

Voice Treatment for Parkinson's Disease (LSVT LOUD): Research Lab to Global Implementation

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****ASHA Foundation YI**

Disclosure

- Lorraine Ramig, PhD, CCC-SLP
- Professor, Senior Scientist, Adjunct Professor, Co-Founder
- Relevant financial relationships:
- Receiving honorarium and travel/expense reimbursement from the ASHA Foundation.
- Receives lecture honorarium and
- has ownership interest in LSVT Global, Inc.
- Relevant non-financial relationships:
- Preference for LSVT LOUD as a treatment technique and equipment which will be discussed

PLAN

- The Origin and Research Pathway
- The Implementation Pathway

“In the beginning...”

Challenges/Opportunities

Progress

Ingredients for Success

- Implementation today
 - Goals and Plans
 - Current Opportunities
- Perspectives

To improve human health,
scientific discoveries must
be translated into practical
applications.

-NIH

Parkinson disease (PD) is a progressive, neurodegenerative disorder with no known cure, which affects nearly 6 million individuals globally (e.g., de Lau & Breteler et al., 2006).

Over 89% of these individuals suffer from voice and speech disorders.

Reduced vocal loudness, hoarse, monotone voice and imprecise articulation (e.g., Logemann et al., 1978; Sapir et al., 2001) are among the classic characteristics.

These voice and speech disorders contribute to *lifelong frustration, embarrassment and social isolation* (e.g., Miller et al, 2006).

Classic Medical Treatments Alone do not Consistently or Significantly Improve Speech in PD

Pharmacological Tx:

“...no evidence of systematic improvement in dysarthria owing to dopamine replacement therapy.” (e.g., Pinto et al, 2004)

Surgical Tx:

Neurosurgical interventions do not consistently or effectively improve speech in PD (e.g., Freed et al., 1992; Goberman, 2005; Pinto et al., 2004; Rousseaux et al., 2000; Tripoliti et al., 2008; Astromet et al., 2010)

Voice and Speech Disorders in PD have been Historically Unresponsive to Speech Treatment

Despite efforts to improve voice and speech in PD

(e.g., Sarno, 1968; Allan, 1970; Greene, 1980; Weiner and Lang, 1980; Robertson and Thompson, 1984 ; Johnson and Pring, 1990).

1987 no effective voice and speech treatments for PD

‘If I have no voice, I have no life.’

-Natalie, individual with PD

The Origin and Research Pathway

“if we could only hear and understand her”

—family of Lee Silverman



Federal & Foundation Funding —
over 20 years and 8 million dollars

Phase I, II

1987-89: Initial invention; Pilot data
1989-91: Office of Education OE-NIDRR

Phase III

1991-94: OE-NIDRR
1990-95: NIH funded RCT
1995-00: NIH funded EMG
2002-07: NIH funded RCT
2007-12: NIH funded RCT

Phase IV, V

2001-02: Coleman Institute
2002-04: NIH and M J FOX Foundation
2002-04: Coleman Institute
2004-06: NIH R21
2004: Coleman Institute
2006: SBIR
2010: SBIR

Conducted THREE Randomized Clinical Trials (RCT) to Test

Efficacy of Treatments to improve Vocal Loudness

Among the first and most pervasive symptoms in PD (e.g., Logemann et al., 1978)

Respiratory (RESP) vs. voice (LSVT) (N=45)

Pre to post (Ramig et al., 1995) e.s. 1.81-1.20

Pre to 12 months follow-up (Ramig et al., 1996) e.s. .85-.65

Pre to **24** months follow-up (Ramig et al., 2001) e.s. 1.03-1.03

Voice (LSVT) vs. Untreated Control groups (PD, Healthy) (N=44)

Pre to Post to **6** months follow-up (Ramig et al., 2001)

e.s. 1.77-1.45, 1.50-1.03

Voice (LSVT) vs Articulation (ARTIC) vs Untreated Control groups (PD, Healthy) (N=84) CONSORT

Pre to Post to **6** months follow-up (Ramig et al., 2014)

e.s. 1.63-2.03, 1.70-1.61

Average SPL effect size 1.23 (.65-1.81) Primary outcome variable

Developed and established the efficacy of voice treatment for Parkinson Disease

	Pre to Post		Pre to FU	
	Rainbow	Monologue	Rainbow	Monologue
LSVT	2.03	1.63	1.70	1.61
ARTIC	0.59	0.45	0.32	0.33
UnTX	0.29	0.18	0.16	0.27
LSVT	1.81	1.20	0.85, 1.03*	0.65, 1.03*
RESP	0.82	0.67	0.06, 0.16*	-0.64, 0.27*
LSVT	1.77	1.45	1.50	1.03
UnTX	0.08	0.03	0.08	0.03

