## **Results from Scientific Studies:**

Fatigue:

Vagus Nerve Activity:

o 61% increase in 5 minutes

o 61% improvement

o 48% improvement

 $\circ$  86% increase after 2 months of daily use

Post-Viral Symptoms (including fatigue, brain fog, GI symptoms, pain):

•	Sleep:
	o 19% improvement
•	Inflammation:
	o 78% improvement
•	Postural Heart Rate Change (POTS):
	o 40% reduction
•	Heart Rate Variability:
	o 18% increase
•	Depressive Symptoms:
	o 45% improvement
•	Oxidative Stress:
	o 28% reduction
•	Memory:
	o 32% improvement
•	Reading & Learning:
	o 29% improvement
•	Macrocirculation:
	o 50% improvement
•	Microcirculation:
	o 39% improvement
•	Attention Deficiency:
	o 11% improvement
•	Anxious States:

- o 35% improvement
- Palpitations:
  - o 85% reduction
- Heart Muscle Function:
  - o 19% improvement
- GI Symptoms:
  - o 80% improvement
- Blood Pressure:
  - o 10% reduction

Simplified

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	Cardiovascular Nurosym Research	Highlights	Link	I 'ANAITIAN	Improvement [%]
1	acutely ameliorates left	The patient showed a decrease in deformation of heart muscle (Global Longitudinal Strain) from -19.3% to -23.1% after 1 hour of active Nurosym neuromodulation, which is a favourable change indicating improved cardiac function.	https://link.springer.com/article/	with preserved ejection	~19% GLS; FMD; LSCI; HRV; quality of life questionnaires (PROMs)
2	nerve stimulation	Review: Nurosym neuromodulation, taking advantage of neural plasticity without destroying the targeted neural tissue. Nurosym has emerged as a novel non pharmacological adjuvant therapy and offers protective effects for the heart, including hypertension.	https://www.tandtonline.com/do	Cardiovascular diseases (atrial arrhythmia, ventricular arrhythmia, ischemia/reper fusion injury, heart failure, and hypertension)	

	TREAT AF (Transcutaneous Electrical Vagus	compared with the control arm	https://www.sciencedirect.com/	Paroxysmal	~85% AF
3.	to Suppress Atrial	lincludes the affective slowing of	•	atrial fibrillation	burden reduction
4.	Stimulation for Atrial Fibrillation: A Glimpse of Hope for Neuromodulation	Editorial Comment: The study (on Nurosym neuromodulation) offers hope for the potential role of neuromodulation in managing atrial fibrillation and other cardiac conditions influenced by the vagus nerve impairment. The study indicated that an implantable device will provide the systematic treatment.	https://www.sciencedirect.com/ science/article/pii/S2405500X2 0300773?via%3Dihub	fibrillation	comment: 23% TNF-a decrease & 116% LF/HF increase; 72% compliance after 6 months
5.	a biomarker for	lineans that it can effectively		Paroxysmal atrial fibrillation	~38% Neuropeptide Y (NPY) levels lower
6.	Non-invasive Low-level Tragus		https://www.aerjournal.com/arti cles/non-invasive-low-level-trag us-stimulation-cardiovascular-d	IDOST-ACHTE	animal and human
7.	Autonomic Modulation of Cardiac Arrhythmias: Methods to Assess	Review: Nurosym neuromodulation holds potential in correcting the sympathovagal imbalance in this cardiovascular disease by improving Heart Rate Variability (HRV). The group using the active treatment had significantly lower levels of atrial fibrillation (AF) burden and tumour necrosis factor (TNF)-a (a marker of inflammation) compared to the sham group.	https://www.sciencedirect.com/ science/article/pii/S2405500X2 0301729?via%3Dihub	fibrillation, inflammatory response	tragus stim. has activated central vagal projections; decrease sympathetic output

