistical analyses were performed utilizing the dichotomous injury variable and each of the selected independent variables. Table 5 provides the odds ratios and 95% confidence intervals for the unadjusted and adjusted odds ratios for the selected independent variables obtained from the various logistic regression analyses described below. Each of these analyses resulted in the finding that only the patient's recoded race was statistically significant and associated with patients who had a medical diagnosis of ADHD and who sustained an injury necessitating treatment in an ambulatory medical care setting (OR=2.38; 95% CI 1.15, 4.92; p=0.02). Compared to those recording their race as Caucasian (reference category), there was no statistically significant difference between those patients who recorded their race as Black/African American (p=0.539). However, those patients recording their race as "Other", including Asian, Native Hawaiian/Other Pacific Islander, American Indian/Alaska Native, and those individuals indicating more than one race, had a unadjusted odds ratio of 6.79 (OR=6.79; 95% CI 2.35, 19.65; p=0.001). This represented

the finding that of those ADHD patients who sustained an injury necessitating medical care in an ambulatory setting, they were nearly 7 times more likely to report their race as one fitting within this "other" category. Analysis of the other independent variables, including; sex, age groups, ethnicities, payment sources, physician specialties, region of the country care was provided, the presence of comorbidities, and even the prescription of a stimulant for ADHD, did not demonstrate a statistically significant association with injury in patients with ADHD. Although only a borderline statistically significant finding, it was determined that, of those patients who sustained an injury necessitating medical care in an ambulatory care setting, the injuries were 2.68 times more likely to have occurred in patients who had been prescribed a stimulant for the treatment of their ADHD, compared to those not prescribed a stimulant for management of their ADHD (OR=2.68, 95% CI 0.92, 7.82; p=0.07).

Inclusion of each of the independent variables in the creation of a full logistic regression model produced adjusted odds ratios once again resulting in only the patient's reported race remaining statistically significant, holding all other variables constant (OR=2.74; 95% CI 1.26, 5.99; p=0.012). Similar to the unadjusted logistic regression analysis, and again compared to Caucasians, it was determined that there was no statistical difference in risk of injury in those patients recording their race as Black/African American (p=0.556). However, those patients recording their race as "Other", including Asian, Native Hawaiian/Other Pacific Islander, American Indian/Alaska Native, and those individuals indicating more than one race, had an adjusted odds ratio of 13.20, representing a more than 13 times greater risk of this joined

race group sustaining an injury requiring ambulatory care medical care (OR=13.20; 95% CI 4.24, 41.09; $p<0.001$). As demonstrated in the individual independent variable analysis, performance of this full model analysis resulted in each of the other independent variables, including the prescription of a stimulant medication in those patients with a diagnosis of ADHD, remaining non-significant for an association with the risk of injury, while holding all other variables constant. Although not statistically significant in the full-model logistic regression, yet similar to the individual analysis that compared patients not prescribed a stimulant medication for management of their ADHD to those patients prescribed a stimulant for the treatment of their ADHD, this full-model demonstrated that the stimulant-treated ADHD patients were 2.9 times more likely to present to an ambulatory medical care setting for the treatment of their injury (OR=2.90, 95% CI 0.98, 8.58; $p=0.055$).

Creation of a final partial logistic regression model using the only independent variable found to be statistically significant on both the individual independent variable and full model analyses, the patient's reported race, and including the stimulant treatment independent variable, it was found that the odds ratio's for each variable did not significantly change from that discovered with previous analyses. The stimulant treatment variable remained borderline significant and the race variable remained statistically significant, similar to all other analyses. Table 6 provides the odds ratios and 95% confidence intervals for the various partial models created by using the injury dichotomous variable as the dependent variable and inclusion of the stimulant variable and separately including each individual independent variable in the partial model. Table

7 provides information describing the stratified analyses using a similar partial model process for all categories of all selected independent variables.

