

# Safety Study of Atomoxetine and Cerebrovascular Outcomes

**Study Type:** Observational

**Study Design:** Cohort, Retrospective

**Official Title:** Atomoxetine and Cerebrovascular Outcomes in Adults

**Trial Alias:** B4Z-MC-B014

**Unique protocol ID:** 12414

## Participant Flow

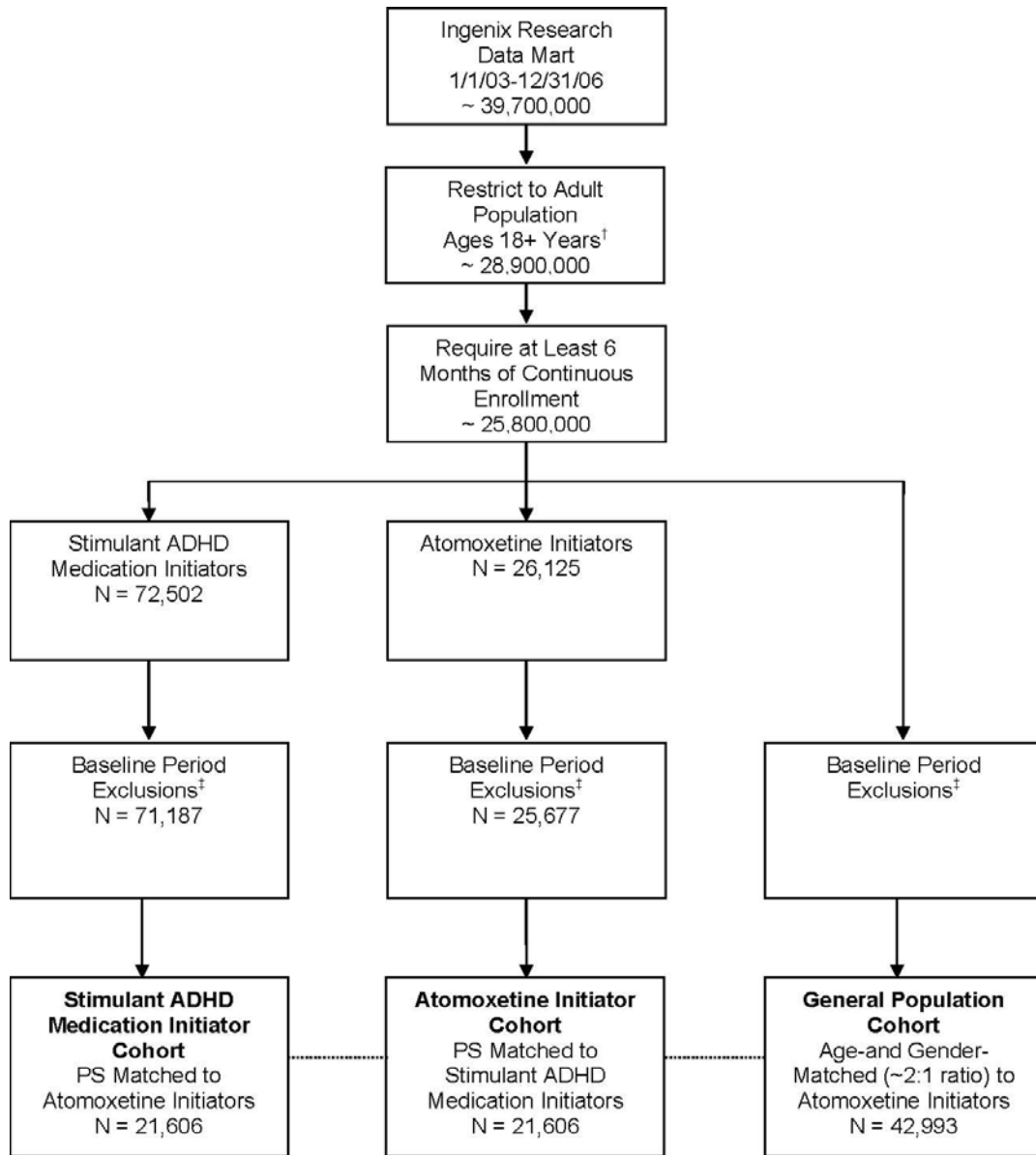
### Recruitment Details

This was an observational database study of health claims for the time period from 1 January 2003 through 31 December 2006 (with follow-up of patients through 30 June 2007).

### Reporting Groups

	<b>Description</b>
<b>Atomoxetine Initiators</b>	All patients 18 years or older who received a first dispensing of atomoxetine during the period from January 1, 2003 through December 31, 2006 with no dispensing of the same drug in the prior 6 months were identified.
<b>Stimulant ADHD Medication Initiators</b>	All patients 18 years or older who received a first dispensing of stimulant (methylphenidate or mixed salts of amphetamine) attention deficit hyperactivity disorder (ADHD) medication during the period from January 1, 2003 through December 31, 2006 with no dispensing of the same drug in the prior 6 months were identified.
<b>General Population</b>	A random sample of patients 18 years or older between January 1, 2003 and December 31, 2006 were selected from the Ingenix Research Datamart (RDM) and assigned index dates so as to be distributed similarly to the initial pool of atomoxetine initiators.

**Figure 1: Study Cohorts**



†Includes patients 18 years or older with commercial health insurance coverage from major markets available for medical record abstraction and complete medical and pharmacy benefits.