8.	low-level tragus stimulation on endothelial function in heart failure with	This might be a helpful way to	https://www.sciencedirect.com/ science/article/abs/pii/S107191 642031589X	Endothelial disease (cells' layer in blood vessels)	~50% Brachial artery diameter increased
9.	vagus nerve stimulation reverses cardiac dysfunction and changes left ventricular gene expression in a rat model of heart failure with preserved	neart failure with preserved	https://academic.oup.com/eurhe artj/article/42/Supplement_1/eh ab724.0736/6393733?login=fals e	fraction	animal model: antifibrotic effect
10	Stimulation Modulates Atrial Alternans and Fibrillation Burden in Patients With Paroxysmal Atrial	The reduction in phase width change (PWA) serves as a valuable biomarker showing the positive effect of Nurosym therapy in patients with paroxysmal AF (62% reduction in AF burden, 6 months treatment, sham vs active group), paving the way for innovative therapy.	https://www.ahajournals.org/doi /10.1161/JAHA.120.020865	Paroxysmal atrial fibrillation	~62% AF burden reduction
111	Microvolt T-Wave Alternans Is Modulated by Acute Low-Level Tragus Stimulation in Patients With Ischemic Cardiomyopathy and Heart Failure		IMC/articles/PIVIC8343129/	Cardiomyopath y Heart Failure	n.s.
12	of Inflammation to Treat Heart Failure With Preserved	Nurosym therapy led to a significant improvement in global longitudinal strain by approximately ~11% to control group, a notable reduction in inflammatory cytokines by about ~23% TNF-α and ~61.3% IL-8 with the enhancement in the quality of life for patients with heart failure with preserved ejection fraction (~35% MLHFQ score).	https://www.ahajournals.org/doi /10.1161/JAHA.121.023582	Heart failure with preserved ejection fraction	~11% GLS, ~23% TNF-α, ~61.3% IL-8 lower, ~35% MLHFQ score increase,

13	Neuromodulation reduces inflammation in HFpEF		https://www.nature.com/articles /s41569-022-00672-2		
14	vagus nerve stimulation, and their effects on		https://www.ncbi.nlm.nih.gov/p	Heart failure with preserved ejection fraction	
15	Effects Of Low Level Tragus Stimulation On Inflammation In Acute Decompensated Heart Failure	Following Nurosym neuromodulation, patients with pre-existing inflammation experienced notable improvements in left ventricular strain and a significant decrease in inflammatory biomarkers, particularly a remarkable ~78% reduction in IL-6.	https://onlinejcf.com/article/S10 71-0164(22)01010-7/fulltavt	Inflammation (heart failure patients)	~78% IL-6 lower, H <sub>2</sub> O <sub>2</sub> reduction
16	Review: Denervation or stimulation? Role of sympatho-vagal imbalance in HFpEF with hypertension		https://www.nature.com/articles /s41440-023-01272-4		
17	Noninvasive Vagus Nerve Stimulation in Postural Tachycardia Syndrome: A randomized clinical trial	After two months of active Nurosym therapy, there was a substantial decrease in orthostatic tachycardia (POTS) compared to the sham group, according to HR analyses that revealed an ~40% improvement during Nurosym neuromodulation. Furthermore, levels of anti-autonomic autoantibodies (α1-AR and β1-AR) were significantly lower (p<0.05) in the active group, indicating a potentially beneficial effect on autonomic function. Importantly, no adverse effects related to the device were observed.	https://pubmed.ncbi.nlm.nih.gov /37999672/	POTS	~40% decrease in postural tachycardia; reduction in antiadrenergic antoantibodies and inflammatory cytokines, improvement in HRV