In conclusion, from the use of this concatenated four-year dataset of the NAMCS, and selecting out those patient office visits associated with a diagnosis of ADHD, it has been demonstrated that of those ADHD patients suffering an injury necessitating treatment in an ambulatory care medical setting there was a borderline statistically significant increase in odds that they were being treated with a stimulant for ADHD. Finally, this research project also demonstrated that compared to Caucasian patients, while holding all other variables constant including, but not limited to, pharmacotherapy, patients reporting their race as other than Caucasian or Black/African American, including those reporting more than one race, were found to be at a statistically significant 13 times greater risk of injury necessitating medical care in an ambulatory setting.

CHAPTER 5

DISCUSSION

The hypothesis for this research project was framed from the standpoint that if ADHD patients were at a greater risk of sustaining an injury requiring medical treatment, as has been reported in previous publications, then appropriate use of the most effective pharmacotherapy for ADHD, the stimulant medications, should impart some level of improvement in the patients' focus, attention, and concentration. This benefit might theoretically translate into a potential reduced risk of injury necessitating medical care in an ambulatory setting. However, this was not the finding from the use of four concatenated years of an ambulatory-based, nationally-representative survey. This dissertation research project reports that of the surveyed ADHD-related patient office visits associated with an injury requiring medical care provided in an ambulatory care setting, there was a borderline statistically significant increase of approximately 2.5 times in these ADHD patients being associated with the prescription of a stimulant for the treatment of their ADHD, compared to those injured ADHD patients not prescribed a stimulant (p=0.055).

It should be stated that since this study is a cross-sectional type of study, there can be uncertainty in the direction of any association. Although debatable, and at times somewhat speculative due to the nature of this study, there may be a few underlying theories related to, or affecting, the finding of this study. Therefore, the possible multiple

interpretations of the discovered temporal relationship between the determinant and outcome will be discussed. To begin the discussion it should be pointed out that even though, for various appropriate reasons, the NAMCS dichotomous injury variable was utilized as the primary dependent variable in this study, the most commonly occurring reason for the injury-related office visits, as captured by use of the ICD-9-CM-based E-codes, was poisoning from medications, specifically CNS depressant medications (Other CNS depressants, *N*=7; Sedatives/Hypnotics, *N*=7). Although not encompassing all of the 21 E-codes captured by the 4 NAMCS study years included in this study, the poisoning-related codes were the majority (14 of 21; 75%). Although the total number of E-codes (*N*=21) did not exactly match the total number of office visits dichotomously cited as being associated with an injury (*N*=25), it could be contemplated by some that the injury concept studied in this research project is more appropriately described by a medication poisoning injury than a physical injury. With this being stated, the following related and alternative relationships between stimulant use in the ADHD population and the risk of injury, more commonly seen in this study as a poisoning by CNS depressant, is offered.

One possible explanation for the finding of this study could be the concept that the frequently injured ADHD patients presenting to their ambulatory care setting for treatment of an injury are more likely to be treated with a stimulant medication than those patients not presenting for care of an injury. It may a situation in which the stimulant-treated ADHD patients had more severe disease and therefore was at a greater risk of being associated with an injury-related event, be it a physical injury or a poisoning-related injury. It is understandable that the more severe diseased patients might be more

likely to be treated with a stimulant medication compared to the less effected, milder cases of ADHD. The use of stimulants to treat ADHD may improve the focus and attention of these ADHD patients but because their disease is more severe, and requiring treatment with pharmacotherapy, their risk of injury is greater than what the pharmacotherapy can reduce or prevent and greater than the less severe cases not being treated. Additionally, it could be that the timing of the diagnosis of ADHD, and more specifically the provision of pharmacotherapy for the disorder, was so acute that there was not enough time to provide clinical benefit from the pharmacotherapy to see a reduction in injury risk compared to those ADHD patients not prescribed a stimulant. A counter conclusion might involve the consideration that some of the study population patients sustained an injury and had ADHD but were undiagnosed when they sustained their injury. It could be that the ADHD patients were prescribed a stimulant and maybe even provided the diagnosis on the same day of the captured injury-related office visit. This would cause the stimulant medication to be on the patients' medication list, and captured by the NAMCS and this study, yet providing no benefit in the reduction of the currently sustained and captured injury. Based on the concept of temporality, it might be that solely from the current injury might it be that the ADHD is diagnosed and a stimulant medication is prescribed thereby providing no benefit to the given level of injury risk for that patient and that particular injury occurrence. This in fact could be considered a form of misclassification as these patients would be considered part of the treatment group when in fact, at the time of the injury, they were not being treated. To further expand this discussion, and as mentioned previously, there is no ability with the

