Conventional, Complementary and Integrative Pain Therapies in a Military Population with chronic Musculoskeletal Pain: Results of a Pragmatic Clinical Trial using SMART Design

Ardith Doorenbos, PhD and Diane Flynn, MD

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Non-Disclosure, Disclaimer, Funding

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- Opinions, interpretations, conclusions, and recommendations are those of the authors and do not necessarily reflect the official policy or position or are endorsed by the Department of the Army, Department of Defense, National Institutes of Health or the US Government. The investigators adhered to the policies for protection of human subjects as prescribed in 45 CFR 46.
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- Approved for public release, Madigan Public Affairs Office, OPSEC and HRPO

Research Team

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  - Larisa Burke, MPH
  - Dahee Wi, PhD

Background

- Physical and occupational therapies are standard rehabilitative care (SRC) for chronic pain
- A growing body of evidence supports complementary and integrative health (CIH) therapies, such as acupuncture, chiropractic, yoga and massage
- Few studies have explored the optimal duration, sequence and combination of SRC and CIH to manage chronic pain

Primary Aim

- Is it better to start with SRC or with CIH in reducing pain impact?

Study Sample

Participants: Active-duty Service Members with chronic pain referred to the Madigan Army Medical Center Interdisciplinary Pain Management Center

Primary outcome measure: Pain Impact Score

- Recommended by NIH Task Force on Research Standards for Chronic Low Back Pain
- Composite measure of PROMIS
  - Pain interference (4-20 range)
  - Reverse Physical function (4-20 range)
  - 7-day average pain intensity (0-10 range)
  - MID = 3

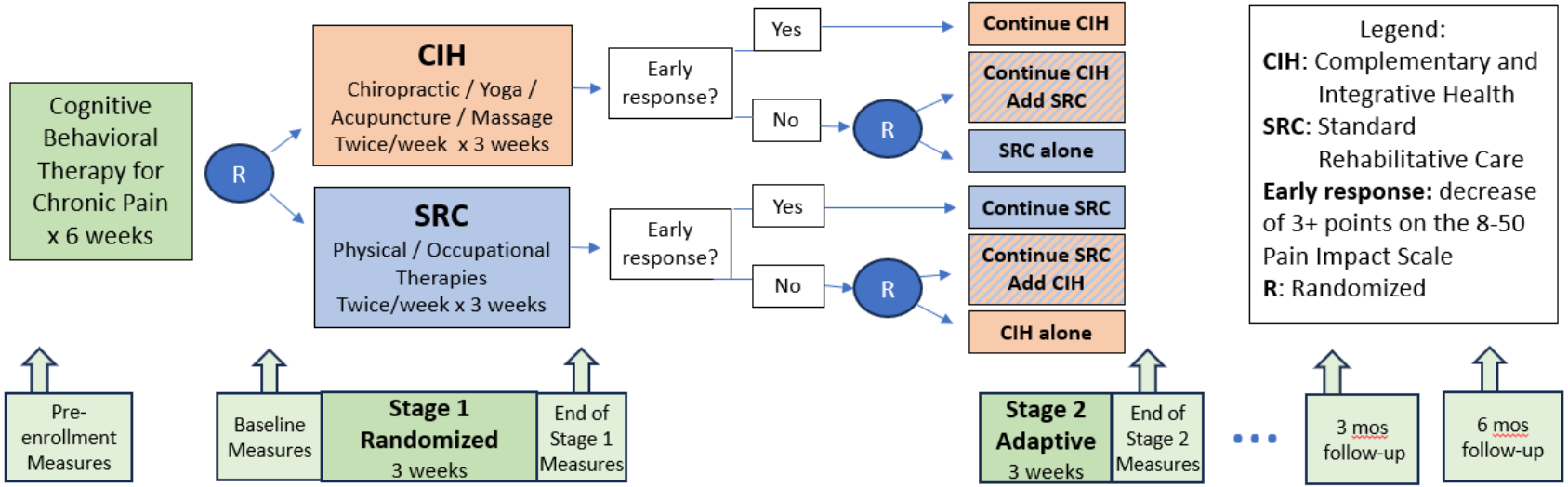
Total range: 8 - 50

Secondary Outcome: Functional Performance

- Treadmill, Lift and Carry (TLC) Battery
  - Treadmill: walk/run on treadmill (METS)
  - Lift:
    - ✓ Lbs lifted from floor to waist
    - ✓ Lbs lifted from waist to shoulder
  - Carry: Lbs carried a distance of 40-ft
- Composite score:
  - 0-100 T-scale
  - MID = 7 points
- Measured by PT/OT professional

Snow T, Burke L, Sanford DC, Mathew A, Steffen AD, Flynn DM, Doorenbos AZ. Use of a treadmill, lift, and carry battery as a composite functional performance test: Analysis of data from a pragmatic randomized controlled trial in a military population participating in a functional restoration program. *Physiotherapy Theory and Practice.* 2024. 40(3): 647-657.

Sequential Multiple Assignment Randomized Trial (SMART) Design



Flynn DM, Eaton LH, Langford DJ, Ieronimakis N, McQuinn H, Burney RO, Holmes SL, & Doorenbos AZ. A SMART design to determine the optimal treatment of chronic pain among military personnel. *Contemporary Clinical Trials.* 2018; 73: 68-74.

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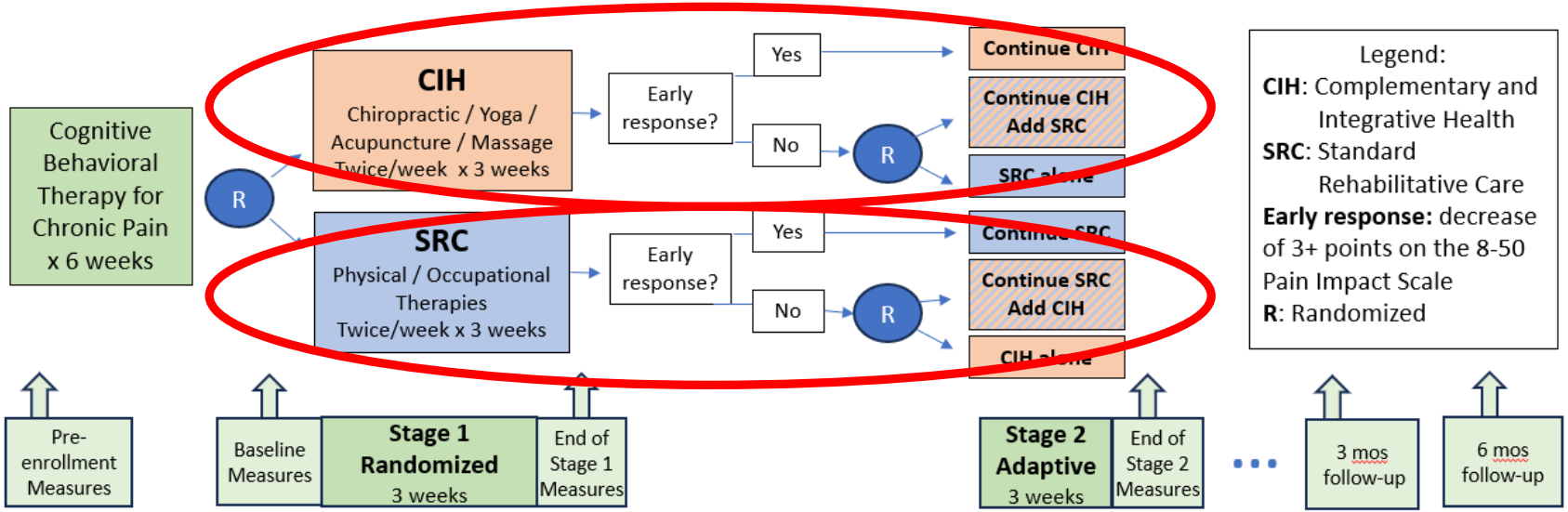