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1:	Afterload reduction after non-invasive vagus nerve stimulation in acute heart failure	Nurosym impact on central blood pressure (BP) in acute heart failure (AHF) patients. Patients receiving active stimulation showed significant reductions in central aortic systolic pressure (CASP), brachial systolic BP (SBP), diastolic BP (DBP), and heart rate (HR), while those in the sham group experienced increases. Nurosym acutely reduces afterload in elderly AHF patients, therefore preventing heart failure decompensation.	https://www.frontiersin.org/articl es/10.3389/fnhum.2023.114944 9/full		Reduction on central blood pressure and parameters SBP, CASP, DBP, and HR
1'.	Electrical Vagus Nerve Stimulation	Effects of Nurosym on electrophysiological parameters and inflammatory markers in patients with AF. Pacing-induced AF, changes in atrial effective refractory period (AERP), and inflammatory cytokines (TNF-α and CRP) were assessed. Nurosym significantly shortened the duration of stimulation-induced AF and prolonged the AF cycle length, and also inhibited systemic TNF-α and CRP levels, while no significant changes were observed in the control group. Two patients suffered minor burns.	https://www.sciencedirect.com/ science/article/pii/S0735109714 075810?via%3Dihub	Atrial Fibrillation	Pacing-induced AF duration decreased; suppressed systemic levels of tumour necrosis factor-alpha (TNF-α) and C-reactive protein (CRP)
2.	effects of low-level vagus nerve stimulation on atrial	Nurosym in the prevention and treatment of atrial fibrillation (AF). Study of atrial electrophysiology by intraoperative epicardial mapping during both acute and chronic use of Nurosym. In acute and chronic Nurosym, a shift of the exit point of the sinoatrial node towards a more cranial direction was observed in 50% of patients. Unipolar potential voltage increases significantly during both acute and chronic Nurosym, which produces an antiarrhythmic effect.		Atrial Fibrillation	50% reduction in arrhythmias; Epicardial mapping showed increased parasympathetic activity

21	Low level transcutaneous vagus nerve stimulation acutely ameliorates diastolic function in humans	A prospective, randomized, double-blind, crossover study examined the acute effects of low-level Nurosym on diastolic dysfunction and autonomic tone in patients with normal left ventricular ejection fraction and evidence of diastolic dysfunction. Echocardiography and a 5-minute ECG assessment were performed before and after the stimulation sessions.  Results showed that Nurosym led to a significant reduction in global longitudinal strain, indicating improvement in diastolic dysfunction, along with favourable modulation of sympathovagal balance, as indicated by a reduced LF/HF ratio.	https://academic.oup.com/eurhe artj/article/38/suppl_1/ehx502.P 2437/4089157	LF/HF at 1 hour decreased; GLS decrease; diastolic dysfunction treatment
22	Autonomic Afferent Dysregulation in Atrial Fibrillation	The aim of this study was to evaluate the role of cardiac afferent reflexes in atrial fibrillation (AF) in terms of efferent autonomic tone in atrial remodelling. Study measurements included beat-to-beat mean arterial pressure (MAP) and heart rate (HR). LBNP-induced reflex vasoconstriction was assessed using forearm blood flow obtained from venous occlusion plethysmography. Reversibility was assessed by repeated LBNP after Nurosym stimulation.  Studies have shown that cardiac afferent reflexes are abnormal in patients with AF.	https://pubmed.ncbi.nlm.nih.gov /35210071/	Improved local blood flow and vascular function (blood vessel tone)

23	Blood Pressure Variability After Non-invasive Low-level Tragus Stimulation in Acute Heart Failure	_	Blood Pressure Variability After Non-invasive Low-level Tragus Stimulation in Acute Heart Failure - PubMed	Hypertension	VAS score improvement; BPV improvement SBP improvement
24	Transcutaneous vagus nerve stimulation restores the cardiac phenotype in heart failure with preserved ejection fraction by modulating the immune cell profile		https://www.ahajournals.org/doi /10.1161/circ.146.suppl_1.1364 5	Heart Failure (mice model)	immune responses -> CAP -> α7nAchR on macrophages; improved cardiac phenotype (mice)