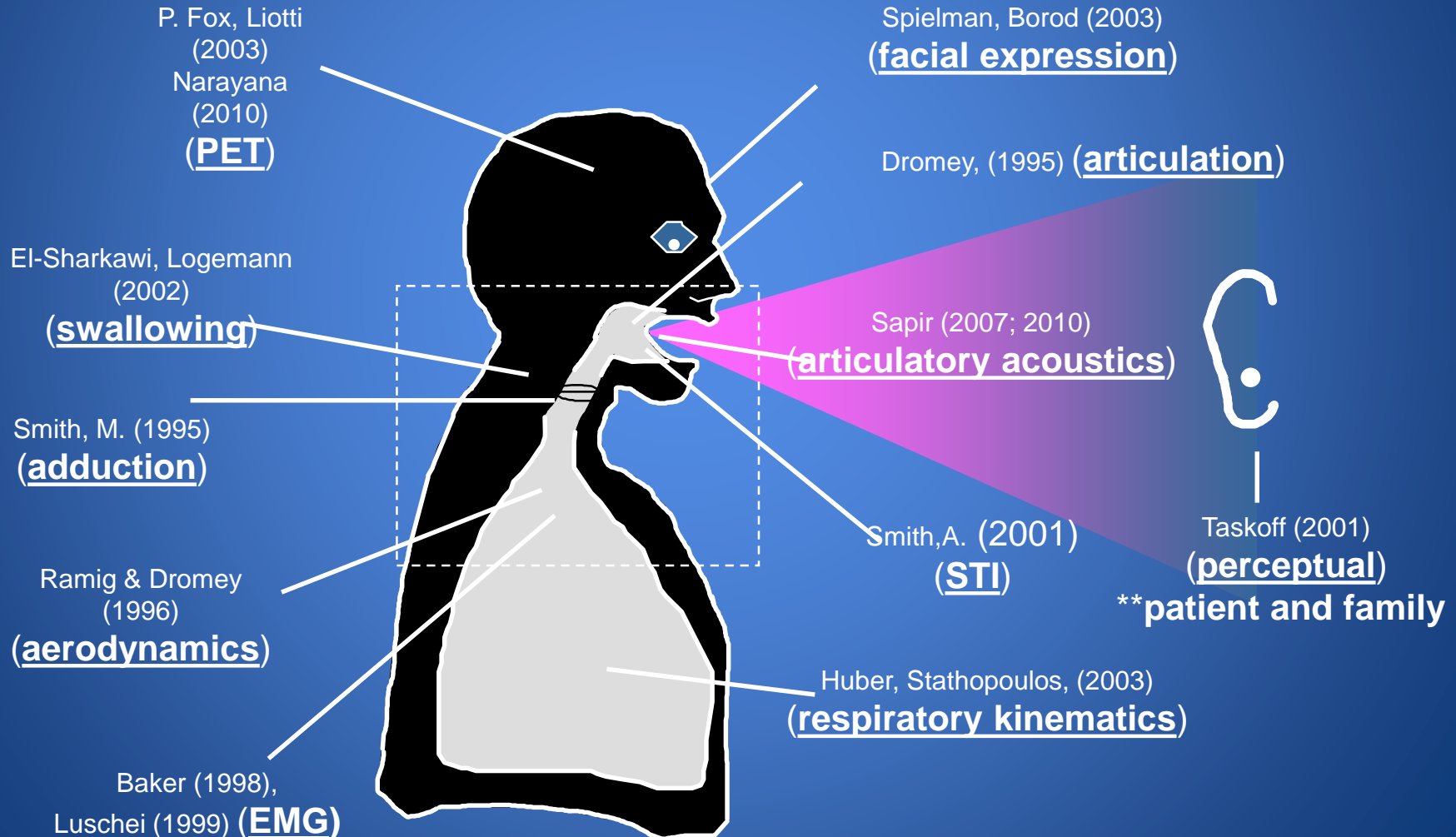
*12, 24M

Since 1987, GOOD PROGRESS establishing efficacy of intensive voice treatment
Level 1 evidence

Advances in Clinical Efficacy

(Ramig et al, 1995; 1996; 2001a; 2001b; Goetz, 2003)

Cross-system effects, Neural changes



The Product: Standardized Research-Based Behavioral Treatment Protocol

Different than previous
speech treatment

Single Target, Mode
(intensive, high effort), Calibration
(in contrast)

Motor, Sensory and
Neuropsychological challenges
in PD

Grounded in principles of
activity dependent neural
plasticity (exercise
science), motor learning,
muscle training

LSVT LOUD

Ramig et al. [87-88, 103]

Intensity: STANDARDIZED

Dosage: 4days/week for 4 weeks (16 sessions in one month)

Repetitions: Minimum 15 repetitions/task

*Effort: push for max patient-perceived effort each day (8 or 9 on scale of 1-10 with 10 being the most)

Simple Focus: LOUD

Increased movement amplitude directed predominately to respiratory/laryngeal systems

Daily Tasks: first half of the treatment session (25 minutes)

Task 1: Maximum sustained movements

15 reps: sustain "ah" in good quality, Loud voice as long as possible

Task 2: Directional movements

15 reps each: say "ah" in Loud good quality voice going high in pitch;

15 reps each: say "ah" in Loud good quality voice going low in pitch

Task 3: Functional movements

Patient self-identifies 10 phrases or sentences he/she says daily in functional living (e.g., "Good morning") 5 reps of the list of 10 phrases. "Read phrases using same effort/loudness as you did during the long 'ah'"

Hierarchy: second half of the treatment session (25 minutes)

-Designed to train rescaled amplitude/effort of movement achieved in CORE exercises from Daily Tasks into in context specific and variable speaking activities

-Incorporate multiple repetitions with a focus on high effort (e.g., list of 20 phrases/sentences repeated 10 times for 200 repetitions)

-Tasks increase complexity across weeks (Words-phrases-sentences-reading-conversation) and can be tailored to each subjects goals and interests (e.g., golf vs. cooking)

-Tasks progress in difficulty by increasing duration (maintain LOUD for longer periods of time) amplitude (loudness - within normal limits), and complexity of tasks (dual processing, background noise and attentional distracters)

Sensory Calibration

Treatment: Focus attention on how it feels and sounds to talk LOUD

Carryover activities: start day one; daily assignments (treatment and non-treatment days); use loud voice in real life situations; - difficulty of the assignment matches the level of the hierarchy where the person is working; make patient accountable and look for comments from patient that people in their daily living have said, such as, "I can hear you better"

Homework practice: start day one: daily assignments to practice at home (Daily tasks and hierarchy exercises); treatment days (one other time for 5-10 minutes); non-treatment days (two times for 10-15 minutes); homework book provided and patient made accountable

Video Example:

59 year old female

2.5 years post-diagnosis

On-meds pre and post video

Pre/post LSVT

(Lee Silverman Voice Treatment)

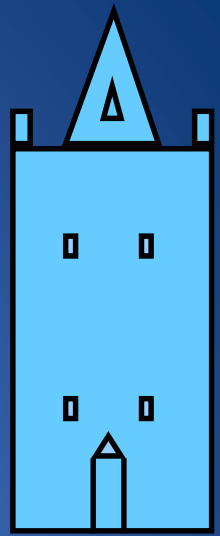
Intensive physical exercise of speech mechanism



Pre-Treatment

“Valley of Death” -NIH

***“Ivory Tower”
Research Lab***



***Real World
“Clinical Trenches”
Patient Populations***

LSVT Implementation Pathway: 1987-1996



The Situation



- 8 Million Parkinson's Disease - 89% degenerative speech problems
- We now have the first evidence that speech treatment can work and last in PD
- 0% Awareness patients, clinicians, neurologists, healthcare professionals, PD
- Conventional wisdom: "changes in the speech treatment room in PD disappear on the way to the parking lot"

The Approach



- Traditional route: wrote a guidebook
- Conducted trainings in response to invitations
- Disseminated to patient and physician groups through lectures

The Opportunities



- Clinicians were implementing only parts of the protocol
- Risk was loss of treatment fidelity "clinician delivery"
- Approached Tech Transfer Office (TTO) to help us protect protocol to insure fidelity
- TTO "didn't want it"
Behavioral treatment???
- If we had been a neuropharmacological treatment...
- What to do?? "Developers make poor disseminators..."