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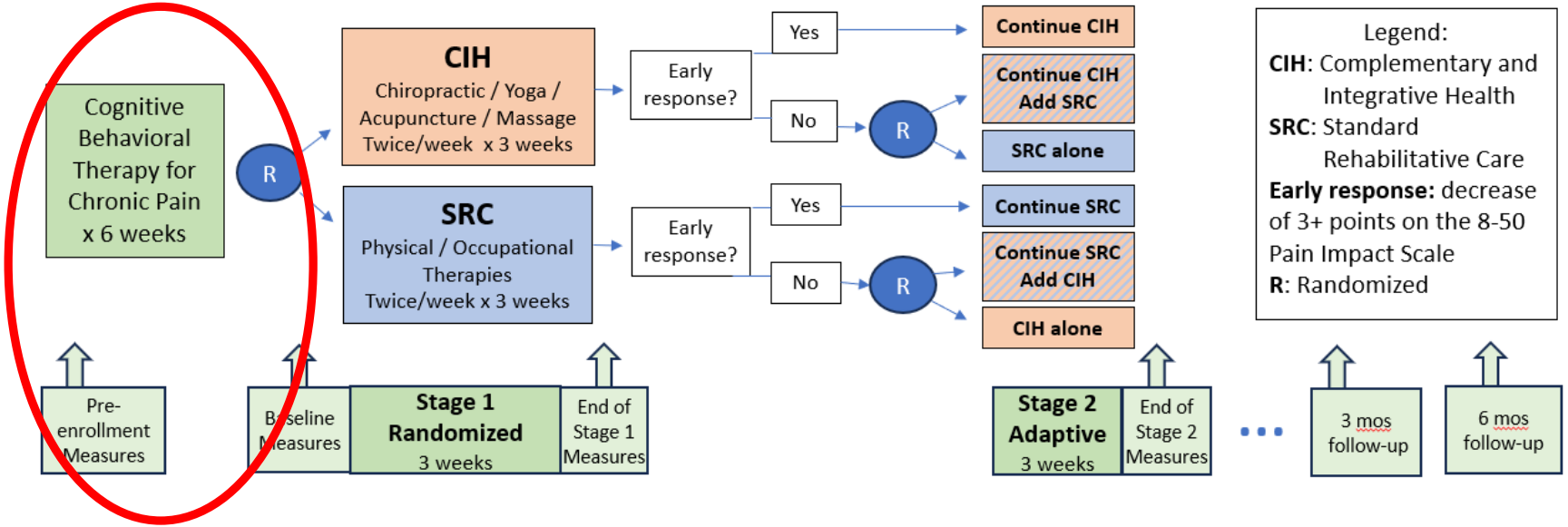

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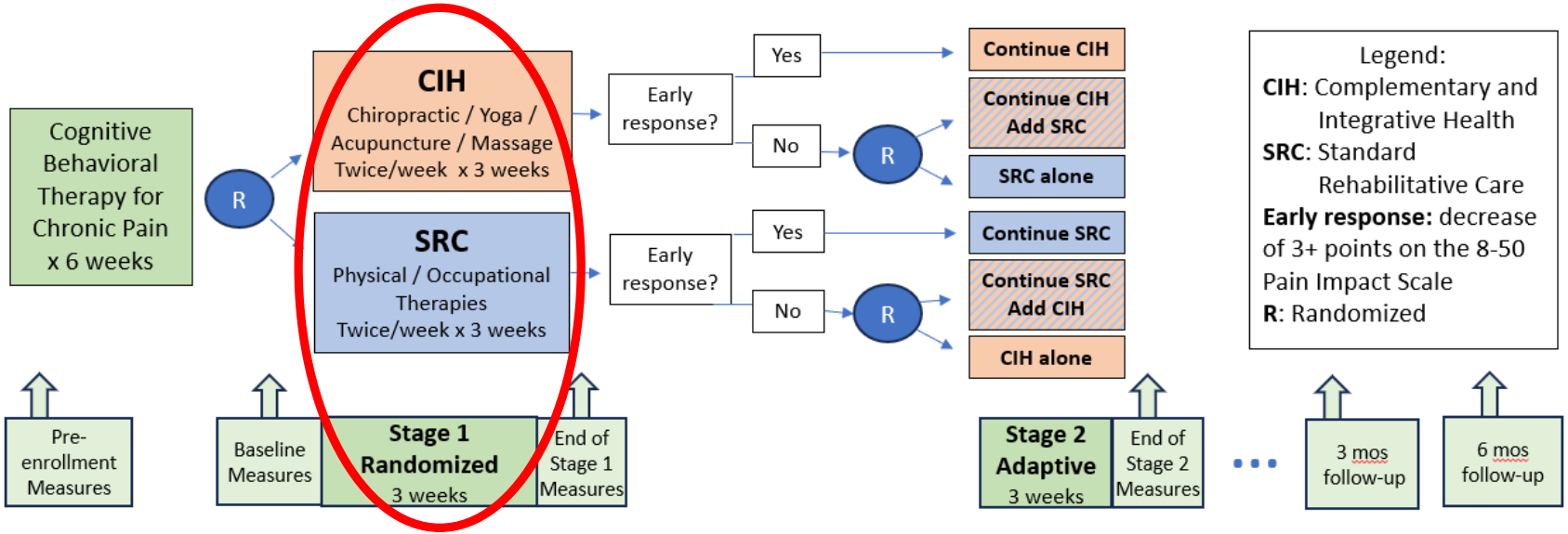

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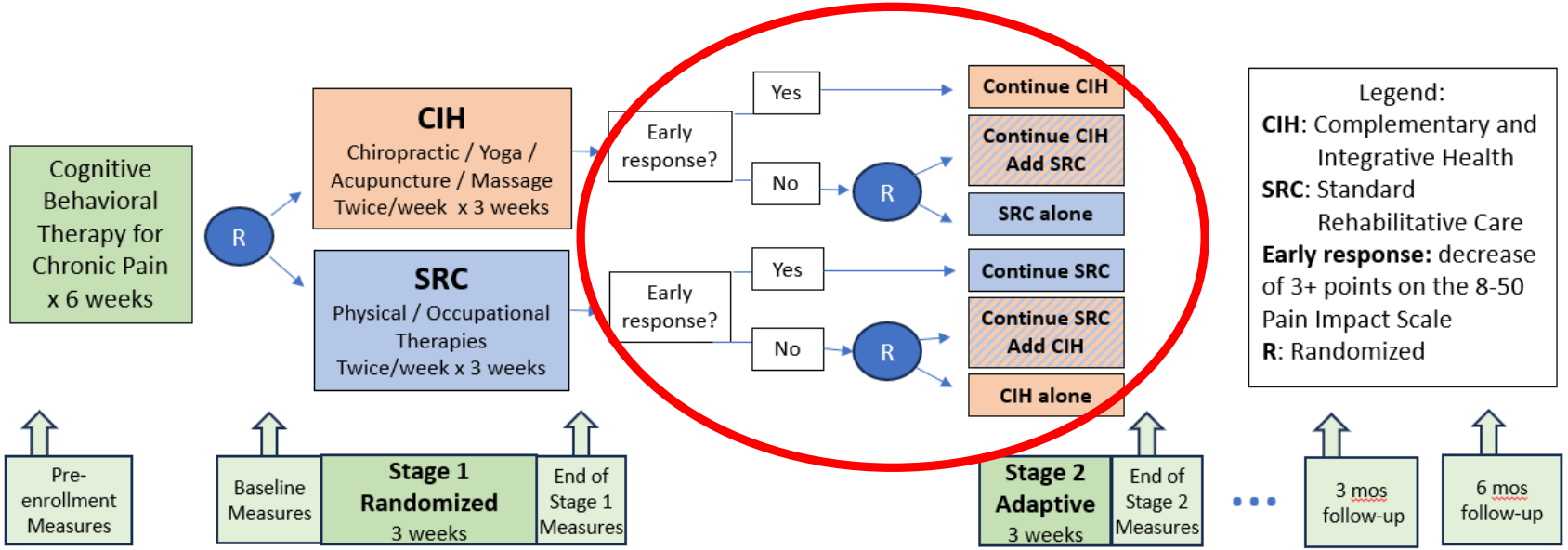

