Journal Club at the Laboratory of Clinical Psychopharmacology of Addictions (LCPA) is a monthly gathering to discuss research papers with a focus on addiction.

Mission: to promote a better understanding of the research process and an improve ability to critically appraise research in addiction and related diseases (e.g. infectious, mental health, etc.).

Discussion topics and learning objectives include (but not limited by) the concepts of addiction, terminology used in the field, socio-cultural and biological risk factors, contemporary public health issues and policies, prevention, treatment and treatment systems.

Values:

- Learning
- Respect
- Collaboration
- Multidisciplinary
- Excellence

Please be open, flexible, realistic, and understanding!

Housekeeping notes

Video-recording

The meeting will be entirely video-recording and published on the Pavlov University website and YouTube, so if you wish not be in the recorded video, please make sure that your webcam off during the meeting.

Q&A

The seminar is interactive and we strongly encourage you to actively ask questions during the presentation but keep in mind that we have dedicated time at the end of the webinar (10 minutes) to group discussion and Q&A. Please raise your hand if you have any questions or comment. You also may use chat option to post your questions or comments.

Mic and Video

Please keep your mic mute during entire meeting unless you want to make a question or comment. We recommend keeping your camera on during the meeting.

Post-meeting survey

After the meeting we would like to send you the survey. Please make sure that we have your email.

A Randomized Trial Comparing Acupuncture, Simulated Acupuncture, and Usual Care for Chronic Low Back Pain

Cherkin et al.

23 June 2020

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The goal of the trial

1. Is acupuncture more effective than usual medical care alone?
2. Is real acupuncture more effective than simulated (noninsertive) acupuncture?
3. Is individualized acupuncture more effective than standardized acupuncture?

Methods

Trial design

7 weeks of treatment

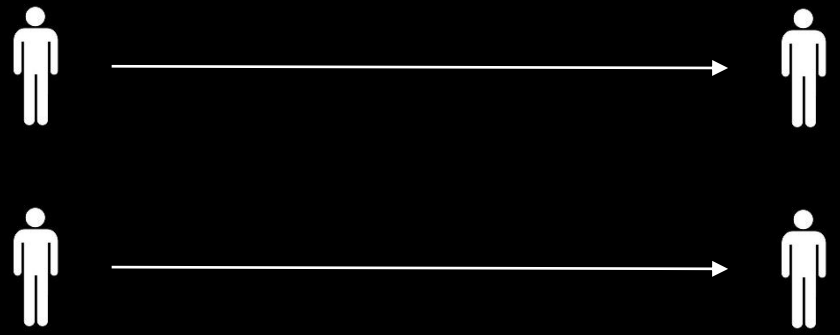
Standardized acupuncture + Selfcare book	(8 weeks)	(26 weeks)	(52 weeks)
Individualized acupuncture + Selfcare book	(8 weeks)	(26 weeks)	(52 weeks)
Sham acupuncture + Selfcare book	(8 weeks)	(26 weeks)	(52 weeks)
Usual care + Selfcare book	(8 weeks)	(26 weeks)	(52 weeks)

Trial design

- ✓ Parallel (randomization to 4 parallel groups)
- ✓ Double blind (triple blind?)
  - Participants were asked to wear eye masks and lie prone with their heads in a face cradle
  - One of 5 diagnostician acupuncturists evaluated participants at each visit and prescribed treatment
  - A therapist acupuncturist then delivered the assigned treatments, interacting minimally with participants and the diagnostician, who remained masked to treatment
- ✓ Controlled
  - Sham acupuncture
  - Usual care

