

The Patient's Perspective on Major Depressive Disorder: What Do We Know?

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Patient Reported Outcomes and Person Centered Care in Mental Health

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Conflict of Interest and Financial Disclosure



- **Susan Ball, Ph.D.**
 - Employee and shareholder of Eli Lilly and Company
- **Cecilia Dedios, MSc. C. Psychol**
 - Employee of Health Research Associates, a consulting firm, which has received funding from the PRO Consortium Depression Working Group
- **Lucy Abraham, MSc. C.Psychol**
 - Employee of Pfizer Ltd
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 - Linda L. Carpenter, MD - Butler Hospital/Brown University, Providence, RI
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- C-Path, in cooperation with the FDA and the medical products industry, formed the **Patient-Reported Outcome (PRO) Consortium** in 2008 for the purpose of developing, evaluating, and qualifying PRO instruments with the FDA for use in clinical trials designed to evaluate the safety and efficacy of medical products
 - Current working groups include: Asthma, Cognition (mild cognitive impairment), **Depression**, Functional Dyspepsia, Irritable Bowel Syndrome, Non-Small Cell Lung Cancer, and Rheumatoid Arthritis

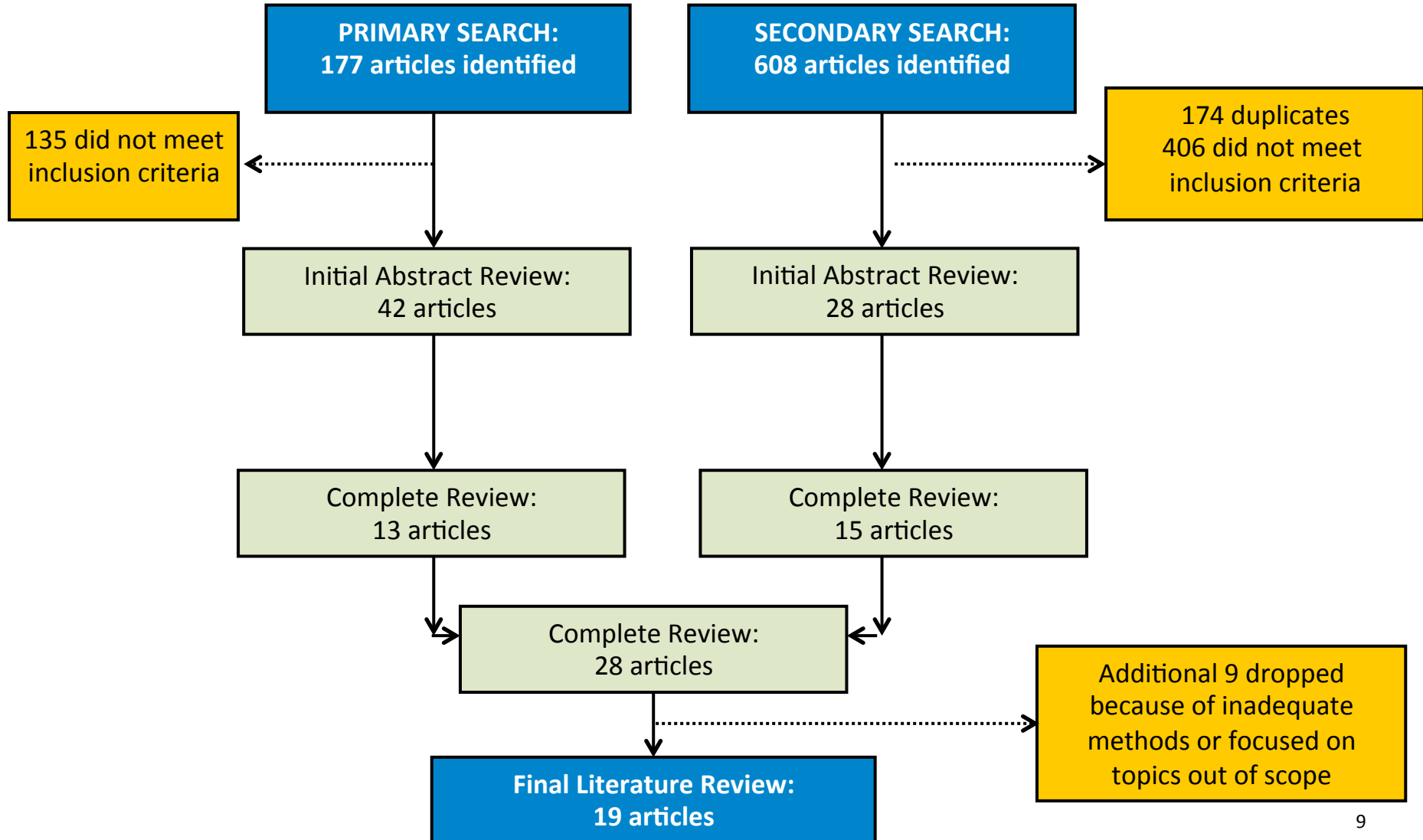
- The Depression Working Group is developing a new PRO instrument intended for use as a primary or key secondary endpoint in clinical trials for major depressive disorder to assess treatment efficacy from the patient's perspective
 - Proposed instrument will be developed and validated following the FDA's Drug Development Tools (DDT) qualification process [Draft guidance issued October 2010]