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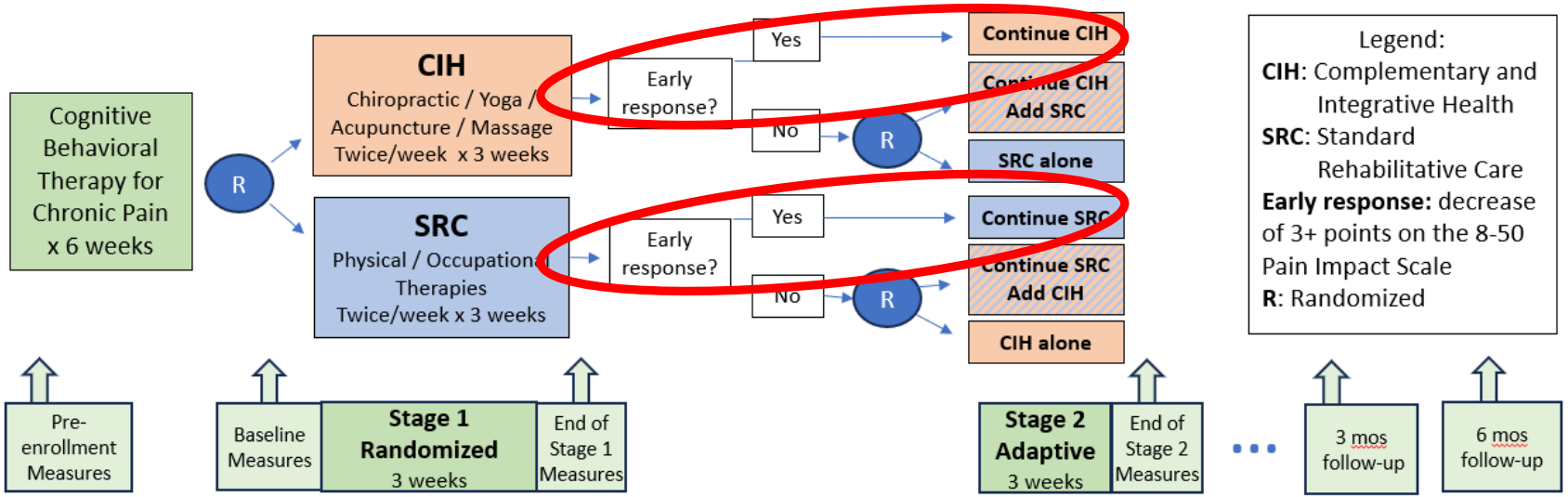

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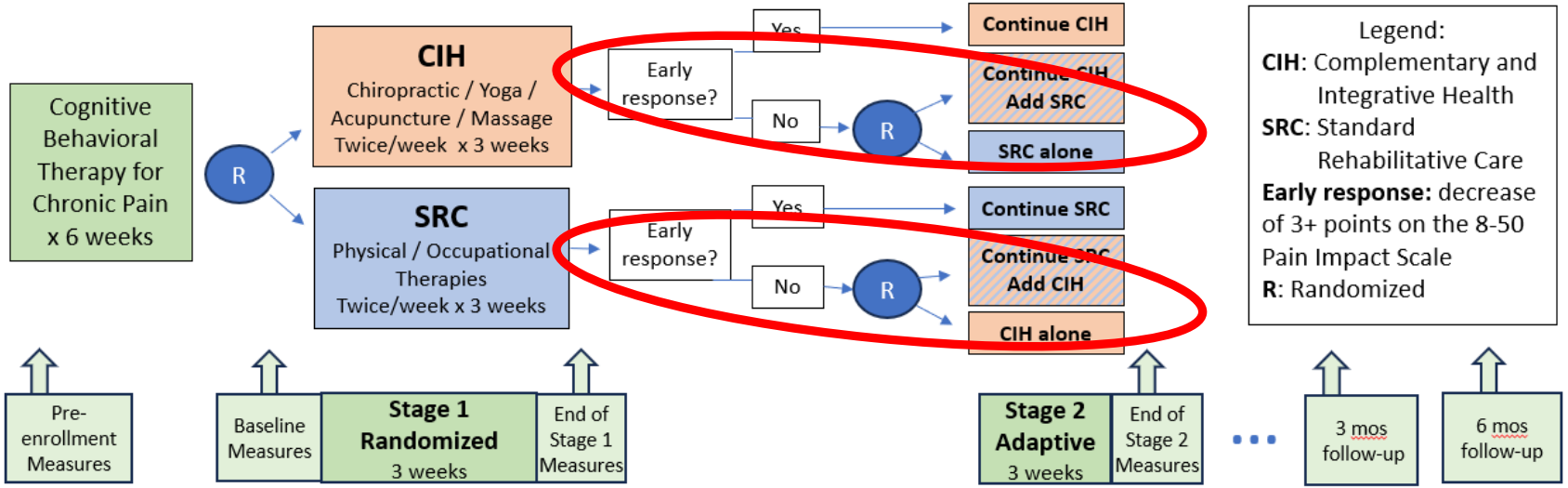

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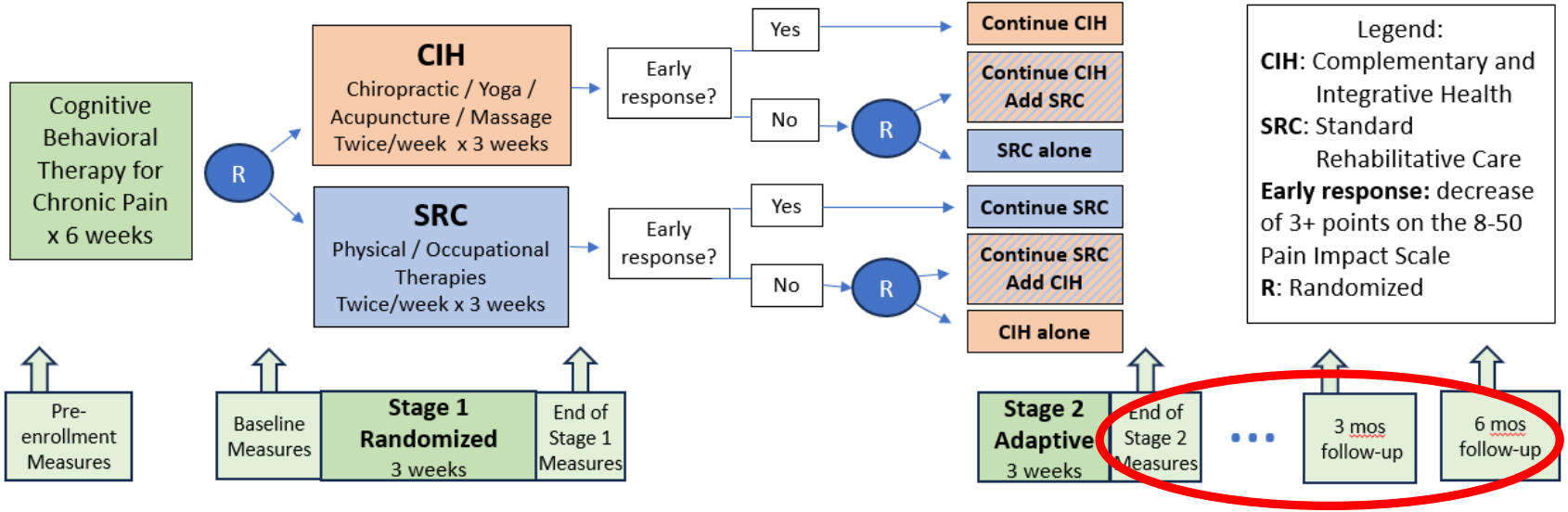
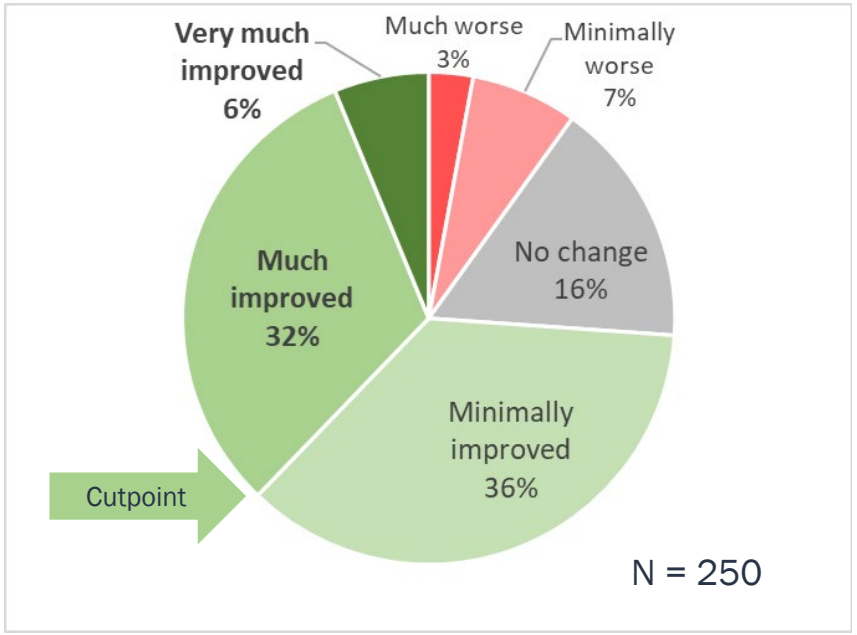