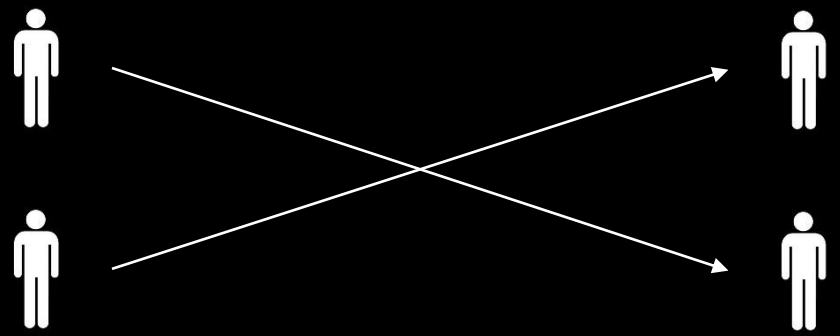
Types of trial design

Parallel



- ✓ Progressive illness (patients' parameters change over time)
- ✓ Unethical to stop treatment (cannot provide a wash-out period)
- ✓ Long period of endpoints evaluation

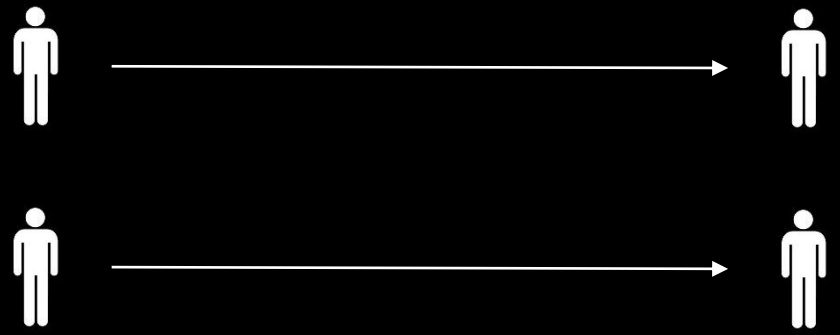
Cross-over



- ✓ Healthy volunteers
- ✓ Stable condition (e.g., chronic pain)
- ✓ Wash-out period is possible (5 x T1/2 – e.g., several days)
- ✓ Short period of evaluation

Design of this trial

Parallel



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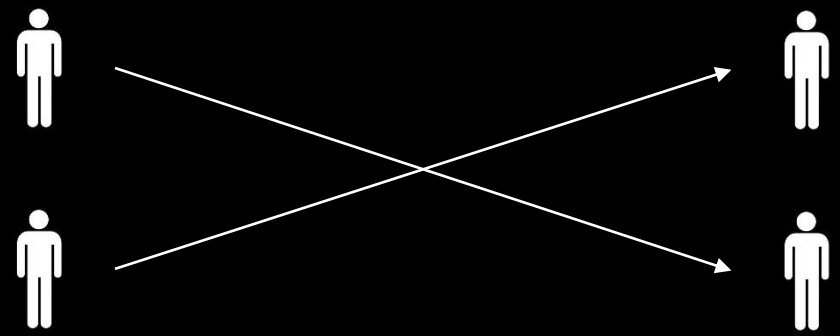

- ✓ Healthy volunteers
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- ✓ Wash-out period is possible (5 x T1/2 – e.g., several days)
- ✓ Short period of evaluation

Blinding

- Only study subjects
- Double blind – subjects and investigators
- Triple blind – subjects, investigators & clinical data evaluators or investigation prescribers
  - MRI / CT / Rg
  - USI / EchoCG
  - Scales subjectively evaluated by a physician
- Quadriple blind – triple blind + data management & biostatisticians

+ data evaluating committees
+ safety committees
+ etc

Control

- Placebo control
- Active control
- Sham control – for non-drug treatment
  - surgery (ethics?)
  - acupuncture
  - physiotherapy
  - psychotherapy (ethics? possibility?)

Acupuncture intervention

Individualized	Standardized	Sham (simulated)
Any points (up to 74)	8 points	8 points
Any (5-20) # of needles	? needles	? needles
15-20 minutes	10+10 minutes	10+10 minutes

Acupuncture intervention

Individualized	Standardized	Sham (simulated)
Any points (up to 74)	8 points	8 points
Any (5-20) # of needles	? needles	? needles
15-20 minutes	10+10 minutes	10+10 minutes

Were patients really masked?
Where therapists really masked?