2:	Impact of optimized transcutaneous auricular vagus nerve stimulation on cardiac autonomic profile in healthy subjects and heart failure patients	The stimulation protocol that yielded the greatest autonomic modulation was 25 Hz applied to the left tragus. In HF patients, the autonomic response was negligible - likely due to reduced vagal sensitivity and beta-blocker use. Left AVNT at 25 Hz: HR reduction of $-1.1 \pm 1.2$ bpm (p < 0.01); RMSSD increase of $+2.55 \pm 4.55$ ms (p < 0.01); HF power increase of $+42.1 \pm 78.4$ ms² (p < 0.05); RR interval increase of $+15 \pm 19$ ms (p < 0.001); 10 Hz, right tragus, and sham stimulation showed minimal or no significant effects.	https://iopscience.iop.org/article /10.1088/1361-6579/ad5ef6	Electrophysiolo gy	One stimulation effect; Left AVNT HR reduction; RMSSD increase; HR power increase
20	Noninvasive low-level tragus stimulation attenuates inflammation and oxidative stress in acute heart failure	Acute decompensated heart failure (ADHF) is characterised by inflammation, oxidative stress, and increased sympathetic nervous system activity. Study of the effect of Nurosym on inflammation and oxidative stress in patients with ADHF. Compared with sham stimulation, neuromodulation led to a significant reduction in circulating serum interleukin-6 levels (-78% vs9%; p = 0.012). Similarly, neuromodulation resulted in reduced oxidative stress on endothelial cells in the neuromodulation group (p = 0.003) compared to sham stimulation (p = 0.094). There were no significant differences in heart rate, blood pressure, or kidney function between the two groups.	https://link.springer.com/article/ 10.1007/s10286-023-00997-z	Heart Failure Chronic Inflammation	~24% ROS (oxidative stress) ~87% IL-6 reduction (compared to placebo)
2.	Stimulation Attenuates Blood Pressure in Young Individuals With Hypertension: Results From a Small-Scale Single-Blind Controlled		https://www.ahajournals.org/doi /10.1161/JAHA.123.032269	Hypertension	Reduced systolic blood pressure (SBP) by 9.7% Diastolic blood pressure (DBP) by 10.2% over three months in young adults with Grade 1 higher blood pressure

28	Acute right-sided AVNT improves cardio-vagal baroreflex gain in patients with chronic heart failure	AVNT shown a significant increase in baroreflex (Mean difference = 1.9 ± 1.6 ms/mmHg from baseline); HRV no significant changes towards vagal predominance. AVNT as a noninvasive alternative to improve sympathovagal balance. Right-sided is more effective than left-sided in improving cardio-vagal baroreflex gain in CHF patients without affecting heart rate, blood pressure, or HRV parameters significantly	https://link.springer.com/article/ 10.1007/s10286-024-01074-9	Eailura	33% relative improvement in baroreflex gain
29	TraNscutaneOus Electrical VAgus Nerve Stimulation to Suppress Premature Ventricular Contractions: a cross-over, randomized clinical trial (NOVA-PVC)		https://www.sciencedirect.com/ science/article/abs/pii/S240550 0X25002646		23% PVC burden reduction

	Cognition Nurosym Research	Highlights		Condition	Improvement [%]
1	The effect of transcutaneous auricular vagus nerve stimulation on reading comprehension	Poster: A positive effect on memory-based aspects of reading comprehension was observed using Nurosym neuromodulation. This suggests that Nurosym Therapy may improve memory and reading comprehension skills.	https://www.sciencedirect.com/ science/article/abs/pii/S01664 32822004326	Reading comprehension	

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2	Auricular Vagus Nerve Stimulation on Reading Comprehension	The study revealed a trend in the main effect of neuromodulation, suggesting that the Nurosym device may have a positive influence on reading comprehension and remove the existing deficit between readers with dyslexia and typically developing individuals.	https://repository.tcu.edu/handl e/116099117/40265	Reading comprehension	n.s
3.	auricular vagus nerve stimulation enhances learning of novel letter-sound	Participants who received Nurosym neuromodulation showed a significant improvement in their performance on the automaticity task compared to the control group, completing it in less time (Nurosym group: 33.14 seconds vs. control group: 46.27 seconds). Additionally, the Nurosym group achieved a higher accuracy rate of ~16% on decoding tasks, compared to the control group.		Cognition improvement	~29% less time on automaticity tasks ~16% accuracy on decoding tasks
4.		The results indicate that there was no significant benefit of 5 Hz Nurosym Neuromodulation on novel language learning.	https://repository.tcu.edu/handl e/116099117/44322		no benefit of 5 Hz AVNT on novel language learning (Palau)
5.		Participants who received active neuromodulation showed a significant ~26% improvement in their performance on all test questions, with a remarkable ~32% boost specifically in answering memory-based questions.		improvement (memory)	~26% better performance ~32% increase memory-based question
6.	from a randomised trial	In the group with an active neuromodulation program, there was a ~13% improvement in global sleep scores, and participants exposed to late stimulation also showed ~15% improvement in answering memory-based questions.	https://www.autonomicneurosci ence.com/article/S1566-0702(2 2)00031-5/fulltext	Insomnia, memory	~13% global sleep score improvement ~15% memory-based questions