Statistical Methods

- Estimating MID for clinically relevant treatment response
  - Receiver Operating Characteristic (ROC) Curve Analysis
  - Euclidean (“Nearest”) method
- Determining treatment response
  - Single time point general linear model regression
    - ✓ Regressed impact score on stage 1 treatment arm
    - ✓ Controlled for baseline impact score
    - ✓ Repeated for each timepoint
      - End of stage 1
      - End of stage 2
      - 3-month follow-up
      - 6-month follow-up

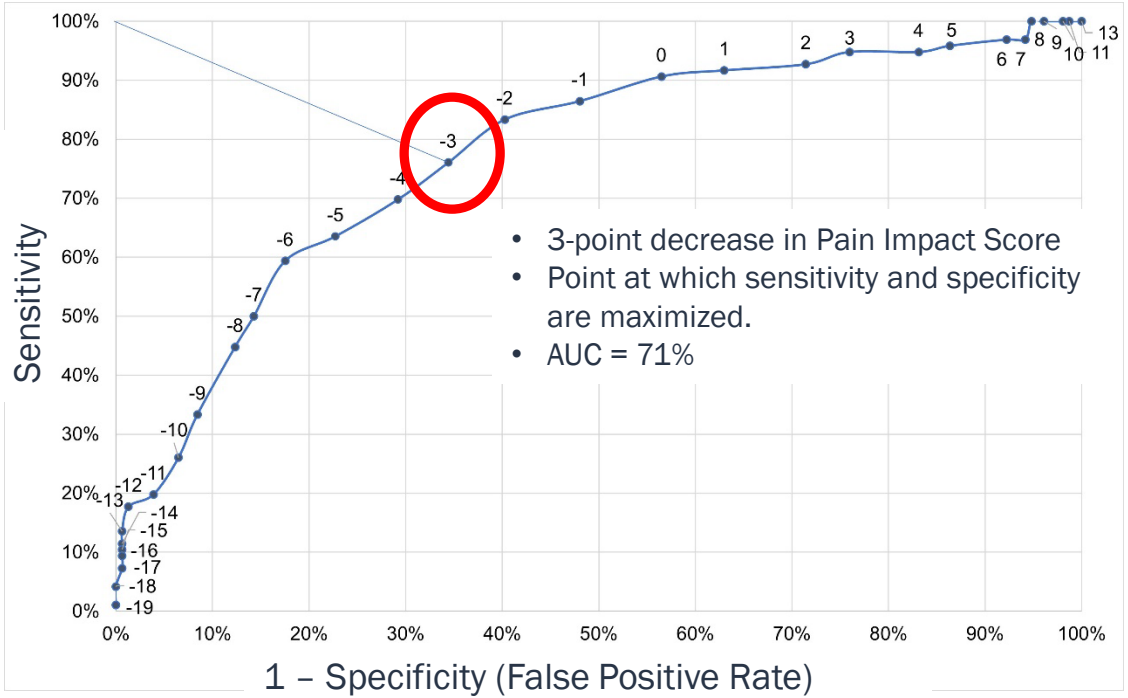
Defining Clinically Relevant Response to Treatment

"Compared to when you started study treatment, how would you rate your overall status?"



Receiver Operating Characteristic (ROC) Curve Analysis to determine MID

Euclidean (“Nearest”) method is point at which both Sensitivity and Specificity are maximized



Other published estimates of PIS MID

Format, author, year	Study population	Anchor	MID method	MID	Number of options	Greater worsening			No change	Greater improvement		
Paper survey; Deyo et al., 2016[4]	Rural Oregon prim care Chr MSK pain, *n* = 198, 66.5 years, PIS = 27.2, 62% women	Pain	Mean score change between "A little" and "Much" less pain	3	5	Much worse	A little worse		About the same	A little less (MID threshold)		Much less
Digital survey; Dutmer et al., 2019[8]	Dutch spine center, Chr LBP, *n* = 223, 49.7 years, PIS = 34.4, 58% women	Treated complaints	ROC curve – Euclidian distance	7.5	7	Extremely worsened	Much worsened	Little worsened	Unchanged	Little improved (MID threshold)	Much improved	Completely improved
Digital survey; Hays et al., 2021[2]	3 US military chiropractic practices, LBP (any duration), *n* = 749, 31 years, PIS 24.0, 24% women	Low back pain	ROC curve – Youden	7	7	Much worse	A little worse		About the same	A little better (MID threshold)	Moderately better	Much better	Completely gone
Two samples. No survey used; Hays et al., 2021[3]	Chiropractic-seeking patients from 6 US states, Chr neck or back pain, *n* = 2024, 49 years, PIS 19.2, 72% women	N/A N/A	Distributive methods: SEM, SEE, SEP, RCI	5-7	N/A N/A	Distributive methods rather than anchor-based survey were used to estimate MID						
Digital CAT survey; current study, 2023	US military interdisciplinary pain management center, Chronic pain (any type), SMART Study *n* =192, PIS = 29.9 22% women IMPPPORT Study *n* = 85 PIS = 26.4 15% women	Pain intensity Physical functioning Pain interference Overall status	ROC curve – Euclidian distance	3	7	Very much worse	Much worse	Minimally worse	No change	Minimally better (MID threshold)	Much better	Very much better

Legend
- MID = minimal important difference
- PIS = pain impact score
- RCI = reliable change index
- ROC = receiver operating characteristic
- SEE = standard error of measurement
- SEP = standard error of prediction

Results - Demographics

	CIH During Stage 1			SRC During Stage 1			*p* value
Sex	**n**	**%**	**Mean (SD)**			**Mean**	
Male	106	**75.7%**		109	**77.9%**		*NS*
Age			34.4 (7.8)			35.1 (8.2)	
18-24	17	12.2%		11	7.9%		
25-34	59	**42.4%**		64	**45.7%**		*NS*
35-44	49	**35.3%**		51	**36.4%**		
45-64	14	10.1%		14	10.0%		
Race							
White	81	**57.9%**		90	**64.3%**		*NS*
Black	31	22.1%		29	20.7%		
Asian	24	17.1%		14	10.0%		
Marital status							
Married	96	**68.6%**		101	**72.1%**		*NS*
Education							
Some college	58	**41.4%**		55	**39.3%**		*NS*
Bachelor's degree	41	**29.3%**		26	**18.6%**		