LSVT Implementation Pathway: 1997-2002



The Situation



Trademarked name
internationally: LSVT Foundation

- Required Training and Certification for use of name LSVT

Change Management Required!
No PAR

- Standardized, evidence-based therapy for PD was novel
- Resistance to a standard protocol (one size fits all?)
- Intensive dosage in a “one time a week” world?
- Vocal hyperfunction (loud is vocal abuse!!)

The Approach



- Clinicians adopted the protocol because they saw impact on their patients; evidence-based practice; underlying mechanism

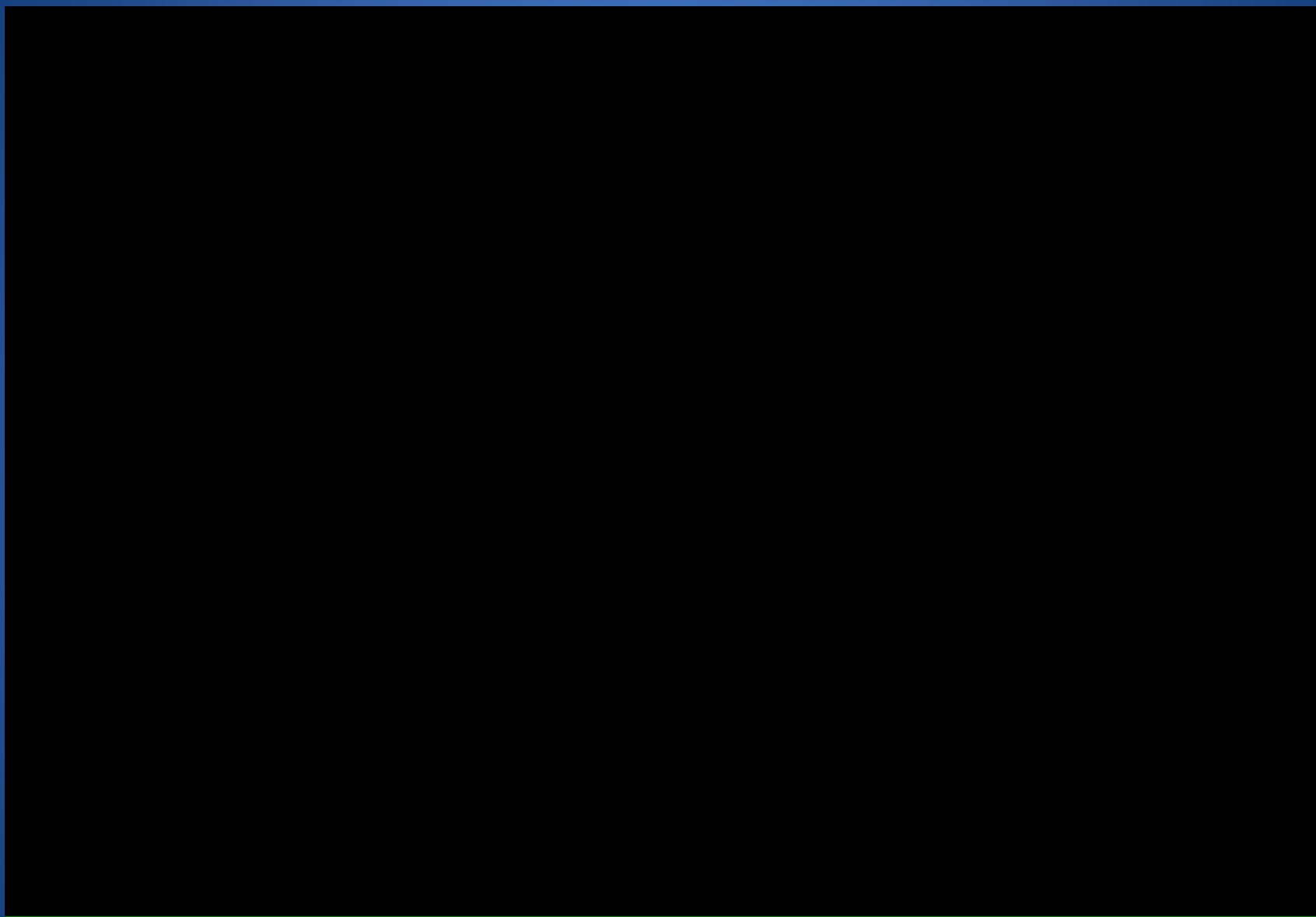
Medical community awareness;
“Rehabilitation revolution”
GAME Changer: Exercise science

Demand for training and treatment increased nationally and internationally

- Application to other disorders (MS, stroke, Cerebral palsy) (e.g., Fox et al., 2012) SS, Small Gr

- Development of LSVT BIG (Physical and Occupational therapy) (e.g., Ebersbach et al., 2010 RCT)





LSVT Implementation Pathway: 1997-2002



The Situation



- LSVT Foundation: Trademarked name internationally
- Required Training and Certification for use of name LSVT

Change Management Required!

- Standardized, evidence-based therapy for PD was novel
- Resistance to a standard protocol (one size fits all?)
- Intensive dosage in a one time a week world?
- Vocal hyperfunction (loud is vocal abuse!!)

The Approach



- Clinicians adopted the protocol because they saw impact on their patients; evidence-based practice
- Medical community awareness; “Rehabilitation revolution”
- Demand for training and treatment increased nationally and internationally; MD and patient lectures
- Application to other disorders (MS, stroke, Cerebral palsy) (e.g., Fox et al., 2011)
- Development of LSVT BIG (Physical and Occupational therapy) (e.g., Ebersbach et al., 2010)

The Opportunity



- Power of RX, Facilitate Growth of Accessibility for patients and clinicians GLOBALLY
- (one clinician can treat 7/month, 6M individuals with PD...) SCALE; # clinicians
- Technology supported training and treatment (e.g., Halpern et al., 2011) LSVT Companion software. FDA cleared.
- Telemedicine (Theodoros et al., 2008)
- Sustainability and growth of entity that will outlast initial founders
- What to do??

LSVT Implementation Pathway: 2003-2009



The Situation



- Transitioned to a Business Model
- Founded for-profit LSVT Global
- Mechanism for software commercialization for LSVT Companion
- Mechanism to develop and assess ONLINE Training and Certification

The Approach



- Back to Tech Transfer Office
- Entrepreneurial Center
- License technology from Universities for LSVT Companion and LSVT BIG
- Submitted product and process patents

The Opportunities



- Under the leadership of TTO:
- CEOs
- Legal teams
- Business plans
- Investment pitches,

BUT.....

No success in the “shark tank”!



What to do?