use of the NAMCS dataset to confirm compliance with therapy in the patients captured by the NAMCS. Patients may have been diagnosed with ADHD and prescribed a stimulant medication but not be compliant with therapy, or only partially compliant, thereby preventing full therapeutic benefit and a reduction in injury risk.

Although this study attempted to control for other psychiatric comorbidities, if the injury topic evaluated in this study is actually more closely related to poisoning from a CNS depressant than a physical injury, it may be that the stimulant-treated ADHD patients are more likely to also be troubled with other psychiatric conditions, poisonings, or other situations which are connected with the use of CNS depressants and these patients are at an increased risk of poisoning themselves from over use of these additional medications. It may be that due to this history these ADHD patients are more likely treated with a stimulant than those ADHD patients without this history. If the injury described in this study is more descriptive of a poisoning from CNS depressants than a physical injury, some may also theorize that the direction of the temporal relationship found in this study could be from a situation in where physicians are more likely to treat ADHD patients previously prone to accidents, injury, trauma, and poisonings to attempt to reduce their subsequent and further need for medical care from ADHD, albeit without success. This could be related to a lack of efficacy, increased severity of disease, or some other unknown factor. Stated another way, it could be that the patients who have ADHD and are also prone to poisoning from CNS depressants and are more likely to have their physicians treat their ADHD with a stimulant medication.

It may also be that treating a patient with a stimulant for their ADHD directly or indirectly increases their risk of an accidental or intentional poisoning-related toxicity and injury from CNS depressants. Although not seriously considered by this researcher, some might speculate that by treating an ADHD patient with a stimulant medication that it induces the patient to over-indulge in the use of additional psychiatric medications, specifically CNS depressants, thereby inducing an injury necessitating ambulatory-based medical care. To continue this line of thought, treatment of ADHD with a stimulant medication may increase a patient's carelessness and lack of attention thereby leading to an increased injury risk.

An additional theory describes the concept that where the non-stimulant treated group still sustained injuries to an equal or even greater rate, but that the injuries sustained by this non-treated group were severe enough to warrant medical care being provided in an emergency room, hospital setting, trauma center, or an institutional-based urgent care center and not in an ambulatory care setting. This would result in a reduction in the number of injuries captured by the NAMCS for the non-stimulant treated group. It may be that stimulant treatment does in fact improve focus in ADHD patients. This improved focus may not, however, completely eliminate the risk of sustaining an injury yet it may reduce the risk of sustaining a more severe level of injury which may be possible without treatment. However, although plausible, this theory was not evaluated by the current research project and requires additional investigation before being considered likely.

One possible limitation that might contribute to the findings of this research project include the fact that the NAMCS does not capture, assess for, or allow control for possible family, home, environmental, or neighborhood injury-related risk factors. Additionally, ADHD patients who are being treated with a stimulant may only be on a stimulant medication during select parts of the year or week but not in others. This describes the concept of "drug holiday" which is commonly employed by both physicians and parents. Physicians and parents may desire the children to only be on treatment during the school week and during the school year (both academic settings) and off treatment during weekends and during the summer (non-academic settings). It might be that some of the injuries could have occurred during the drug holiday periods when pharmacotherapy benefit is not being provided. The NAMCS does not capture aspects related to compliance or drug holidays.