Results – Baseline Clinical Characteristics

	CIH During Stage 1		SRC During Stage 1		*p* value
Pain type	n	%	n	%	
Musculoskeletal	124	88.6%	124	87.9%	*NS*
Nerves/senses	11	7.9%	10	7.1%	
Other	3	2.1%	4	2.9%	
Missing	2	1.4%	3	2.1%	
Pain duration 1+ year	91	65.0%	85	60.7%	*NS*
Pain persistence Every/nearly every day	99	70.7	94	67.1	*NS*

Results – Baseline Clinical Characteristics

	CIH Treatment Group			SRC Treatment Group			*p* value
Avg pain intensity Moderate (4-6)	n 95	% **67.9%**	Mean T score (SD) 5.4 (1.5)	n 88	% **62.9%**	Mean T score (SD) 5.5 (1.5)	*NS*
Pain interference Moderate	93	**66.4%**	64.0 (5.7)	91	**65.0%**	64.7 (5.8)	*NS*
Physical function Moderate impairment	80	**57.1%**	38.5 (4.4)	74	**52.9%**	38.2 (5.5)	*NS*
Anxiety WNL Moderate	53 45	**37.9%** 32.1%	57.0 (9.7)	42 42	**30.0%** **30.0%**	57.6 (10.7)	*NS*
Depression WNL Moderate	54 36	**38.6%** 25.7%	55.3 (10.3)	61 37	**43.6%** 26.4%	54.8 (10.5)	*NS*
Anger WNL Moderate	65 35	**46.4%** 25.0%	55.1 (11.8)	61 35	**43.6%** 25.0%	56.3 (10.9)	*NS*

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Results – Baseline Clinical Characteristics

	CIH Treatment Group			SRC Treatment Group			*p* value
	n	%	Mean T score (SD)	n	%	Mean T score (SD)	
Sleep-related impairment			62.7 (8.8)			62.2 (9.0)	*NS*
Moderate	57	**40.7%**		63	**45.0%**		
Severe	27	19.3%		20	14.3%		
Fatigue			60.1 (9.2)			59.6 (8.5)	*NS*
Mild	31	22.1%		32	22.9%		
Severe	54	**38.6%**		62	**44.3%**		
Satisfaction with Social Roles and Activities			38.2 (7.2)			38.1 (6.8)	*NS*
Average	59	**42.1%**		51	36.4%		
Moderate dissatisfaction	59	**42.1%**		58	**41.4%**		

Results – Engagement in Treatment unrelated to Study

	CIH Treatment Group		SRC Treatment Group		*p* value
	Baseline through 6-months follow-up				
Medications					
NSAIDs (topical or oral)	53	37.9%	45	32.1%	
Muscle relaxants	25	17.9%	18	12.9%	
TCAs / SNRIs	40	28.6%	37	26.4%	*NS*
Gabapentinoids	27	19.3%	30	21.4%	
Opioids	2	1.4%	2	1.4%	
Procedures					
Epidural steroid injections(s)	15 (10.7)	10.7%	16	11.4%	
Joint injection (non-spine)	10 (7.1)	7.1%	5	3.6%	*NS*
Peripheral nerve block	7 (5.0)	5.0%	4	2.9%	
Trigger point injection(s)	7 (5.0)	5.0%	5	3.6%	
	End of Stage 2 through 6-months follow-up				
Additional SRC or CIH	83	59.3%	94	67.1%	*NS*

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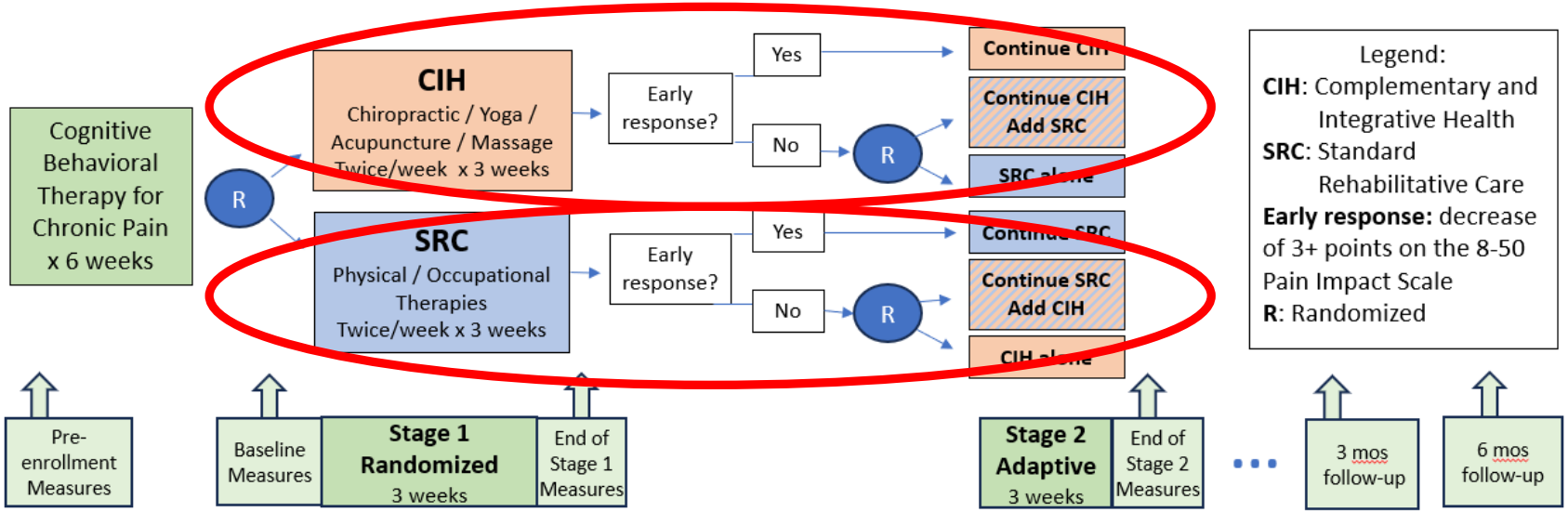
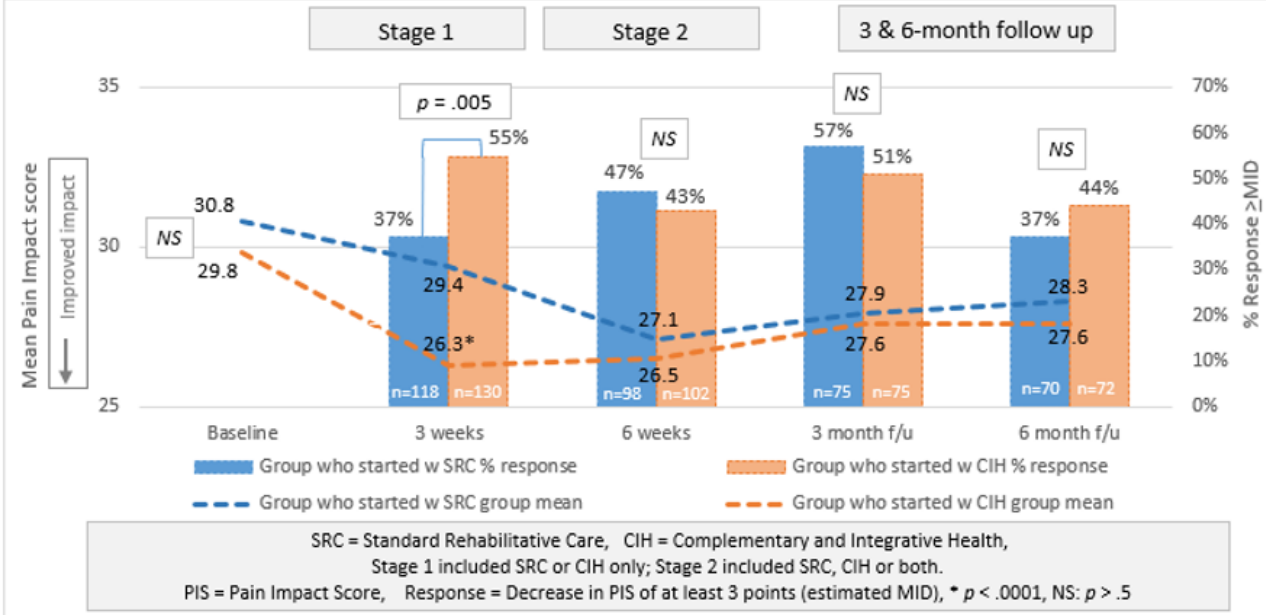