The Situation



Organic growth business model

Maintain FIDELITY of training and treatments and increase ACCESSIBILITY

Need to do more than initial training of clinicians, support their implementation; Sustainability; research advances

Support patients lifelong practice

The Approach



SBIR Funding

•Technology partners for LSVT Companion and ONLINE training

• Offer clinician support: webinars, forums, online tools, renewal

•Enhance Clinician database for access

•www.lsvtglobal.com

The Opportunities



Harness clinician power globally; effectiveness studies (are the treatments working in the 'real world'?)

**•Grow technology to support lifelong training and treatment (translations)
•LSVT HYBRID, LOUD for LIFE and BIG for LIFE**

•Partner Healthcare companies (Amedysis, Residential) and training institutions (e.g., Columbia, Colorado, Rush, Purdue)

Use research data to support rehabilitation reimbursement

• Continued dissemination with medical, professional and patient communities

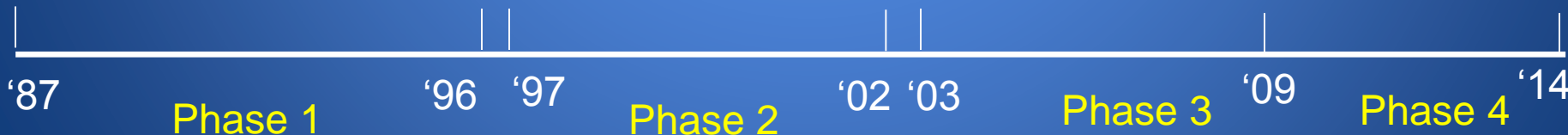
LSVT Global EVOLUTION:

Using a successful business model to impact Fidelity and Accessibility

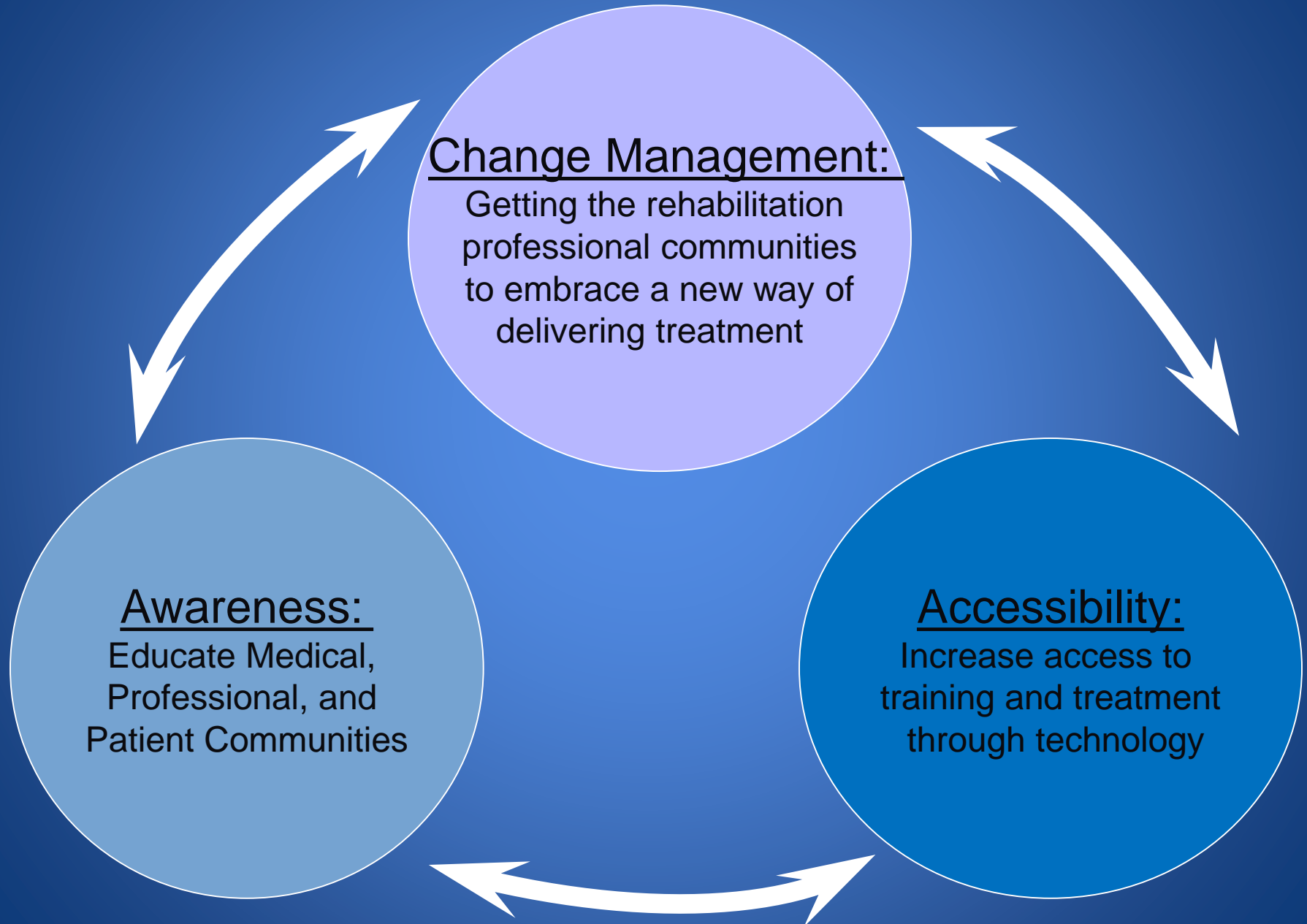
Global Scalability
LSVT Global, Inc.

Information Dissemination and Training
LSVT Foundation, a 501c3 organization

Scientific Research Underlying Biobehavioral Treatments
National Center for Voice and Speech, over 8 million in NIH and other funding



