

The Preventive Potential of Bupropion on Aortic Aneurysm Progression: A Real-World Data Analysis

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Epidemiology and Challenges:

- Aneurysm pathogenesis encompasses various disorders affecting the aorta, with both thoracic and abdominal regions affected.
- Approximately 26,000 people die from AAs annually in the U.S., making it a significant health concern.
- Aneurysm disease is a leading cause of death, and its prevalence is expected to rise, imposing a substantial burden on healthcare resources.
- Surgical intervention is resource-intensive, emphasizing the need for novel therapeutic modalities to alleviate the associated costs.

1. Elefteriades JA. Thoracic aortic aneurysm: reading the enemy's playbook. *Yale J Biol Med.* 2008;81(4):175-86

2. Dua A, Kuy S, Lee CJ, Upchurch GR, Jr., Desai SS. Epidemiology of aortic aneurysm repair in the United States from 2000 to 2010. *J Vasc Surg.* 2014;59(6):1512-7.

Background/Significance

- Aortic aneurysms (AAs) are a significant cause of morbidity and mortality, posing challenges for cardiovascular surgeons.
- No effective medical therapy currently exists; aortic rupture is a common cause of death.
- The FDA-approved antidepressant Bupropion has shown promise in regulating pathways associated with aneurysm progression.

1. Eleftheriades JA. Thoracic aortic aneurysm: reading the enemy's playbook. *Yale J Biol Med.* 2008;81(4):175-86

2. Dua A, Kuy S, Lee CJ, Upchurch GR, Jr., Desai SS. Epidemiology of aortic aneurysm repair in the United States from 2000 to 2010. *J Vasc Surg.* 2014;59(6):1512-7.

Background/Significance

- Bupropion modulates pathways in aortic aneurysm progression.
- It suppresses IL-6, MMP-2, and MMP-9 while increasing TIMP-1.
- Dual action aims to mitigate aortic aneurysm advancement.

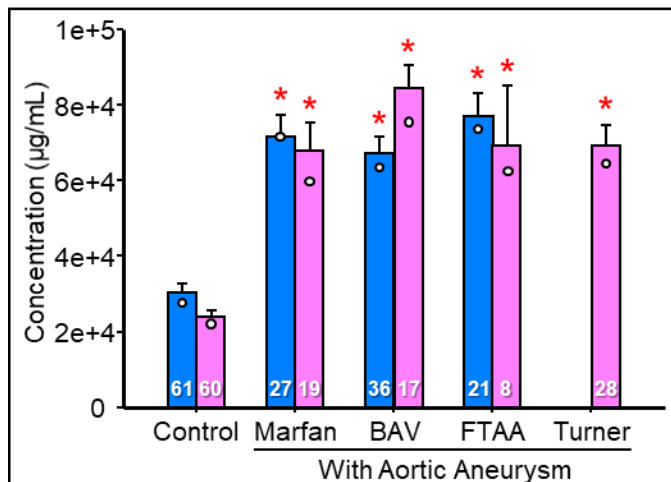


Figure 1. Human Plasma MMP-2 Levels. Circulating levels of MMP-2 are **elevated** in different etiologies of thoracic AA patients. All data is displayed as mean (bar) ± standard error of the mean. Median is displayed as a white circle, sample sizes are denoted at the base of each bar. *p<0.05 vs sex-matched non-AA control. Abbreviations: Bicuspid Aortic Valve (BAV), Familial thoracic AA