Participants rated the acupuncture and simulated acupuncture treatments almost identically with regard to provider skills and caring.
The diagnostician acupuncturists rated the acupuncture and simulated acupuncture groups very similarly with regard to apparent efficacy and likelihood of receiving individualized treatment.

Endpoints (outcome measures)

- ✓ Computer-assisted telephone interviews by interviewers masked to treatment
- ✓ Estimated at 8, 26 & 52 weeks
- ✓ Backrelated dysfunction – Roland-Morris Disability Questionnaire (RMDQ)
- ✓ Symptom bothersomeness at end of treatment – how bothersome their pain had been during the past week on a scale of 0 (“not at all bothersome”) to 10 (“extremely bothersome”)

Did we need blinding?

Definitely yes!

Highly subjective endpoints, very high risk of placebo/nocebo effect if unmasking
Unmasked therapist or interviewer can unintentionally influence subject’s feelings

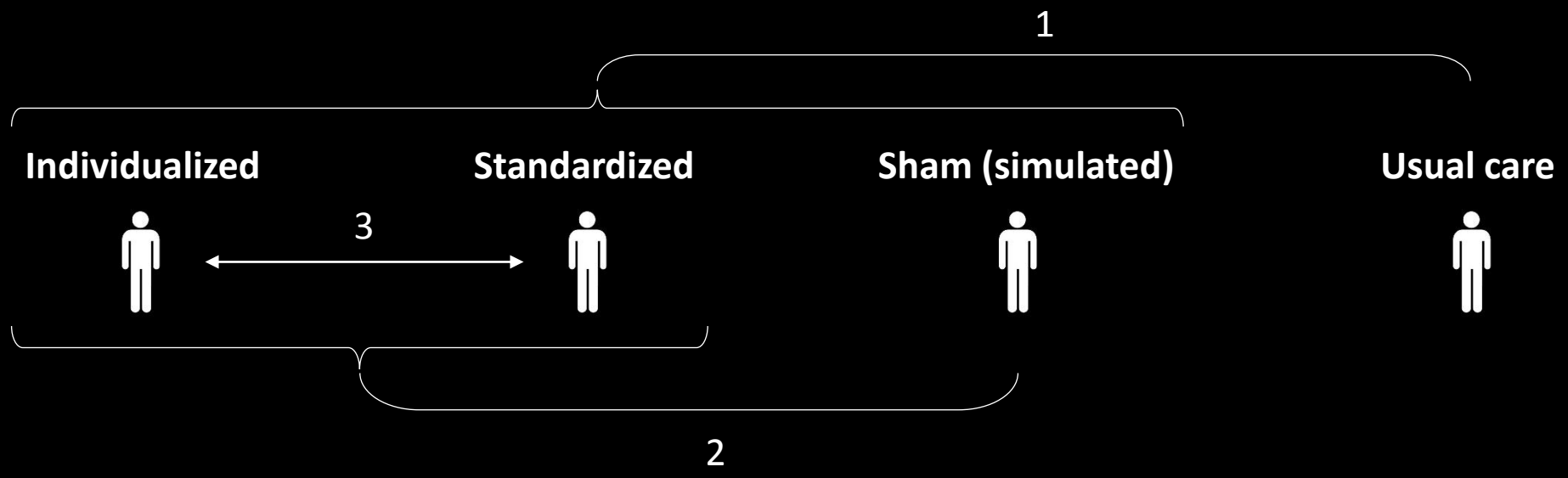
And please...

… never use 0 to 10 scales for by-phone evaluation

These scales MUST be evaluated using a line on a paper source.
And the line must always be the same length. No matter what printing problems you have.

What we compare?

1. Is acupuncture more effective than usual medical care alone?
2. Is real acupuncture more effective than simulated (noninsertive) acupuncture?
3. Is individualized acupuncture more effective than standardized acupuncture?