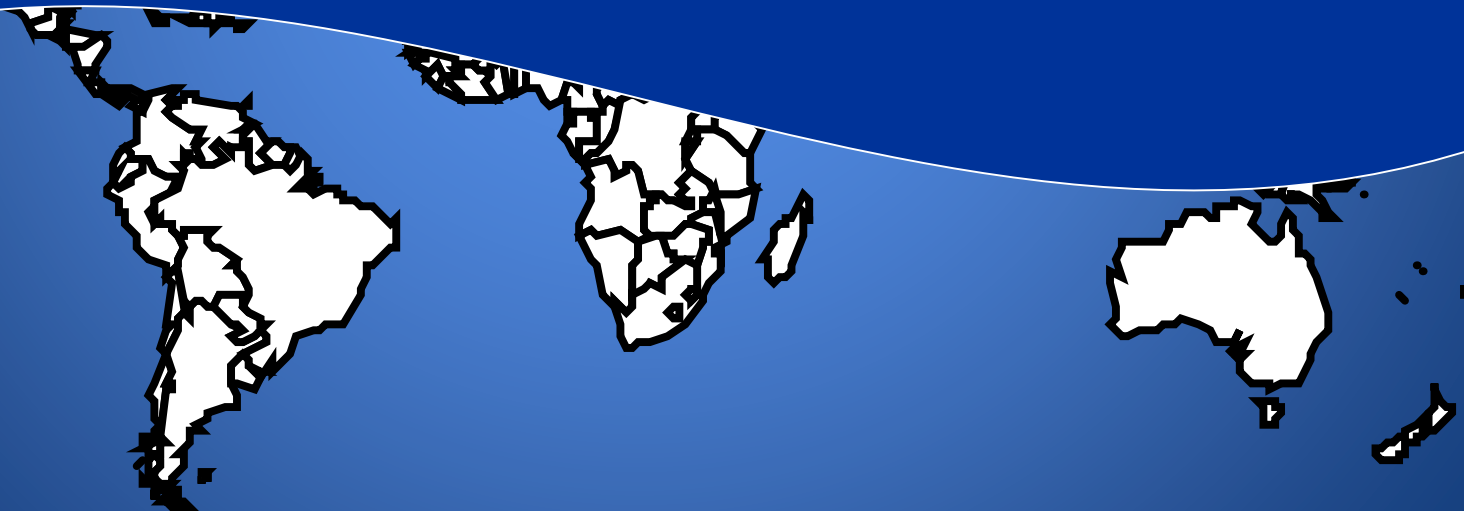
LSVT Global: Impact in relation to our goal



***LSVT® LOUD global standard for Speech Treatment
for PD (Pinto et al., 2004) NICE Great Britain***

Maintain Treatment Fidelity:

*Global Standardized Treatment “LSVT is LSVT is LSVT”
Standardized Training*



Summary of Progress

- Training (0)
- 15,000 trained
- 54 countries
- Online training
- Renewal
- Webinars
- Modules
- Sustain and enhance fidelity “life long”
- Treatment (0)
- Estimate 150,000 treated globally
- LSVT Companion FDA (German)
- LSVT Telepractice (module)
- LSVT-Hybrid
- LOUD BIG for LIFE
- Beyond PD

Summary of Progress

- LSVT administered in medical centers, university clinics, private practice, healthcare networks
- Successful Implementation?

Amedysis quote *“So prior to LSVT we had 0% NOMS FCM Voice Progress. At the close of 2013 we had FCM Voice Progress Numbers of 61.54%”.*

OpenlinesNYC Communication quote *“97.42% of PD demonstrated improved SPL (loudness) in speech; 87.53% had lower total VHI (Voice Handicap) scores, and all people reported an improvement in voice. All patients and families reported functional voice improvement, reduced communication breakdowns, and greater QOL in both the patients and their caregivers' lives.”*

Ingredients for using a Business Model for Implementation

Team

- Rock Solid product
- Thick skin
- Identify gate keepers
- Focus on first adopters
- Span research and treatment
- Ever evolve

Essential to have a 'Fundamental Passion' for the vision JOY!

Fueled by seeing the direct impact on patients lives
Clinicians 'EMPOWERED' by delivering efficacious
treatment

Impact on the fields of neurology and rehabilitation
'taking rehabilitation seriously'

Perspectives Gained and Lessons Learned

This world is not for “the faint of heart”

Change management, translating research treatment to real world ‘scope of practice’ requires seeing the ‘world through many eyes’ Open your mind and be persistent!

Recognize your competence
‘trust yourself’

“you need to be surrounded by good advisors
but you also have to trust your instinct”

Chris Hughes Co-Founder Facebook

Perspectives Gained and Lessons Learned

- “Don’t stop believing”
-Journey

Our field is rich with potential to dramatically improve quality of life.

To a patient.....major life impact

“My voice is alive again”

“I can talk to my grandchildren!”

“I feel like my old self”

“LSVT BIG has changed my life...the impact is beyond a miracle!”

“I am confident I can communicate!”







Ramig, L., Sapir, S., Countryman, S., Pawlas, A., O'Brien, C., Hoehn, M., Thompson, L. (2001). Intensive voice treatment (LSVT) for individuals with Parkinson disease: a two year follow-up. *J, Neurology, Neurosurgery and Psychiatry*, 71, 493-498.

Ramig, L., Sapir, S., Fox, C., & Countryman, S. (2001). Changes in vocal intensity following intensive voice treatment (LSVT) in individuals with Parkinson disease: a comparison with untreated patients and normal age-matched controls. *Movement Disorders*, 16, 79-83.

Sapir, S., Ramig, L., Fox, C. (2011). Intensive voice treatment in Parkinson's disease: Lee Silverman Voice Treatment (LSVT). *Expert Reviews in Neurotherapeutics*, 11(6), 815-810.

Liotti, M., Vogel, D., Ramig, L., New, P., Cook, C., Ingham, R., Ingham, J., & Fox, P. (2003). Hypophonia in Parkinson's disease: neural correlation of voice treatment revealed by PET. *Neurology*, 60, 432-440.

Narayana, S., Fox, P., Zhang, W., Franklin, C., Robin, D., Vogel, D., Ramig, L. (2010). Neural correlates of efficacy of voice therapy in Parkinson's disease identified by performance-correlation analysis. Human Brain Mapping, 31, 222-236.

Fox, C., & Boliek, C. (2012). Intensive voice treatment (LSVT LOUD) for children with spastic cerebral palsy and dysarthria. J. Speech Language Hearing Research, 55, 930-945.

Ebersbach, G., Ebersbach, A., Edler, D., Kaufhold, O., Kusch, M., Kupush, A., & Wissel, J. (2010). Comparing exercise in Parkinson's disease-the Berlin LSVT®BIG study. Movement Disorders, 25 (12): 1902-1908.

Halpern, A., Ramig, L., Matos, C., Petska-Cable, J., Spielman, J., Pogoda, J., Gilley, P., Sapir, S., Bennett, J., McFarland, D. (2012). Innovative technology for the assisted delivery of intensive voice treatment (LSVT®LOUD) for Parkinson disease. Am. J. Speech-Language Pathology, 21 (4), 354-367.

