Discovery, Design, and Proof-of-Concept: ORBIT Phases I and IIa

Lynda H. Powell, PhD

Rush University Medical Center Chicago, IL Ipowell@rush.edu

The "Nuts and Bolts" of Behavioral Intervention Development

International Behavioral Trials Network Conference Montreal, Canada

26 May 2018

ور والمتناقيل بوليده

ومحمد والمحمد وبالأبر ومريس المحمد والمحمد ومحمد والمحمد والمحمد والمحمد والمحمد والمحمد والمحمد والمحمد والمحم

PROCESS OF BEHAVIORAL TREATMENT DEVELOPMENT



Czajkowski, Powell et al., 2015; Powell, Freedland, Kaufmann, in press

PROCESS OF DRUG DEVELOPMENT



| PHASE | GOAL | STRATEGY | MILESTON | |
|--------------|---|--|--|--|
| Discovery | Identify candidate | Integrate clinical need with basic science | Biologic activity | |
| Non-Clinical | Non-human safety, biologic activity | Animal, in vitro laboratory studies | FDA approval for testing in humans | |
| Phase I | Human Pharmacology | Small N, healthy, close monitoring, no controls | Safe and biologic activity in healthy | |
| Phase II | Therapeutic Efficacy | Small N, patients, close monitoring, no controls | Safe and biologic activity in patients | |
| Phase III | Therapeutic Confirmatory | Randomization efficacy trial with morbidity/mortality outcomes | FDA permission to market drug | |
| Phase IV | Therapeutic Use | Long-term surveillance, no control, diverse patients | Optimization, refinement | |

ومرأته والبنائي وتحديد أساميه وبالتلافي والترج

والمتحاذ والمحاجبين والمحاجبين والمحاجبين والمحاجبين والمحاجبا والمحاجبا والمحاجب والمحاجبا والمحاجب



Development of a Lifestyle Intervention for Remission of the Metabolic Syndrome:

Discovery through Proof-of-Concept

والمستحدين ومحاجزا والمراجع أأناع والمتناقص وتحديث أمرأ ومحمدها التناقي والمعرجة الألالي

والمستجد والمناطقة فالمحاجب والأمريس والمتكليل المحافظتين والمحافظ والمعاد



Discovery: Significant Clinical Question:

Sustained Change in Lifestyle

international behavioural trials network



BASIC PRINCIPLES

- 1. Target diet, physical activity, and stress simultaneously.
- 2. Real time patient discovery more powerful than education.
- 3. Immediate benefits more powerful than distal negative consequences.
- 4. Embed program into medical care.



ومحاجزته والمشارية والمتناقية وتحصر أساحهم والتكافية والأنتاج

والمتحاذ المتحاد والمتحاج والمحاجب والمحاجب والمحاجب والمحاجب والمحاجب والمحاجب والمحاجب والمحاج

Standard Strategy for Lifestyle Changer in the standard strategy for the standard strategy for Lifestyle Changer in the standard strategy for Lifestyle Changer in the standard strategy for standard strategy for the standard strategy for strategy for standard st

ihtn

international behavioural





Standard Strategy for Lifestyle Change



Strategy: Self-management skills

Hall & Marteaux, 2014



ibtn international behavioural trials network

Problem with the Standard Strategy for Lifestyle Change



international behavioural trials network

Revised Strategy for Lifestyle Change From Neuroscience



Foerde et al., 2015 Guo et al., 2014 Schwabe & Wolf, 2009



ibtn international behavioural trials network

Revised Strategy for Lifestyle Change From Basic Neuroscience



والمستحد والمتحافظ فالمتلاصين والأمريون ويراب المتقاصل والمحافظ والمتحافظ والمتحاط والمحا

PROCESS OF BEHAVIORAL TREATMENT DEVELOPMENT



Czajkowski, Powell et al., 2015; Powell, Freedland, Kaufmann, in press

Phase Ia: Define

HYPOTHESIZED TREATMENT PATHWAY

Behavioral Risk behavioural Component Habit ("ELM Leaf") Primary **Treatment Target** trials network Factor Outcome "Perfect Plate" ½ plate vegetables/day Vegetable Intake DIET $(\geq 3 \text{ servings/day})$ "HALT" Stop and breathe before emotional eating "Play" Engage in enjoyable physical activities and notice sensory **Physical Activity** \geq 50% with experiences PHYSICAL (≥ 150 min remission of moderately ACTIVITY metabolic "Use It or 30 min moderately vigorous vigorous /week) syndrome Lose It" physical activity on most days 10,000 steps on most days "Waste Energy" "Discover this Practice staying in the present while Moment" engaging in health behaviors "Recognize Put time between a stressor and Hooks" emotional reaction to it Depression STRESS (reduce) Practice kindness to self and others "Smile First" "Important Trumps Prioritize an ELM hour on most days Urgent"

and the second

ibtn

The ELM Lifestyle Program

Central Fat



Hypertension



▲ Triglycerides

Glucose

HDL Cholesterol



ibtn

international behavioural trials network



You are invited to the ELM Dinner Club





Phase IIa: Proof-of-Concept

After 6 of intensive treatment:

• 61.5% no longer met criteria for metabolic syndrome

- Energy/vitality, social support, and depression improved
- Drug use decreased

After 2.5 years:

- 53.8% maintained remission of the metabolic syndrome
- 38.5% maintained clinically significant weight loss
- 25% no longer needed anti-hypertensive medications
- Sustained improvement in diet, physical activity, stress, mood, social support, energy/vitality.
- Metabolic syndrome remission was highly related to loss of <u>></u> 5% of baseline weight



ibtn international behavioural trials network

Phase Ib: Refine



TINKERING

- **DEFINITION** Attempt to repair or improve something in a casual way.**USAGE** He tinkered endlessly with the car
- **SYNONYMS** adjust, fix, mend, play with, fiddle with, fool with, take apart

"A new treatment is born into a hostile environment. It must be kept alive in infancy. It needs to mature until it reaches a point at which it can be brought into contact with the abundance of problems that could undermine it. Scientists should protect early development; not contribute to premature death."

Feyerabend, 1965

international behavioural

trials network

والمستجد والمناطقة والمناصبين والمرجون والمتعالية والمعاد والمتعادي والمستعد والمتعاد والمتعاد

البناكي وليبو أوراز

Phase Ib: Refine



7-Year Follow-Up of Proof-of-Concept Participants

international behavioural trials network

In those in remission at 2.5 years, at 7 years:

50% lost or stayed the same weight

What helped the most?

- 93%: Nutrition education
- 86%: Reducing emotional reactivity to stress
- 71%: Physical activity

Health Network

- 43%: Still connected with ELM friends
- 57%: Connected with a health conscious friend > once a week

ومحجل والبول والمتكرك والمتناقية والمربع أور المحج وخلاليك

Technology

43% Use Fitbit for health





Phase Ib: Refine

ELM Experimental Group N=10

international behavioural trials network

Physical Activity



Cooking Demonstration





Group Discussion (Share a Meal)





Phase Ib: Refine Update Technology

international behavioural trials network





Phase Ib: Refine Neutralize Desire With Mindfulness-Based Habits

international behavioural trials network

| AIM | ELM LEAF (HABIT) | PREPARE FOOD | EATING HABITS | PHYSICAL ACTIVITY | STRESS |
|-----------------------|---------------------------|--|--|---|--|
| Attention Control | "Be Here Now" | Experience taste of salt, fat, sugar. Notice smell, aroma, color of vegetables. | Become sensitive to emotions that trigger eating. | Notice judgmental thoughts during activity. | Experience body's reaction to stress and relaxation. |
| Emotion Regulation | "Stop, Breathe, Be" | Cutting vegetables cues breathing | Stop and breathe before opportunistic eating | Replace judgmental thoughts with deep breathing before activity. | Breathe before reacting to interpersonal "hook" |

والمراجع أأترج والمتناقين وتنبعه أمراجهم وخالباته فالتلمين والأنتاجي

20

| Component | ELM (2011) | ELM (2017) trials netw | |
|-----------------------|-----------------------|------------------------------|--|
| Treatment Strategies | Feedback, Support | Habit Change (added) | |
| Number of Habits | 9 | 4 | |
| Wearable Technology | Pedometers | Fitbits | |
| Cooking Demonstration | Full meal | Vegetable dishes | |
| Stress Management | Variety of techniques | 2 Mindfulness-Based Habits | |
| Duration of Sessions | 2.5 hours | 1.5 hours | |
| Health Network | Evolved organically | Fitbit-assisted connectivity | |

PROCESS OF BEHAVIORAL TREATMENT DEVELOPMENT



Czajkowski, Powell et al., 2015; Powell, Freedland, Kaufmann, in press

Phase IIb: Pilot Feasibility Pilot Study (N=12)

- Aims: 1. To explore feasibility at a different site
 - 2. To explore acceptability to patients and providers
 - 3. To determine rate of recruitment
 - 4. To explore impact on weight and metabolic syndrome after 6 months.





Kevin Masters, PhD Anschutz Health and Wellness Center University of Colorado at Denver



SUMMARY OF THE PROCESS OF BEHAVIORAL TREATMENT DEVELOPMENT USING THE ORBIT MODEL





المتحد ومتحا فتنافأ فالجاري والأبريس والمتناط الالمحتقصان وترجيها الطريبي

It takes a village . . .

Behavioral Science

Lynda Powell, PhD Brad Appelhans, PhD Elizabeth Lynch, PhD Jennifer Ventrelle, MS, RD Patricia Normand, MD

Medicine

Steven Rothschild, MD Laura Zimmerman, MD Rasa Kazlauskaite, MD

Public Health

Rebecca Dawar

Community

Joyce Mack

Biostatistics and Data Management

DeJuran Richardson, PhD Liz Avery-Mamer, MS Kelly Karavolos, MS Tami Olinger, MS

Rush Philanthropy

Sophia Worobec



ibtn

international

behavioural



a di na sen dell'Arte dell'en en e

ومحمد والمحمد المحمد المحمد والمحمد والمراجع والمحمد والمحمد