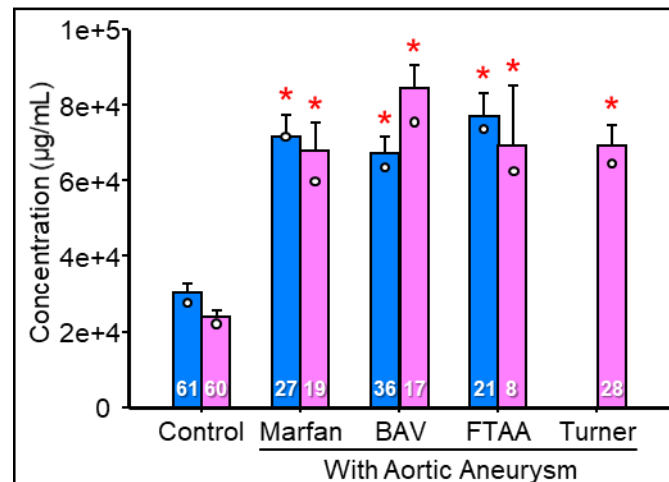


Figure 2. Human Plasma MMP-2 Levels. Circulating levels of MMP-2 are **elevated** in different etiologies of thoracic AA patients. All data is displayed as mean (bar) ± standard error of the mean. Median is displayed as a white circle, sample sizes are denoted at the base of each bar. *p<0.05 vs sex-matched non-AA control. Abbreviations: Bicuspid Aortic Valve (BAV), Familial thoracic AA

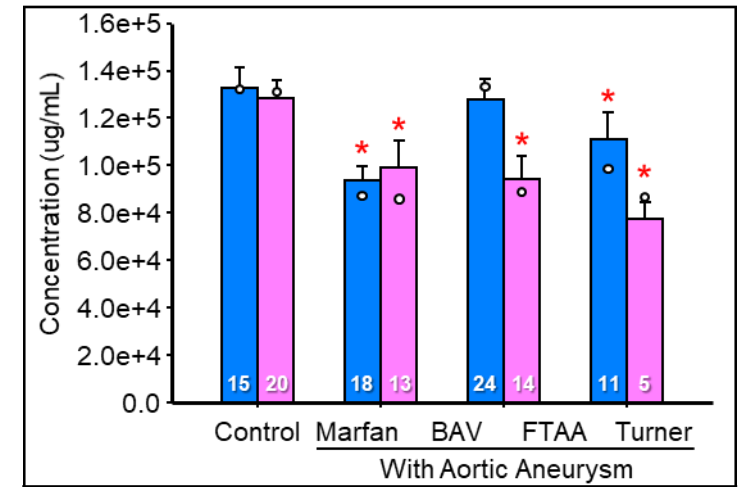
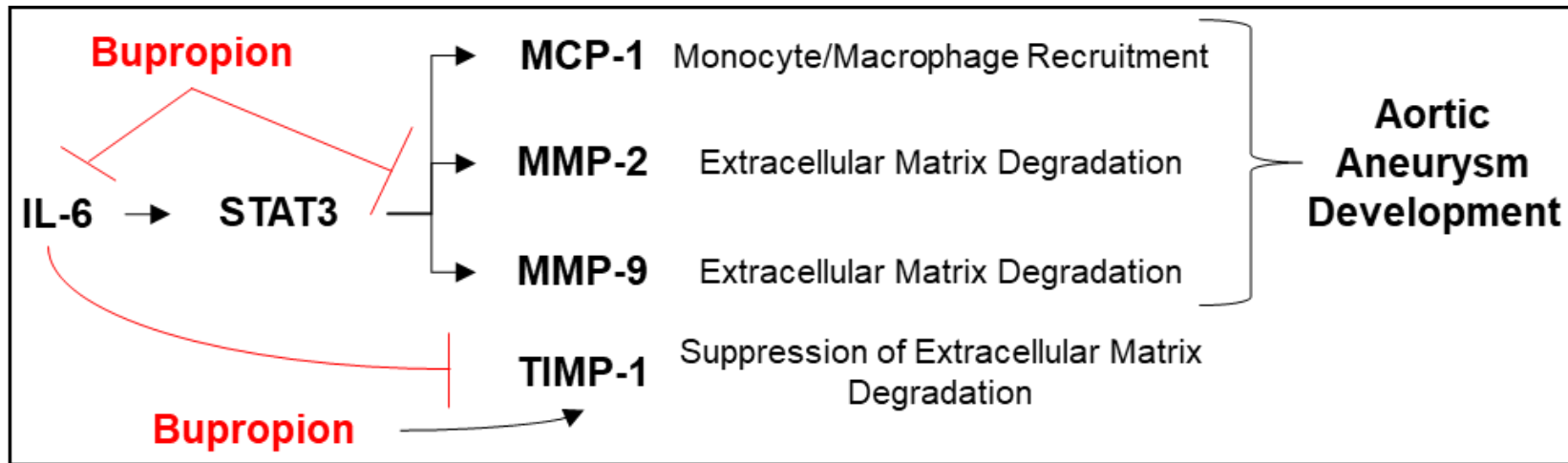