No adjustment for multiple comparisons provided

Multiple comparisons

Many ways to adjust
Needed if multiple primary endpoints are evaluated

Examples of multiple endpoints

1. Decrease in pain and/or increase in ability to take care of themselves (statistics depends on OR/AND)
2. Decrease in pain at week 8 and/or week 12

Statistical analysis

Analysis of covariance was used to test for treatment differences at the follow-up assessment, adjusting for the **baseline** measure. We also adjusted for **site**, **age** group (18-29, 30-39, 40-49, 50-59, and > 60 years), and **sex**.

therapist (limited amount; highly important)

+ previous experience of acupuncture
+ need for other treatment of pain

Results

Describing results

Table 2. Mean RMDQ Score and Symptom Bothersomeness Score at Baseline and Follow-up by Randomized Treatment Assignment

Score	Mean (SD)			
	Baseline	8 wk	26 wk	52 wk
RMDQ				
Individualized acupuncture	10.8 (5.2)	6.4 (5.3)	6.8 (5.5)	6.0 (5.4)
Standardized acupuncture	10.8 (5.6)	6.3 (5.7)	6.7 (5.8)	6.0 (5.8)
Simulated acupuncture	9.8 (5.2)	5.4 (4.9)	6.4 (6.0)	6.2 (5.8)
Usual care	11.0 (5.2)	8.9 (6.0)	8.4 (6.0)	7.9 (6.5)
Unadjusted *P* value		<.001	.01	.02
Adjusted *P* value[a]		<.001	.003	.001
Bothersomeness				
Individualized acupuncture	5.0 (2.5)	3.4 (2.7)	3.8 (2.5)	3.7 (2.6)
Standardized acupuncture	5.0 (2.3)	3.3 (2.5)	3.7 (2.6)	3.5 (2.7)
Simulated acupuncture	4.9 (2.4)	3.0 (2.4)	3.5 (2.7)	3.4 (2.7)
Usual care	5.4 (2.4)	4.7 (2.6)	4.4 (2.6)	4.1 (2.6)
Unadjusted *P* value		<.001	.03	.12
Adjusted *P* value[a]		<.001	.04	.12

compared to baseline?
compared among groups?