Next, the CDC and the NCHS recommend using caution when conducting statistical analysis on cells with fewer than approximately 30 office visits. The dichotomously-captured NAMCS injury variable for the ADHD subpopulation only comprised 25 office visits. The borderline statistically significant finding might have been moved to statistical significance had the number of office visits captured for the ADHD subpopulation been larger. Although demonstrating an increase in odds in the stimulant ADHD group, there might have been a greater likelihood of demonstrating statistical significance of the increased odds had our study population had a larger sample size of injuries. And finally, the results might have been different had the patients who were prescribed a stimulant medication but did not have either an official diagnosis of

ADHD or a captured diagnosis of ADHD been included in the study population. Over 400 office visits were found to be associated with the prescription of a stimulant medication but not associated with the medical diagnosis of ADHD. The NAMCS only captures up to three medical diagnoses yet captures up to six medications. It could be that physicians would have documented the known and previously determined diagnosis of ADHD if the NAMCS captured more diagnoses. For example, the patient may have had four or more medical diagnoses at the time of the injury-related office visit, one being ADHD, yet the NAMCS patient record form only allowed the capture of three medical diagnoses. Had a fourth or fifth diagnosis been captured by the NAMCS patient record form the diagnosis of ADHD might have been captured thereby increasing the over study population sample size and the potential number of injury-related office visits.

By utilizing the study design developed for this research project and by using the NAMCS dataset, this research project overcame most of the limitations of prior published studies evaluating the presence of an association between ADHD, or it's associated behavioral characteristics, and injury. First of all, by use of 4 concatenated years of the NAMCS, the total weighted population and the total weighted ADHD subpopulation numbers were greater than would have been available if less than 4 years had been utilized. The office visits captured by the NAMCS included patients with medical diagnoses and medications prescribed by a physician. This study was not limited by the use of surrogate markers for ADHD or individual, select behavioral characteristics frequently found in those with ADHD. The ADHD patients included in this study were drawn from the full 4-year concatenated dataset by use of standard ICD-9-CM diagnosis

codes, representing medical diagnoses. Injuries were captured on the NAMCS patient form, directly from the patients' medical chart, via the survey question of whether or not the office visit was associated with an injury or poisoning. Due to the methodology of this research project and the use of the NAMCS, there is minimal to no selection or recall bias to negatively impact this study.

In spite of the enhancements to the methodology of this study provided by use of the NAMCS dataset there are minor limitations that must be mentioned, most of which do not directly explain the findings of this study. First, it is assumed that the medical diagnosis of ADHD was properly determined by qualified medical professionals using validated rating scales and official DSM-IV diagnostic criteria. Some patients may have been prescribed a stimulant for what parents, teachers, or family members are calling ADHD-like symptomatology and convincing primary care physicians of this non-medically based opinion. The patients may have been, over time, subsequently labeled as having ADHD because the parents or teachers say they believe the patient is hyperactive or has symptoms commonly associated with ADHD. The parents, teachers, or family members might have convinced the physician of this fact, without conducting a full and formal medical evaluation and disease diagnosis review, who then prescribes a stimulant for treatment of the disorder. It also might occur that physicians do not fully utilize the full DSM-IV diagnostic criteria and simply ask a few common questions related to ADHD before rendering their diagnosis. Secondly, this study assumes that due to the probabilistic, national aspect of the NAMCS that the ADHD patients captured by the

survey during the four selected survey years are representative of the non-surveyed patients with ADHD.

This research project was also limited by the fact that the NAMCS does not include federally-funded ambulatory sites in the survey and excludes hospital-related medical facilities (although the NHAMCS does capture hospital-related sites but this dataset was not utilized for this study). This becomes important for those individuals with no medical care insurance coverage and who utilize federally-funded or hospital-based indigent care medical facilities for treatment of their injuries and other medical conditions. Patients being treated in these types of facilities are not captured by the NAMCS and therefore would not be represented in the current study. However, the NAMCS does include patients of all age ranges, ethnicities, races, regions of the country, and forms of payment, including self-pay, Medicare/Medicaid, workers compensation and no charge/complimentary care. The NAMCS strives to over-sample under-represented patient populations which may, in part, overcome some of the limitations imparted by the exclusion of federally-funded and hospital-related facilities.