Figure 3. Human Plasma TIMP-1 Levels. Circulating levels of TIMP-1 are **reduced** in different etiologies of thoracic AA patients. All data is displayed as mean (bar) ± standard error of the mean. Median is displayed as a white circle, sample sizes are denoted at the base of each bar. *p<0.05 vs sex-matched non-AA control. Abbreviations: Bicuspid Aortic Valve (BAV), Familial thoracic AA (FTAA).

Background/Significance



Methods

- Utilized Medicare Claims database (2007-2017)
- Diagnosis of major depressive disorder, seasonal affective disorder, and tobacco use patients.
- Intervention: Bupropion
- Comparative group: SSRIs, SNRIs, mirtazapine, buspirone, nefazodone, trazodone, vilazodone, vortioxetine, varenicline, and nicotine
- Outcome: Aortic aneurysm development and aortic interventions
- Analysis: Descriptive statistics and Kaplan-Meier method

Results

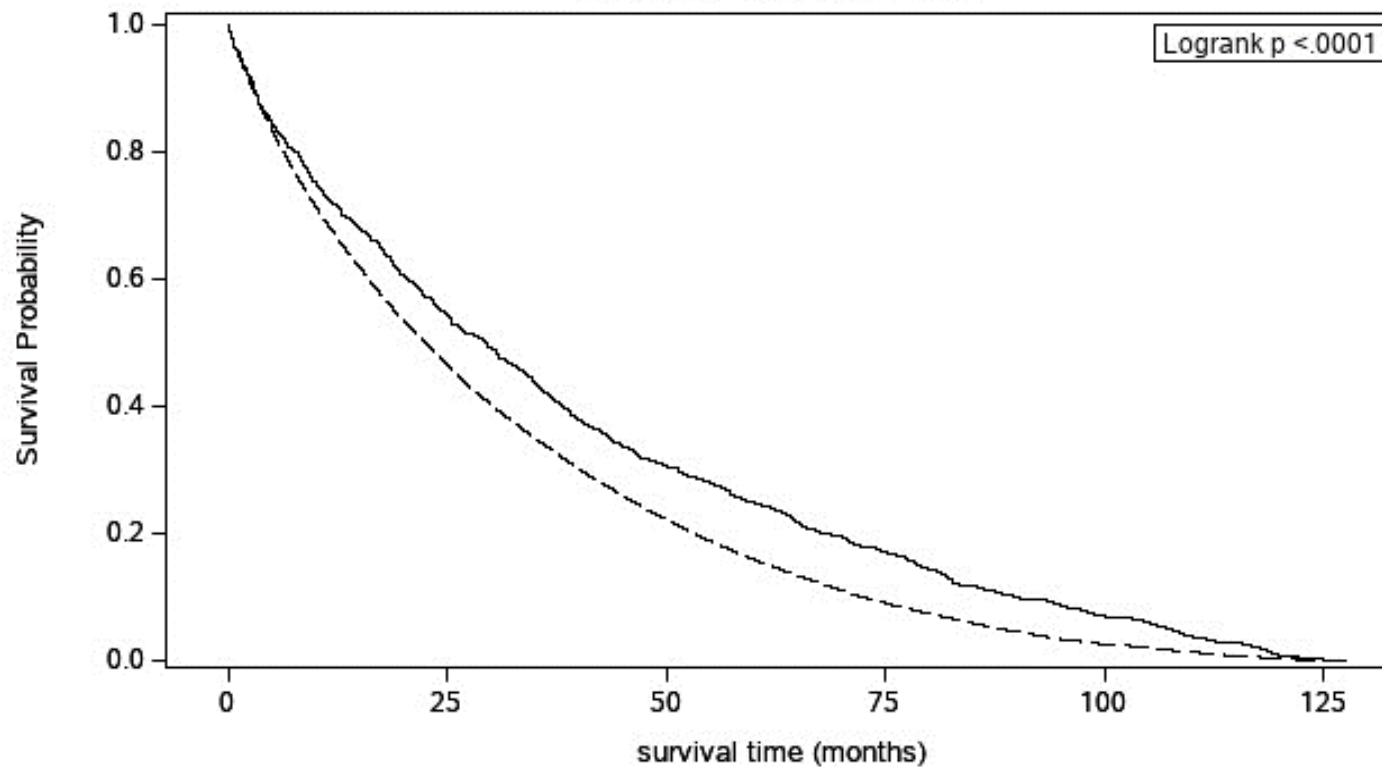
Characteristic	Comparator N=46052		Bupropion N=916	
	Frequency	%	Frequency	%
Male	17652	38.3	352	38.4
Age 65-74 years	26816	58.2	625	68.2
Age 75-84 years	14736	32.0	242	26.4
Age 85+ years	4500	9.8	49	5.3
Race: Black or African American	2184	4.8	33	3.6
Race: Hispanic	1305	2.8	22	2.4
Race: Other	1407	3.1	23	2.5
Race: White	41012	89.3	835	91.5
CCI cat 0	11991	26.0	292	31.9
CCI cat 1	11516	25.0	247	27.0
CCI cat 2+	22545	49.0	377	41.2
Current smoker	14677	31.9	228	24.9
Former smoker	19287	41.9	369	40.3