SRC start vs CIH Start - Outcomes

Figure 1. Change in Mean Pain Impact Score and Percentage of Responders during and up to 6-months after Treatment between Group that started with SRC (n=130) vs CIH (n=135)



Key

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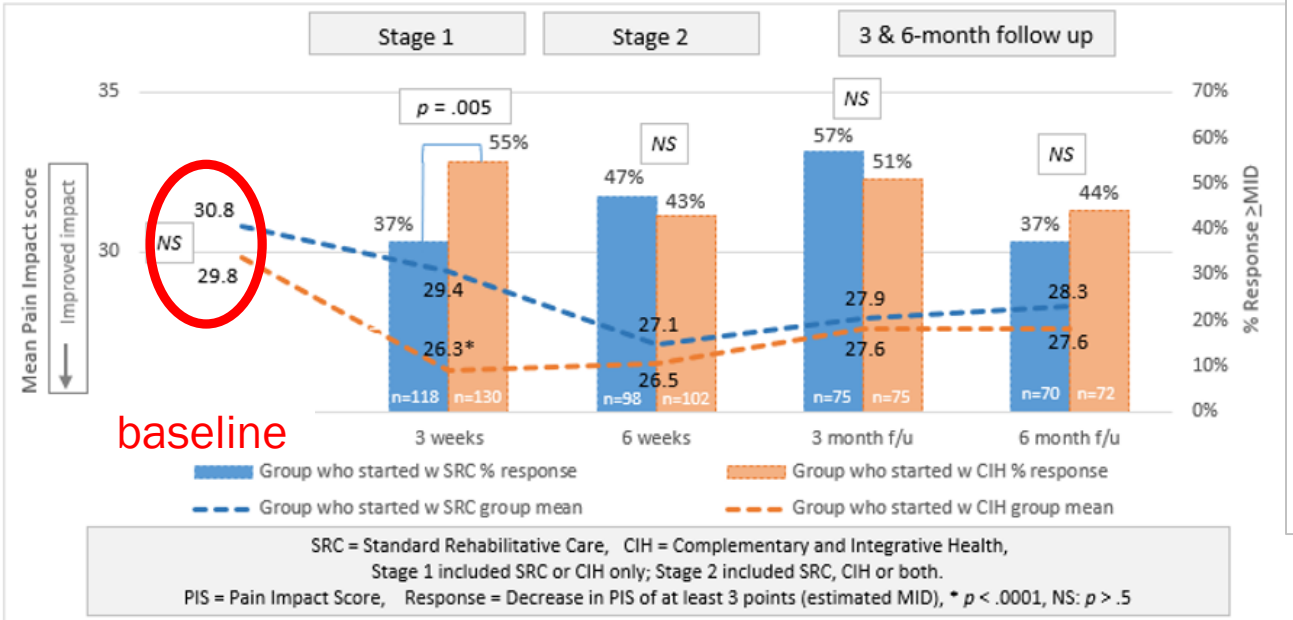

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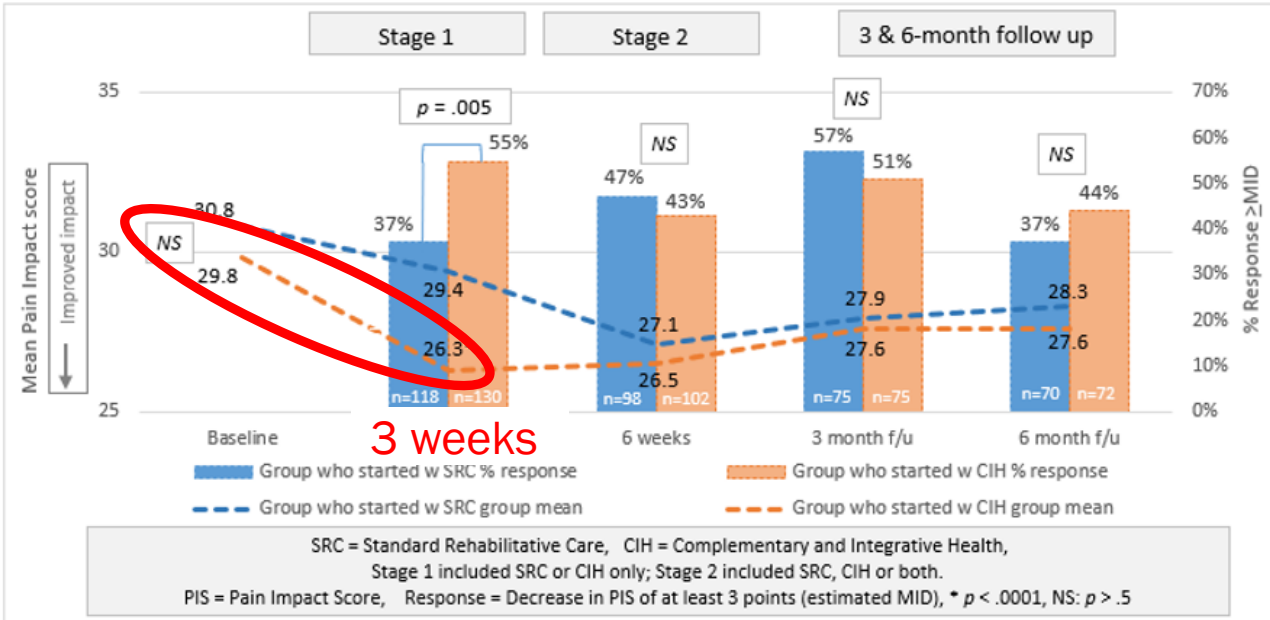

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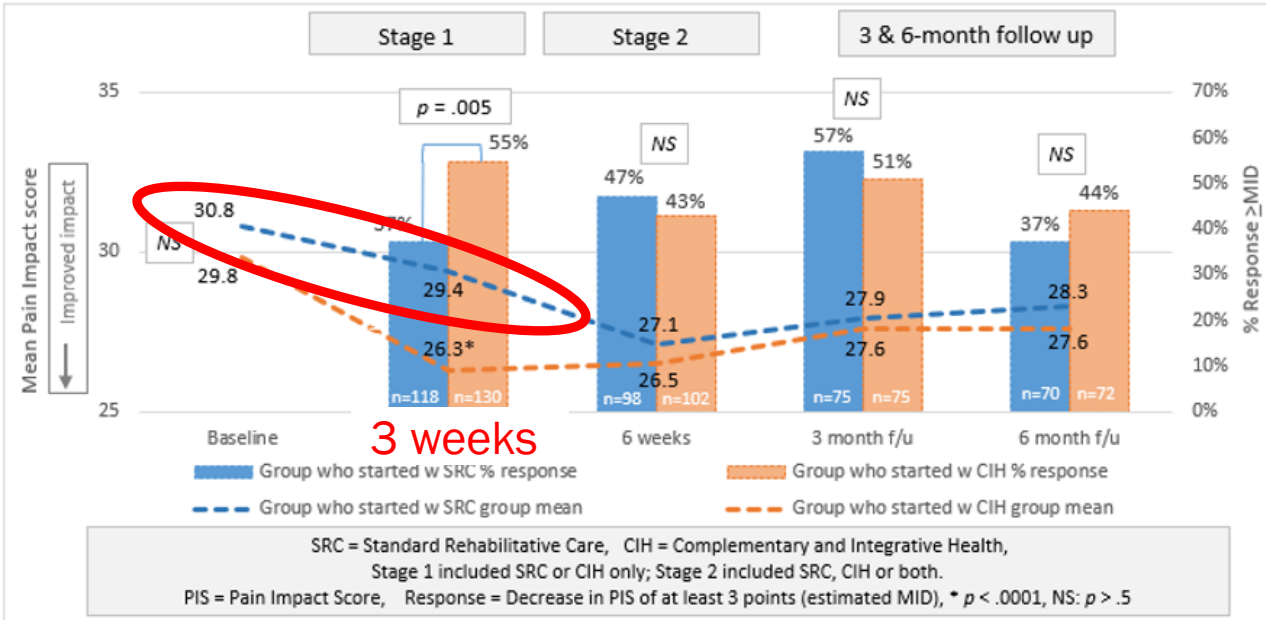