Implementation process today:

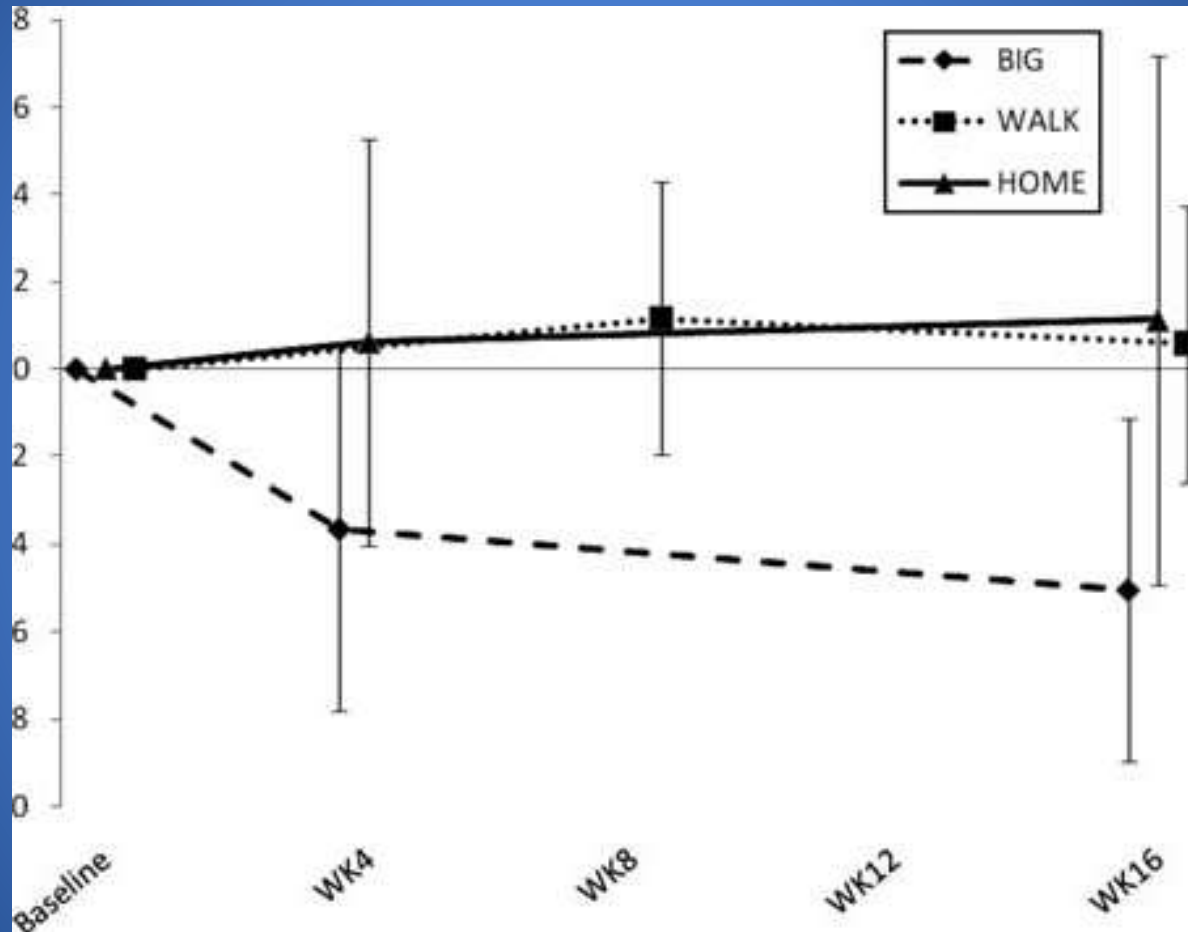
Goals and Plans

- **1) Scale**
- Training and access to treatment
- Partner with organizations, training institutions, medical networks
- --bottom up “grassroots” top down
- Application to other disorders (e.g., MS, stroke, CP, Downs)
273M need lifelong intervention
- LSVT BIG
- **2) Follow-up driven by exercise science**
- LOUD for LIFE, BIG for LIFE

Comparing Exercise in Parkinson's Disease — The Berlin LSVT BIG Study (2010, Movement Disorders)

Georg Ebersbach,^{*} Almut Ebersbach, Daniela Edler, Olaf Kaufhold, Matthias Kusch,
Andreas Kupsch, and Jo"rg Wissel

3



UPDRS motor score (blinded rating), mean change from baseline (vertical bars 5 standard deviations). Change between baseline and follow up at week 16 was superior in BIG (interrupted line) compared to WALK (dotted line) and HOME (solid line), $P < 0.001$. ANCOVA did not disclose significant differences between in intermediate and final assessments.

Our Implementation Pathway

2014 Progress:

- _____ LSVT LOUD Clinicians in _____ countries
LSVT LOUD Training materials in _____ languages

In addition...

- _____ Online LSVT LOUD Training
- _____ Online LSVT LOUD Renewal
- _____ Webinars, listserv, Expert hotline

Is the treatment effective (working in the real world?)

DATA from Amedysis, other?

- _____ patients globally receive LSVT LOUD
- _____ website database of XXX LSVT LOUD clinicians

Add numbers of clinicians who participated

Other stuff: clinicians are taught the published research in PD and outcome data, given dissemination materials

As a part of every workshop patient lecture and practice session XX number of patients globally

MDs refer clinicians globally!!

Quotes from clinicians? Pride about delivering evidence based practice

Value to their community and company

LSVT Global, Inc. IP



Trademarks: words, names, symbols distinguish goods

- LSVT ®
- LSVT COMPANION®
- LSVT BIG™
- LSVT LOUD™
- (US, EU, AU, BR, CA, CH, JP, SG, WO)

Copyrights: works of expression, granted for originality

- LSVT Training and Certification Workshop Binders and Lectures
- Patient Presentation
- LSVT BIG and LSVT LOUD Marketing Brochures
- LSVT LOUD Patient Assessment and Treatment Pack
- LSVT WEBSITE

LSVT Global, Inc. IP



Patent:

- LSVT® HYBRID
- SPL calibration

Licenses:

- University of Arizona, University of Colorado
- All LSVT LOUD and LSVT BIG Certified clinicians globally
- Healthcare Organizations: HealthSouth, Amedysis

Regulatory affairs:

FDA Clearance (510K)