Obese	2439	5.3	43	4.7
Marfan syndrome	25	0.1	1	0.1
Turner syndrome	19	0.0	1	0.1
Ehlers Danlos syndrome	11	0.0	0	0.0
Loeys Dietz syndrome	46	0.1	0	0.0
Familial TAA	833	1.8	15	1.6
ACTA2/FBN1/MFAP5	507	1.1	5	0.5
Bicuspid aortic valve	199	0.4	4	0.4
Giant cell arteritis	918	2.0	14	1.5
Takayasu arteritis	32	0.1	0	0.0
Genetic predisposition	2519	5.5	39	4.3

Results

	Comparator						
	mean	std	range	median	p25	p75	
	30.8	27.8	127	22	8	46	p-value
Time to aneurysm Diagnosis or repair	Burpopion						<.0001
	mean	std	range	median	p25	p75	
	38	33	127	29	10	60	

Results

Kaplan-Meier Plot: Survival time to aneurysm diagnosis or repair by bupropion/comparator drugs in the Medicare database 2007-2017, n=46968
With Number of Subjects at Risk



Type of drug ——— Bupropion - - - Comparator

Bupropion	916	500	280	158	65	2
Comparator	46052	21368	10243	4197	1234	42

Conclusions

- **Key Finding from Real-World Data Analysis:**
 - Bupropion demonstrates a potential protective effect against aneurysm development and progression.
- **Implications of our Findings:**
 - Challenge Bupropion's conventional views of its pharmacological effects.
 - Expand Bupropion's scope beyond antidepressant use.
 - Suggest a novel avenue for preventive cardiovascular interventions.
- **Call to Action:**
 - Further research and exploration are warranted for the potential clinical application of Bupropion in preventing aortic aneurysms.