7	The effect of long-term non-invasive vagus nerve stimulation on cognitive performance: results from a randomized placebo controlled trial	recall but without satistically significant difference.	https://www.brainstimjrnl.com/a rticle/S1935-861X(23)01728-X/f ulltext	memory recall	significant improvement in recall (early and late tVNS phase)
8	The effect of non-invasive vagus nerve stimulation on memory recall in reading	In a pilot study, improvements in memory recall of previously read material were observed, representing higher levels of reading skills in participants who received active Nurosym neuromodulation.	https://linkinghub.elsevier.com/r etrieve/pii/S0166432822004326	memory recall	
9	The effects of transcutaneous auricular vagus nerve stimulation on language retention in college-aged students	The Nurosym effect in memory-based reading comprehension and associative memory, and examining the effects on long-term language retention. During this training, participants received sham stimulation, 5 Hz stimulation, or 25 Hz stimulation towards the posterior aspect of the left tragus. There was no significant difference in performance between the sham and 5 Hz taVNS groups. Those receiving 25 Hz stimulation significantly improved retention of learned words after one week.	https://repository.tcu.edu/bitstre am/handle/116099117/59369/ CrupperJordan-Honors_Projec t.pdf?sequence=1	memory recall	improved verbal and visual working memory

	Cancer Nurosym Research	Highlights	Link	
1	Effects of non-invasive vagal nerve stimulation on radiation-induced inflammation and cancer prognosis	The preliminary findings of the study suggest that vagal neuromodulation has the potential to improve the body's ability to fight tumours by reducing the presence of Myeloid-Derived Suppressor Cells (MDSC), which can support tumour growth. Vagal neuromodulation encourages the growth of beneficial cells like conventional dendritic cells, natural killer cells, and CD8+ T cells, while decreasing harmful MDSC populations.	https://researchportal.vub.be/en /publications/effects-of-non-inv asive-vagal-nerve-stimulation-on -radiation-indu-2	

2	Vagal Nerve Stimulation Alone or in Combination With Radiotherapy Stimulates Lung Tumor Infiltrating Lymphocytes But	mouse models and in a small	nttps://www.frontiersin.org/artic les/10.3389/fimmu.2021.77255 5/full	Non-small cell	~25% NK cells i(NSCLC patients, non-significant )
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	Post-Viral Autonomic Dysfunction Nurosym Research	Highlights			Improvement [%]
1	Transcutaneous auricular vagus nerve stimulation (tVNS) can reverse the manifestations of the Long-COVID syndrome: a pilot study	Fatigue (~48% on Pitchot Fatigue Scale) and improved	https://emrespublisher.com/ope n-access-pdf/transcutaneous-au ricular-vagus-nerve-stimulation-c an-reverse-the-manifestations-of -the-long-covid-syndrome-a-pilot- study-100011.pdf	Chronic fatigue, Depression, inflammatory response	~48% on Pitchot Fatigue Scale ~45% on Beck depression score ~185% IL-1ra improvement (compared to median baseline vs. median 3rd visit)
2	Transcutaneous vagus nerve stimulation in the treatment of long covid-chronic fatigue syndrome	In a study of patients experiencing chronic fatigue symptoms after Covid-19 infection, approximately 40% of the participants showed positive responses to treatment involving Nurosym neuromodulation, as evidenced by improvements in fatigue, brain fog, and widespread pain.	https://www.medrxiv.org/conten t/10.1101/2022.11.08.2228180 7v1	Fatigue, Brain Fog	~60% patients has shown improvement; 57% improvement VAS rate