Expect to see changes from baseline, not absolute values

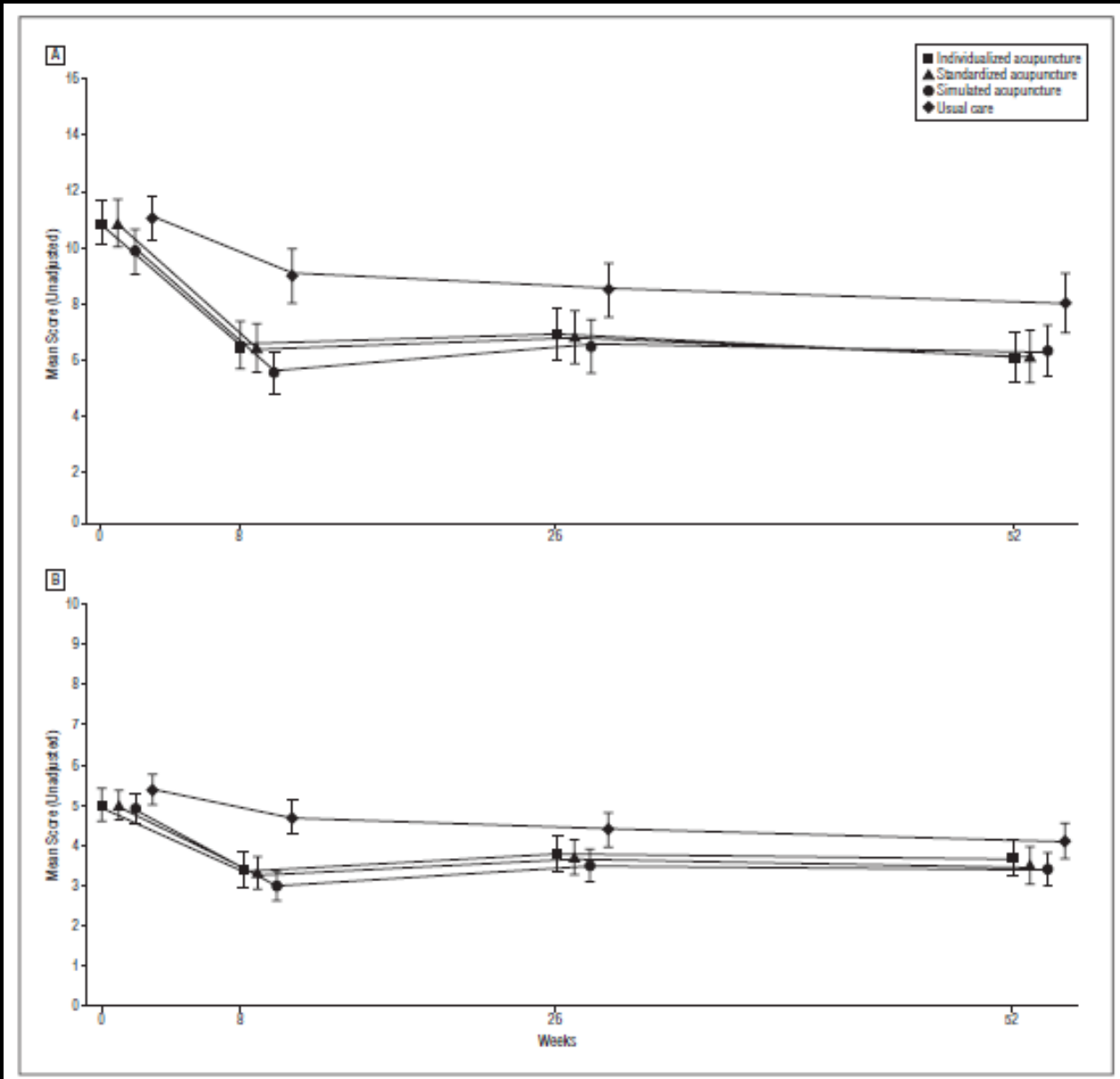


Figure 2. Mean Roland-Morris Disability Questionnaire scores (A) and symptom bothersomeness scores (B) and 95% confidence intervals by treatment group and time since randomization.

There is a picture, but no p-values for change for baseline provided (or you need to read very carefully to find it in the text)

Interpretation of results

1. Is acupuncture more effective than usual medical care alone?
2. Is real acupuncture more effective than simulated (noninsertive) acupuncture?
3. Is individualized acupuncture more effective than standardized acupuncture?

1. Compared with usual care, individualized acupuncture, standardized acupuncture, and simulated acupuncture had beneficial and persisting effects on chronic back pain.

2. One German trial found that both real acupuncture and sham acupuncture had similar effects… A second German trial found that both real and sham acupuncture were … not significantly different from each other.
Our trial extends the findings from these studies by demonstrating that needle insertion is not necessary to achieve therapeutic benefits and by measuring longer-term outcomes.

3. No comment on the third question.

Placebo effect

Collectively, these recent trials provide strong and consistent evidence that real acupuncture needling using the Chinese meridian system is no more effective for chronic back pain than various purported forms of sham acupuncture. However, both real and sham acupuncture appear superior to usual care.
(= any acupuncture-like intervention causes placebo effect)

Possible explanations for these findings include the following:

1. Superficial acupuncture point stimulation directly stimulates physiological processes that ultimately lead to improved pain and function,
2. participants' improved functioning resulted from nonspecific effects such as therapist conviction, patient enthusiasm, or receiving a treatment believed to be helpful (placebo effect).

When placebo effect is a problem?

Psychoactive drugs
Emotional distress
Psycho-somatic symptoms (anxiety and depression related)
Populations seeking for physicians attention (Russian population!)
Children

Could we say that the drug is ineffective under these circumstances?

Nocebo effect

Psychoactive drugs
Emotional distress
Psycho-somatic symptoms (anxiety and depression related)

Pain (if said “this will not help”)
Generic and biosimilar drugs (if open-label)

Thanks for your attention!

Any questions?

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