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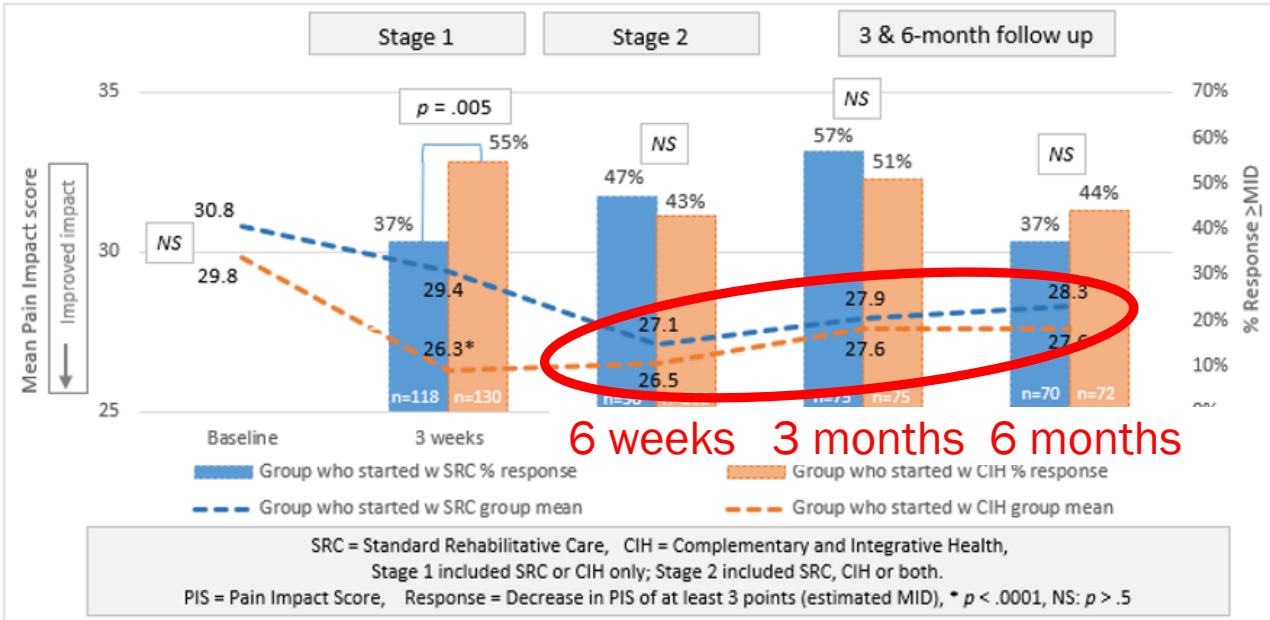

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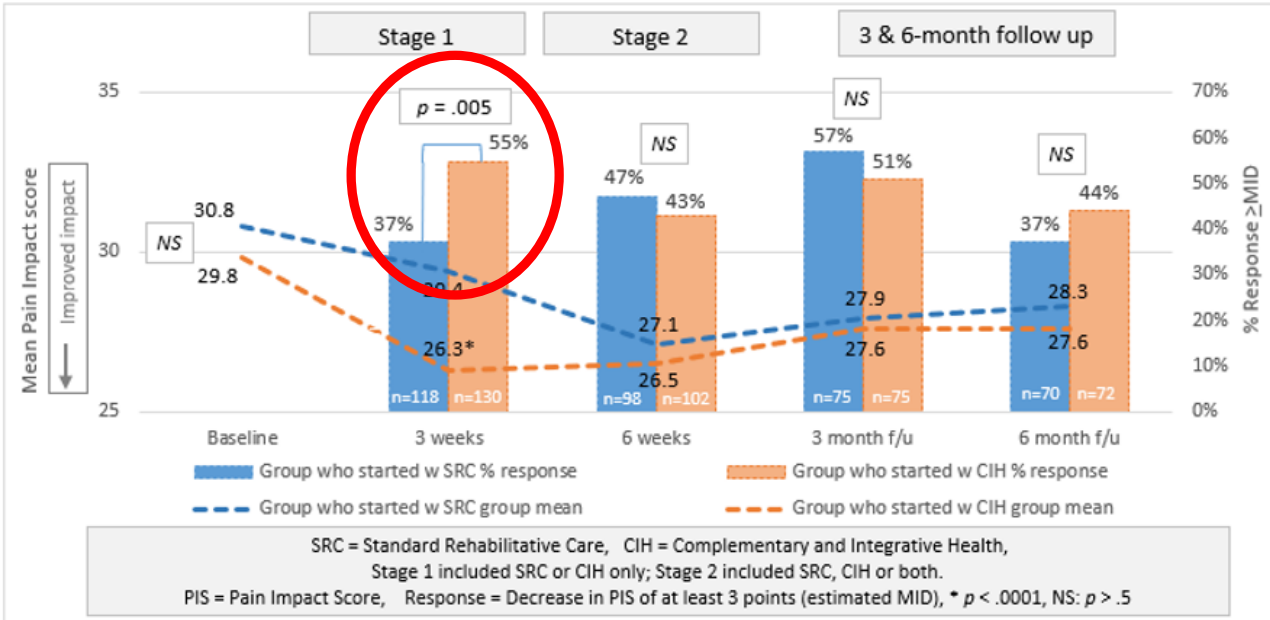

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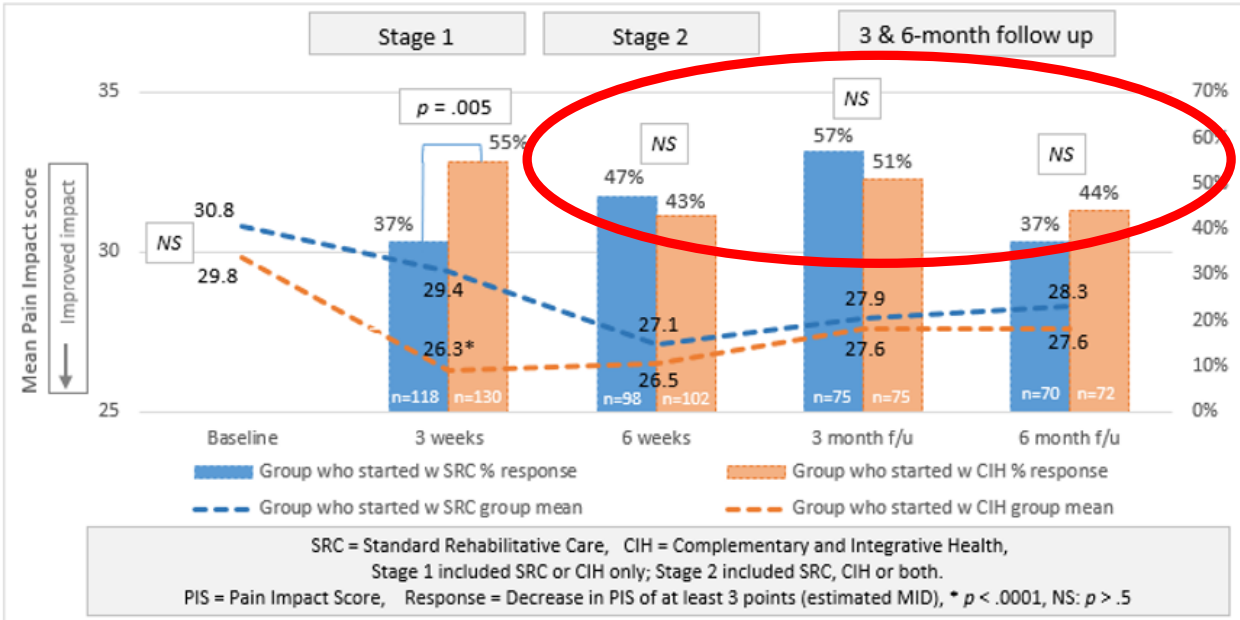