‡Patients were excluded at baseline if they had a history of arrhythmia (diagnosis or medication use), history of heart failure (diagnosis or medication use), or atomoxetine or stimulant ADHD medication daily dose values (not applicable for the general population cohort) greater than 240 mg per day.

## Baseline Characteristics (after matching)

Characteristic	Atomoxetine Initiators (N=21,606)	Stimulant ADHD Medication Initiators (N=21,606)	General Population (N=42,993)
Age (mean)	35.87	35.79	35.95
Gender (N/%)			
Female	10,363/48%	10,361/48%	20,711/48%
Male	11,243/52%	11,245/52%	22,282/52%

## Results

**Table 1: As-Treated Comparison of Current Use of Atomoxetine to Current Use of Stimulant ADHD Medication, Cerebrovascular Accident (CVA)**

	N	Person-Years (PY)	Incidence Rate per 1000 PY	Crude RR (95% CI)
Atomoxetine	5	9,579	0.52	1.38 (0.42-4.54)
Stimulant ADHD	7	18,417	0.38	1.00 [REF]

Abbreviations: RR=Rate Ratio, 95% CI = 95% Confidence Interval, REF=reference

**Table 2: As-Matched Comparison of Atomoxetine to Stimulant ADHD Medication, Cerebrovascular Accident (CVA)**

	N	Person-Years (PY)	Incidence Rate per 1000 PY	Adjusted HR (95% CI)
Atomoxetine	10	31,442	0.32	0.86 (0.36-2.04)
Stimulant ADHD	11	31,499	0.35	1.00 [REF]

Hazard ratio (HR) and 95% CI comparing all follow-up time for atomoxetine initiators to all follow-up time of stimulant ADHD medication initiators for CVA (secondary analysis) adjusted for age, gender, calendar year, prior use of heroin, diuretics, sedative hypnotics, and warfarin, prior stroke, and foot x-ray procedure (CPT 73630).

**Table 3: As-Treated Comparison of Current Use of Atomoxetine to Current Use of Stimulant ADHD Medication, Transient Ischemic Attack (TIA)**

	N	Person-Years (PY)	Incidence Rate per 1000 PY	Crude RR (95% CI)
Atomoxetine	1	9,580	0.10	0.31 (0.04-2.63)
Stimulant ADHD	6	18,416	0.33	1.00 [REF]

**Table 4: As-Matched Comparison of Atomoxetine to Stimulant ADHD Medication, Transient Ischemic Attack (TIA)**

	N	Person-Years (PY)	Incidence Rate per 1000 PY	Adjusted HR (95% CI) <sup>†</sup>
Atomoxetine	7	31,441	0.22	0.71 (0.26-1.93)
Stimulant ADHD	9	31,496	0.29	1.00 [REF]

<sup>†</sup> Hazard ratio (HR) and 95% CI comparing all follow-up time for atomoxetine initiators to all follow-up time of stimulant ADHD medication initiators for TIA (secondary analysis) adjusted for age, gender, calendar year, prior use of heroin, diuretics, sedative hypnotics, and warfarin, prior stroke, and foot x-ray procedure (CPT 73630).

**Table 5: As-Matched Comparison of Atomoxetine and Stimulant ADHD Medication Initiation to the General Population Cohort, Cerebrovascular Accident (CVA)**

	N	Person-Years (PY)	Incidence Rate per 1000 PY	Adjusted HR (95% CI) <sup>†</sup>
ADHD Medication Cohort <sup>‡</sup>	21	62,941	0.33	0.71 (0.34-1.47)
General Population Cohort	23	65,880	0.35	1.00 [REF]

<sup>†</sup> HR and 95% confidence interval (CI) adjusted for age, gender, calendar year, history of psychiatric diagnoses (psychotic disorders, neurotic disorders, and adjustment reaction), stroke risk factors (hypertension, diabetes, hyperlipidemia, coronary artery disease, smoking, and alcohol abuse), depressive disorders, and allergic rhinitis, and prior use of medications (antihypertensives, antilipemics, antidepressants, antipsychotics, anxiolytics, sedative hypnotics, anticonvulsants, narcotic analgesics, and cyclooxygenase-inhibitor-type non-steroidal anti-inflammatory drugs).

<sup>‡</sup> Defined as the combined atomoxetine and matched stimulant ADHD medication

**Table 6: As-Matched Comparison of Atomoxetine and Stimulant ADHD Medication Initiation to the General Population Cohort, Transient Ischemic Attack (TIA)**

	N	Person-Years (PY)	Incidence Rate per 1000 PY	Adjusted HR (95% CI) <sup>†</sup>
ADHD Medication Cohort <sup>‡</sup>	16	62,937	0.25	3.44 (1.13-10.60)
General Population Cohort	5	65,888	0.08	1.00 [REF]

<sup>†</sup> HR and 95% confidence interval (CI) adjusted for age, gender, calendar year, history of psychiatric diagnoses (psychotic disorders, neurotic disorders, and adjustment reaction), stroke risk factors (hypertension, diabetes, hyperlipidemia, coronary artery disease, smoking, and alcohol abuse), depressive disorders, and allergic rhinitis, and prior use of medications (antihypertensives, antilipemics, antidepressants, antipsychotics, anxiolytics, sedative hypnotics, anticonvulsants, narcotic analgesics, and cyclooxygenase-inhibitor-type non-steroidal anti-inflammatory drugs).

<sup>‡</sup> Defined as the combined atomoxetine and matched stimulant ADHD medication