3	Transcutaneous vagus nerve stimulation improves Long COVID symptoms in a female cohort: a pilot study	Improvements in cognitive	https://www.frontiersin.org/jour nals/neurology/articles/10.3389 /fneur.2024.1393371/full	Long-Covid	~35% Anxious States improvement ~19% PROMIS sleep disturbances improvement ~19% improvement in Attention Deficiency Symptom
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and entransa 1 nerve a coho with d	bility, safety fficacy of auricular vagus stimulation in ort of patients disorders of ciousness	iconeciolienace aenacialivin	https://linkinghub.elsevier.com/ retrieve/pii/S1935861X1930476 0	Coma	Improvement in CRS-R (Coma) (Parameters: EKG, blood pressure, heart rate)

	Optimization Nurosym Studies	Highlights	Link	Condition	Improvement [%]
1	The effect of transcutaneous auricular vagus nerve stimulation on HRV in healthy young people	The Nurosym neuromodulation group was associated with significantly higher measures of cardiac vagal activity (~61% HF, ~18% RMSSD, ~25% pRR50 and ~14% SDRR parameters improvement, compared to control group), and thus activation of the parasympathetic system responsible for regeneration and rest.	https://journals.plos.org/ploson e/article?id=10.1371/journal.po ne.0263833	Parasympathetic activity	~61% HF, ~18% RMSSD, ~25% pRR50, ~14% SDRR improvement

2	Circadian stage-dependent and stimulation duration effects of transcutaneous auricular vagus nerve stimulation on heart rate variability		https://journals.plos.org/ploson e/article?id=10.1371/journal.po ne.0277090	Parasympathetic	~39% HF, ~16% RMSSD improvement	
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	Sensory Nurosym Research	Highlights		Condition	Improvement [%]
1	controlled study	A neuromodulation study of Nurosym with chronic tinnitus did not result in significant improvement in tinnitus measures compared to controls. The study showed a significant increase in theta band activity in quantitative electroencephalography (qEEG) in the study group compared to the control group, which proves the influence of neuromodulation on brain activity.	https://www.tandfonline.com/d oi/full/10.1080/14992027.2023 .2177894?scroll=top&needAcce ss=true&role=tab	Chronic tinnitus	n.s.
2	reduces eympathetic	Nurosym for autonomic nervous system (ANS) imbalance in patients with tinnitus-induced stress. The results showed that approximately three-quarters of 97 patients had sympathetic predominance or reduced parasympathetic activity before treatment. Nurosym caused a significant increase in R-R interval variability in 75% of patients and a decrease in HRV age in 70% of patients (15 - 60 min). 90% of patients either had increased R-R interval variability or decreased HRV age, indicating a shift in ANS function from a sympathetic to a parasympathetic predominance.	https://www.tandfonline.com/d oi/full/10.1080/00016489.2016 .1269197	Chronic tinnitus	90% of patient had increased R-R interval variability or decreased HRV age; stress index reduction (graphical representation )

3	Transcutaneous vagus nerve stimulation via tragus or cymba conchae: Are its psychophysiological effects dependent on the stimulation area?	differences in nost-arror	https://pubmed.ncbi.nlm.nih.go	Targeted stimulation	No difference between concha cymbae and tragus stimulation and physiological effect
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	Pain Nurosym Research	Highlights		
1	Use of tVNS as a new therapeutic option in a cohort of patients with Fibromyalgia Syndrome: Pilot Study	Dysfunctions in the Autonomic Nervous System (ANS) are implicated in fibromyalgia (FMS). Nurosym improved disease activity and sleep quality in FMS patients. Within 2 weeks of tVNS, reductions were seen in Wide Pain Index (WPI) and Fibromyalgia Impact Questionnaire Total (FIQR). After 4 weeks, FIQR scores, physical function, general health, symptoms, Symptom Severity Score (SSS), and WPI significantly decreased. Sleep quality improved according to PSQI. However, perceived diffuse pain, measured by visual analogue scale (VAS), remained unchanged after 2 or 4 weeks of treatment. Future studies should explore disease biomarkers like brain-derived neurotrophic factor (BDNF).	Fibromyalgia	31% PSQI; 27% FIQ; 22% SSS; 36% WPI n.s. VAS