CE EU

AU, NZ, CA

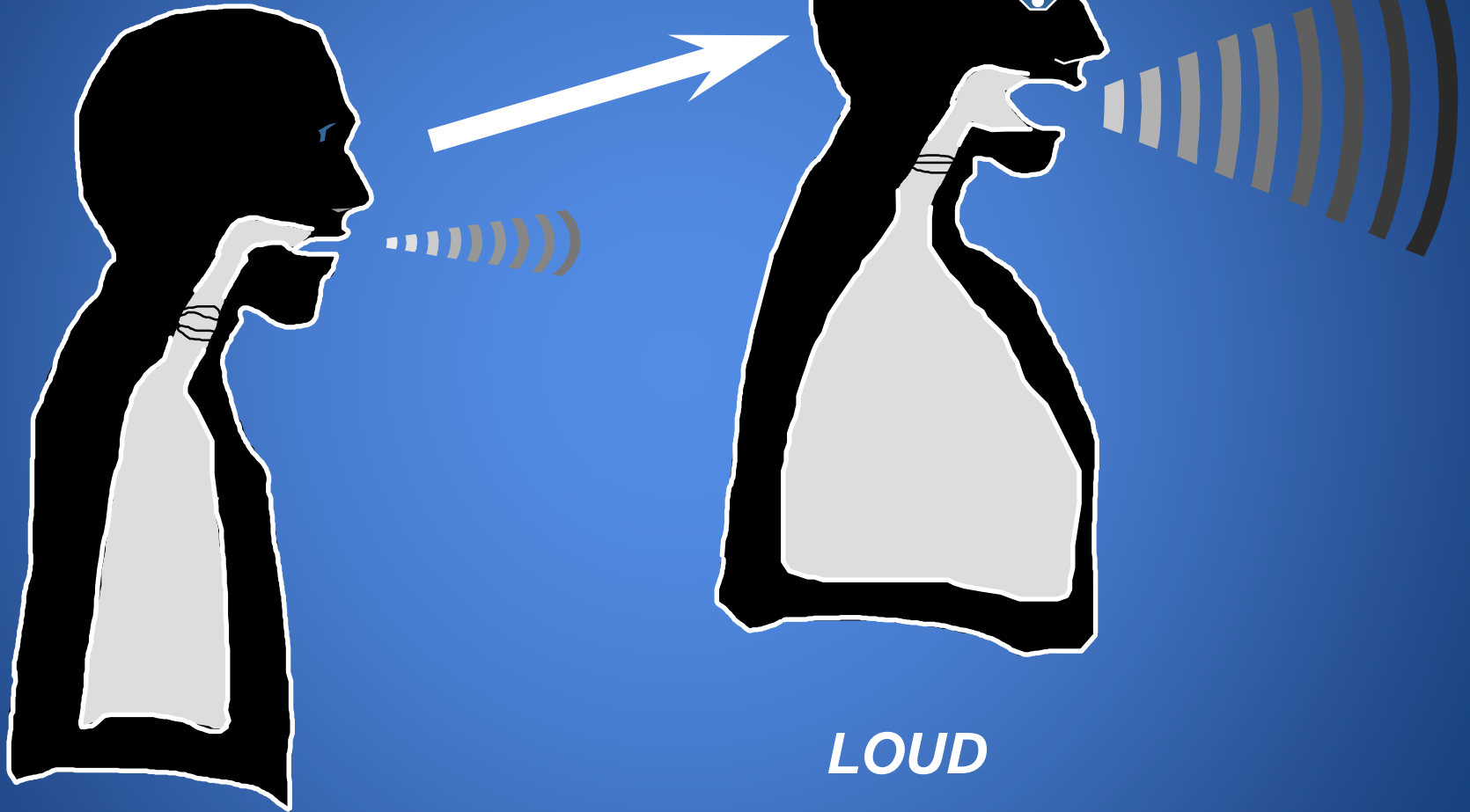
- LSVT Companion Software

LSVT LOUD Applications

- **Parkinson Plus** (Countryman et al., 1994)
- **Post Surgery, Fetal cell** (Countryman, et al., 1993)
- **Stroke** (Fox et al, 2002; Mahler et al., 2009)
- **Multiple Sclerosis** (Sapir et al., 2001)
- **Ataxia** (Sapir et al., 2003)
- **Cerebral palsy** (Fox et al, in press)
- **Down Syndrome** (Robinson et al., 2004; Petska et al, 2006)
- **Aging** (Ramig et al., 2001)