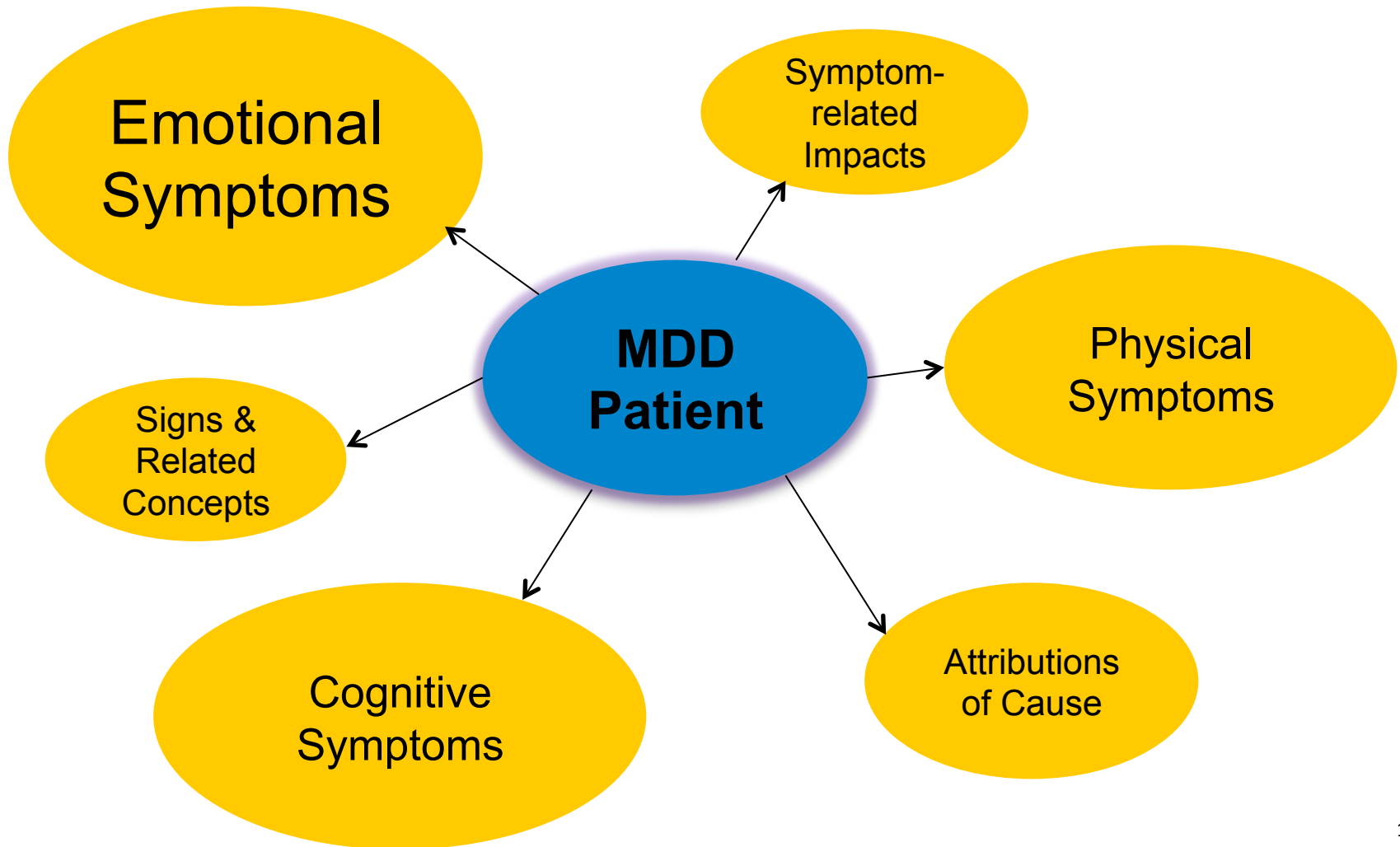
- Depression is a disease whose experience includes a wide range of symptoms that are subjectively experienced by patients
- However, efficacy of new treatments for MDD are typically evaluated using clinician assessment of symptoms, as defined by DSM-IV
- Assessing symptoms from the patient's perspective is critical to fully evaluate a treatment's risk/benefit ratio
- While many MDD PRO tools exist, none have yet been accepted by regulators to evaluate treatment efficacy to support labelling
- PRO Instrument Qualification requires a robust development process
 - Literature review, qualitative interviews with patients, expert panel review, item generation, cognitive interviews, quantitative testing
- As a first step towards seeking Regulatory Qualification of a PRO instrument to assess MDD symptoms in clinical trials, a systematic literature review was conducted to understand the patient's perspective