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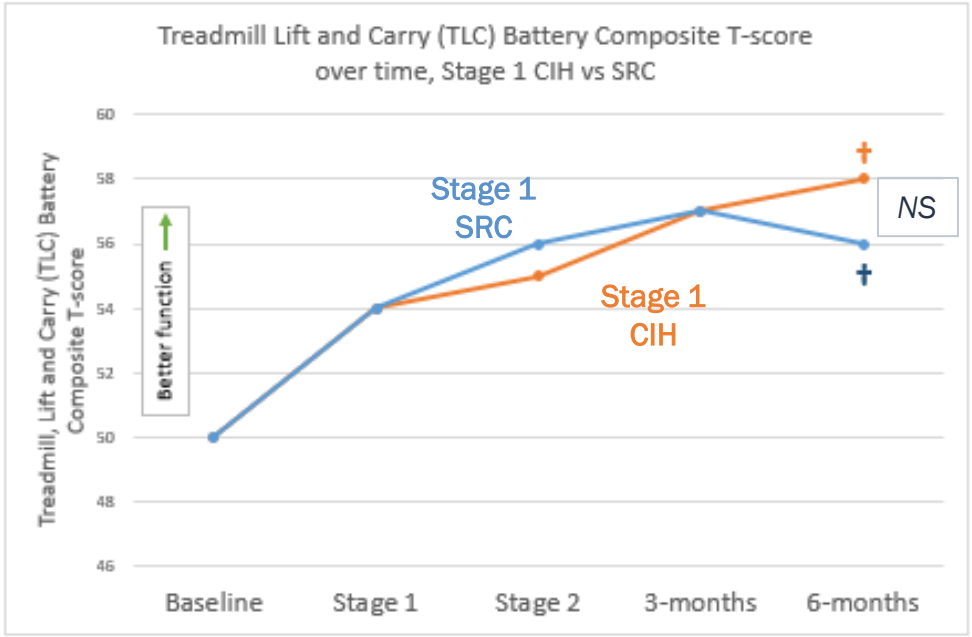
Functional Performance (TLC battery) Outcomes by Stage 1 Treatment Group



Legend: † Mean improvement from baseline exceeded MID at 6-month follow-up, MID = 6 for TLC T-score

SRC start vs CIH Start – Outcomes Summary

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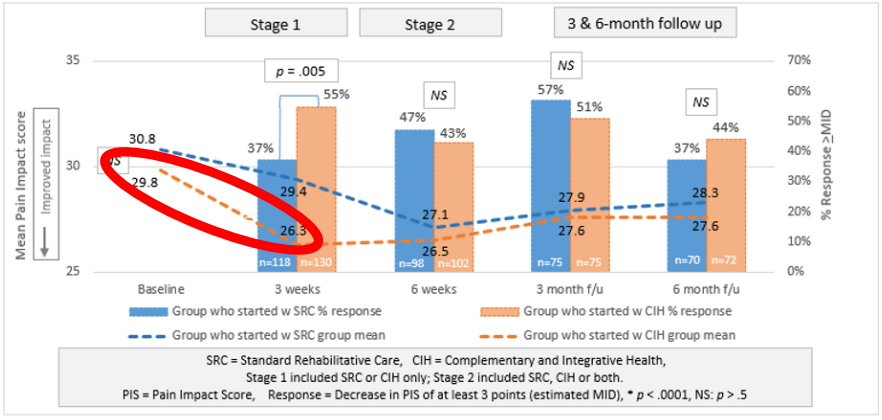
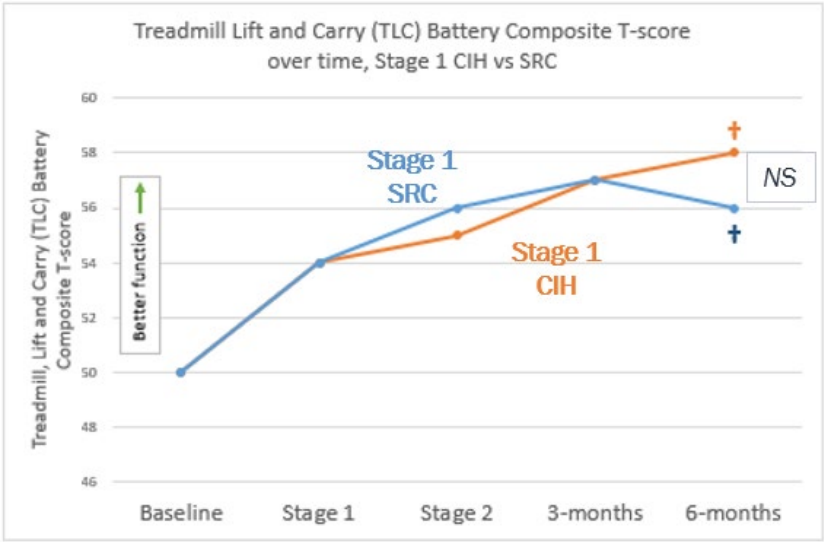


Pain Impact

Functional Performance



SRC start vs CIH Start – Clinical Implications

- Clinicians can feel confident recommending patients start with CIH therapies if that is the patients' preference
- Findings lend support to expanding access to CIH approaches

Questions

Thank you!

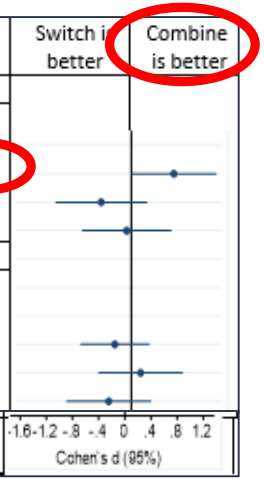
Additional slide

Secondary Aim and Results

Secondary Aim: Among non-responders to stage 1 treatment, determine the best follow-on approach

Outcome	Time point	Mean (SD)	Mean Δ[a] (95% CI)	Mean (SD)	Mean Δ[a] (95% CI)	*P* value
		CIH → SRC		CIH → both		
Pain impact score (8-50; higher score = worse impact)	Pre-stage 1	26.6 (7.7)		31.3 (8.2)		
	Post-stage 1	27.0 (8.0)		31.6 (8.1)		
	Post-stage 2	26.3 (9.7)	2.3 (−0.2, 4.7)	29.6 (10.0)	−1.6 (−3.6, 0.5)	.022
	3 months	23.0 (11.0)	−3.4 (−6.5, −0.3)	31.9 (9.2)	−0.6 (−3.3, 2.0)	.205
	6 months	25.3 (9.9)	−1.1 (−3.9, 1.7)	30.4 (6.6)	0 (−2.9, 2.8)	.601
		SRC → CIH		SRC → both		
	Pre-stage 1	31.0 (8.1)		29.8 (7.9)		
	Post-stage 1	32.3 (7.5)		31.6 (7.2)		
	Post-stage 2	28.0 (9.5)	−1.8 (−3.6, 0.1)	28.1 (9.8)	−0.4 (−2.3, 1.5)	.320
	3 months	31.9 (10.4)	1.3 (−1.9, 4.5)	28.5 (9.3)	−0.5 (−3.8, 2.9)	.460
	6 months	30.2 (9.5)	−0.5 (−3.2, 2.2)	30.7 (7.3)	1.3 (−1.4, 4.0)	.364

[a]Δ = change in mean from pre-stage 1 baseline between SRC and CIH stage 1 groups. CIH = complementary & integrative, SRC = standard rehabilitative, TLC = treadmill, lift, and carry battery.[16]



- For non-responders to CIH start
  - It was better to combine SRC w/ CIH than switch to SRC alone
  - Only at end of active treatment, not at follow-up
- For non-responders to SRC start
  - No difference between switch to vs. combine with CIH