A final aspect that may be contemplated by some as a limitation of the NAMCS is the fact that the survey does not strive to capture repeat office visits of individual patients. The NAMCS is not a panel survey and does not permit statistical evaluation of repeated measures. Again, the NAMCS is not structured to provide this aspect which may appear to some as a limitation.

Two aspects aiding in the improvement of the internal validity of this research project is the fact that the ICD-9-CM diagnostic codes for ADHD did not significantly

change during the four selected study years. Additionally, the medication class code used to capture stimulant medications also did not change and is a nationally supported and recognized FDA coding system. Furthermore, other than use for treatment of ADHD, there are no other FDA-approved indications for the stimulant medications, although there are several off-label uses. However, these off-label uses would have to occur concomitantly with the medical diagnosis of ADHD since in this study these medications were captured only in those patients who also had the diagnosis of ADHD. Therefore, it was assumed that the capture of both the diagnosis of ADHD and the prescription of a stimulant indicated those patients being treated with a stimulant for their ADHD.

The only statistically significant finding discovered by this research project indicated a difference in the patients' reported race and the risk of injury in ADHD patients requiring medical care in an ambulatory care setting. It was found that compared to those patients reporting their race as Caucasian (White), there was an approximately 13 times greater risk in those patients either reporting more than one race or one of the races collapsed into the "Other races" category; including those patients reporting their race as Asian, Native Hawaiian/Other Pacific Islander, or American Indian/Alaska Native. No previous publication could be located describing a difference in risk of injury in ADHD patients with the races listed in this study's "Other races" category. This unique finding warrants further study to evaluate and attempt to elucidate possible rationale.

APPENDIX

DSM-IV Criteria for the Diagnosis of ADHD (APA, 1994)

A. Either 1 or 2:
   1. Six (or more) of the following symptoms of inattention have persisted for at least six months to a degree that is maladaptive and inconsistent with developmental level:
      a. Often fails to give close attention to details or makes careless mistakes in schoolwork, work or other activities
      b. Often has difficulty sustaining attention in tasks or play activities
      c. Often does not seem to listen when spoken to directly
      d. Often does not follow through on instructions and fails to finish schoolwork, chores or duties in the workplace (not due to oppositional behavior or failure to understand instructions)
      e. Often has difficulties organizing tasks and activities
      f. Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework)
      g. Often loses things necessary for tasks or activities (e.g., toys, school assignments, pencils, books, or tools)
      h. Is often easily distracted by extraneous stimuli
      i. Is often forgetful in daily activities
   2. Six (or more) of the following symptoms of hyperactivity-impulsivity have persisted for at least six months to a degree that is maladaptive and inconsistent with developmental level:
      Hyperactivity
      a. Often fidgets with hands or feet, or squirms in seat
      b. Often leaves seat in classroom or in other situations in which remaining seated is expected
      c. Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)
      d. Often has difficulty playing or engaging in leisure activities quietly
      e. Is often "on the go" or acts as if "driven by a motor"
      f. Often talks excessively
      Impulsivity
      g. Often blurts out answers before questions have been completed
      h. Often has difficulty waiting turn
      i. Often interrupts or intrudes on others (e.g., butts into conversations or games)

B. Some hyperactive-impulsive or inattention symptoms that caused impairment were present before the age of seven years.

C. Some impairment from the symptoms is present in two or more settings (e.g., at school [or work] and at home).

D. There must be clear evidence of clinically significant impairment in social, academic, or occupational functioning.

E. The symptoms do not occur exclusively during the course of a pervasive developmental disorder, schizophrenia, or other psychiatric disorder, and are not better accounted for by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, or a personality disorder).

DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Washington, D.C.

ADHD = Attention Deficit/Hyperactivity Disorder.

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