TARGET

*Loud is more than a laryngeal event
– spread of effects*



SOFT

LOUD

HEALTHY LOUDNESS

20+ year journey from invention to scale-up

Phase I, II

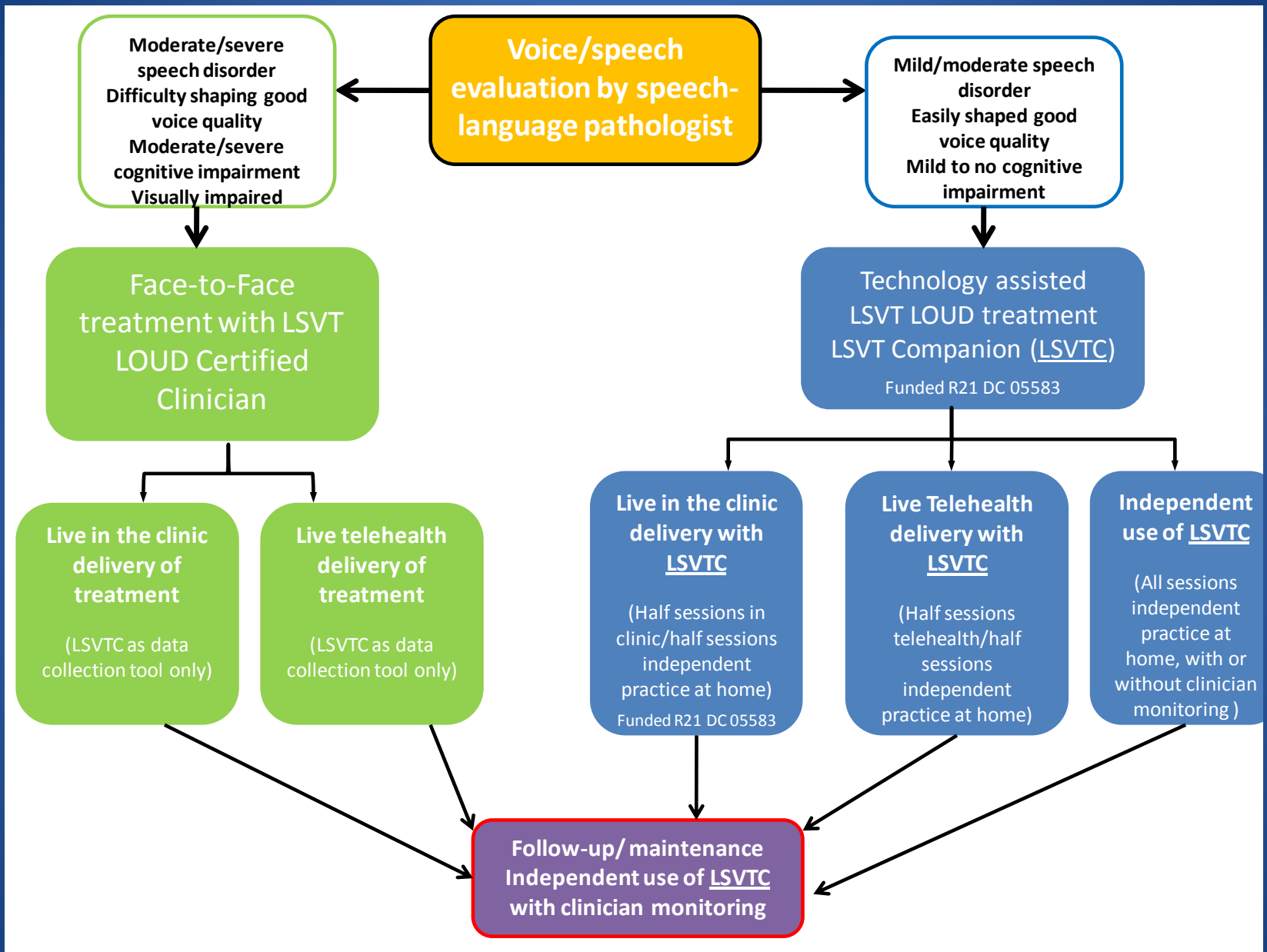
Development

Phase III

Efficacy

Phase IV, V

Clinician Training & Treatment
Accessibility



We have been chipping away for twenty years...



Today LSVT® LOUD has Level 1 evidence for speech treatment for Parkinson disease, is being delivered in over 50 countries and has been endorsed by the National Institute of Clinical Excellence (NICE) in Great Britain.

LSVT Global, Inc. Products

emerged from core LSVT protocol and supported by outcome data

- Training
- In person training LSVT LOUD, LSVT BIG (Physical therapy)
- Online LSVT LOUD training
- Online Renewal
- Online training modules

- Treatment
- LSVT LOUD standard protocol
- LSVT BIG standard protocol
- LSVT Hybrid standard protocol
- LSVT Companion software**
- LSVTeLOUD** telepractice delivery
- LSVT Homework Helper



LSVT eLOUD

Telepractice

(Theodoros et al, 2006)

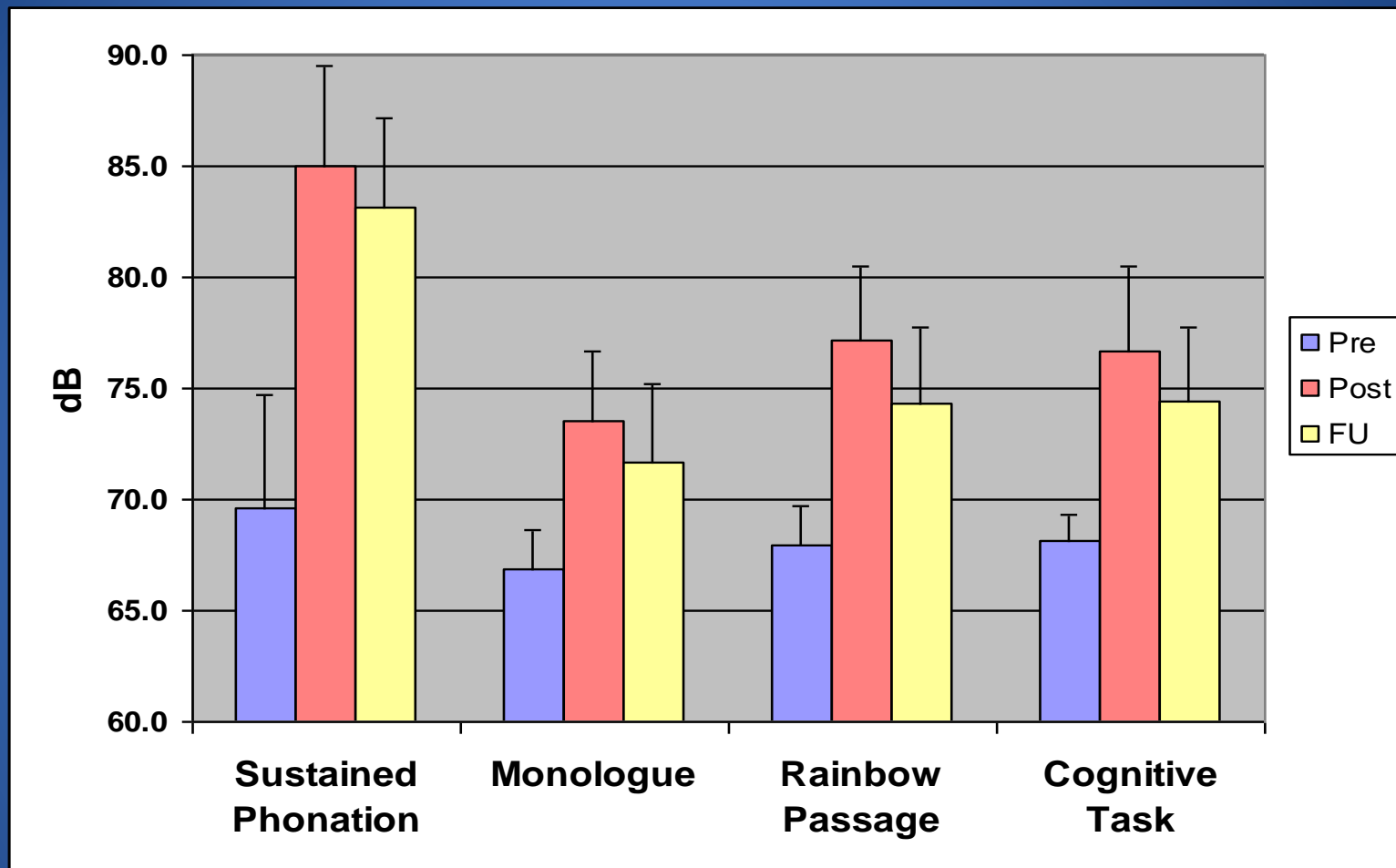


LSVT Companion

Funded by: NIH-NIDCD &
Michael J. Fox Foundation

Perceptive, independent

50% of sessions delivered by LSVTCOMPANION ($p < 0.001$) $n=16$



Changes consistent with those reported in previously published data (*Halpern et al, 2011*)