- To conduct a systematic literature review of published qualitative studies to understand the patient's perspective on MDD, including the language patients use to talk about their condition, and the symptoms and disease impacts of greatest importance to them

- **Systematic search of MEDLINE and PsychINFO**
 - **Primary Search Strategy**
 - Published in English language between 1991 and 2011
 - Peer-reviewed journal
 - Included community trials, case control studies, cohort studies, cross sectional studies, and qualitative studies
 - Studies had to include adults with diagnosed MDD
 - Principal search terms (used alone and in combination)
 - Major depression
 - Qualitative
 - Focus groups
 - Symptoms
 - Impacts
 - Patient attitude
 - **Secondary Search Strategy**
 - Searched for 'depression' AND 'qualitative' since January 2009

Articles Identified





Symptoms of Depression: Emotional

Symptoms

Sadness/wanting to cry

“...when I got to work and got into the office, I would just sit there and cry.”

Guilt

“It’s embarrassing, you feel guilty, you feel weak”

Low self-esteem/self-efficacy

Irritability/Anger

“Avoiding things, denying things, being more agitated and aggressive for no apparent reason”

Helplessness/Hopelessness

Loneliness

“It’s like a doorway that I know I can’t go through. I can’t do that to my parents....but I so much would just like to go to sleep and not wake up”

Thoughts of death

Symptoms of Depression: Physical

Symptoms

Fatigue

“You feel as though you are walking through a bog in the fog, like you’re dragging your limbs around”

Sleep Disturbance

Bodily Aches & Pains

“For me, it’s the sleeping and the withdrawing [that] are a key that something’s wrong”

Heart Palpitations

Chest Pressure

“I get real, what I think is physical pain in my arms, my shoulders, my chest, I have headaches at the back of my head”

Tingling in extremities

Dizziness

Gastrointestinal problems

“Everybody notices the weight loss. Everybody would be like, ‘Oh my God, what’s going on, what happened to you?’

Weight Changes

Symptoms of Depression: Cognitive

Symptoms

Intrusive thoughts

“I will be released from all of this, all of these thoughts”

Desynchrony with environment

“I just started waking up early...two in the morning, wide awake ...and you start worrying about the next day, and then... you worry about not sleeping. It’s a vicious cycle”

Cognitive Lethargy

“And my mental acuity also went.. it just scared the bee-gee-bees out of me, the lack of concentration I had at work”

Impacts

Social isolation, decreased social support, stigma

“you want to isolate yourself and you don’t actually want to be a part of all the normal things”

Relationship difficulties

“You don’t like to admit you’re a depressed person... there’s a negative view of someone with depression so you didn’t really let a lot of people know about it.”

Difficulties at work

Difficulties doing chores at home

“I get depressed and I don’t wanna do anything. If I didn’t have those symptoms I believe that I would be more active or more motivated to do more”

Decreased self-care

- **Concepts not easily defined by patients as symptoms, impacts or a cause of MDD**

Concept

Significant life changes

“I had to actually leave the province, how’s that for embarrassment?”

Stress

“Extremely stressed at work and feeling physiological effects of the stress . . .”

General anxiety

“Because of being depressed I have made really stupid choices... I started having sex with heaps of different people, and drugs and alcohol were even worse. And then the depression came...”

Drug & alcohol abuse

Concept

Life events, significant losses

“One of the things that affected me is the two children that died so close together...”

Discrimination

“I know a lot of black people that's depressed. Every black person I know is depressed”

Poverty

“Poverty is the reason. If you can meet your needs, the problems will lessen”

- **However, many patients reported limited or no understanding of the condition or its causes**
 - Increased feelings of despair and impotence, anxiety, shame and guilt
 - Made it more likely that patients would blame external factors for their symptoms

- **Depression is understood by patients in the terms of the symptoms, signs and disease-related impacts they are experiencing.**
- **Patients with depression focus their discourse more on their emotions as compared with other known clinical symptoms, such as cognitive and executive functioning symptoms**
- **A range of concepts not easily defined as symptoms of depression or as disease-related impacts were also a substantial focus of patient discourse, suggesting that from the patient's perspective comorbid symptoms are not distinctively derived from other conditions**
- **Patients' attributions of cause of depression should be investigated in detail during the qualitative interviews to provide important information on how they see the causes and impacts of their disease, but it may not be relevant for assessing illness severity**

- **Patients' discourse focused primarily on their emotional symptoms suggesting these are the most burdensome and should be the focus of a PRO instrument**
- **Impacts and attributions were more distal from symptoms, and while relevant to the understanding of the patient, these were supplementary to the core patient experience**
- **Implications for future research**
 - To assess efficacy from the patient's perspective, instruments for measuring clinical improvement in depression may need a more patient-centered foundation than used previously

- **Systematic Review of PRO instruments used to Assess Symptoms Associated with MDD**
 - Being presented in the PROs: Mood & Anxiety Symposia
- **Qualitative Concept Elicitation Interviews with Patients with MDD**
 - to determine the adoption, adaptation, or creation of a PRO instrument fit for the purpose of assessing MDD treatment benefit in clinical trials

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