A Systematic Approach to the Pharmacotherapy of Late-Life Depression

Benoit H. Mulsant, MD, MS, FRCPC

camh
Centre for Addiction and Mental Health
Centre de toxicomanie et de santé mentale

Psychiatry
UNIVERSITY OF TORONTO

Faculty/Presenter Disclosure

- **Relationships with commercial interests (past 5 years):**

Grants/Research Support: Brain Canada, CAMH Foundation, Canadian Institutes of Health Research (CIHR), US National Institute of Health (NIH), US Patient-Centered Outcomes Research Institute (PCORI)

Capital Solution Design LLC and HAPPYneuron: software used in studies founded by CAMH Foundation and Brain Canada

Bristol-Myers Squibb, Eli Lilly, and Pfizer: medications (or matched placebo pills) for NIH-funded clinical trials

Speakers Bureau/Honoraria: None

Consulting Fees: None

Other: Income from Center for Addiction and Mental Health, University of Toronto, University of Pittsburgh; directly held stocks from General Electric (less than $5,000)

Potential for Bias and Mitigation

- The use of some antidepressants, antipsychotics, and several other psychotropic medications will be discussed during this program.
- Generic names will be used
- Generic forms are available for almost all medications that will be mentioned.

Outline

- Prevalence and treatability
- Clinical course under usual care conditions
- Argument for a systematic approach (“protocol”, “algorithm”, “clinical pathways”, “stepped care”)
- Role of clinical skills
- Treatment-resistant depression

Treating Late-Life Depression: Fighting therapeutic nihilism

One of the few medical conditions in which treatment can make a rapid and dramatic difference in an elderly patient's level of function and quality of life

Major Depressive Disorder in Older Adults
Prevalence and Treatability

- High prevalence!
  - 3 to 5% in the community
  - 10 to 15% in clinical settings

- Absolute numbers increasing with greying population

- Highly treatable!

  173 patients treated over one year with five-step algorithm:

  87% response – 4% non-remission – 9% drop-out

Blazer et al, 2003, Whyte et al, 2004

Major Depressive Disorder in Older Adults
Clinical Course Under Usual Care Conditions

- Low initiation of treatment
- Poor adherence
- Early treatment drop-outs
- Partial remission
- Recurrence
- Chronicity

↑ Disability
↑ Use of health care resources
↑ Morbidity and mortality
Suicide

“How do we improve the quality of mental health care? […] We can do much better by delivering the treatments we have today. We can save lives –many lives – simply by closing the unconscionable gap between what we know and what we do.”

Tom Insel
Final blog as NIMH director
October 29, 2015

A Tale of Two Approaches

What we know:

Systematic Approach

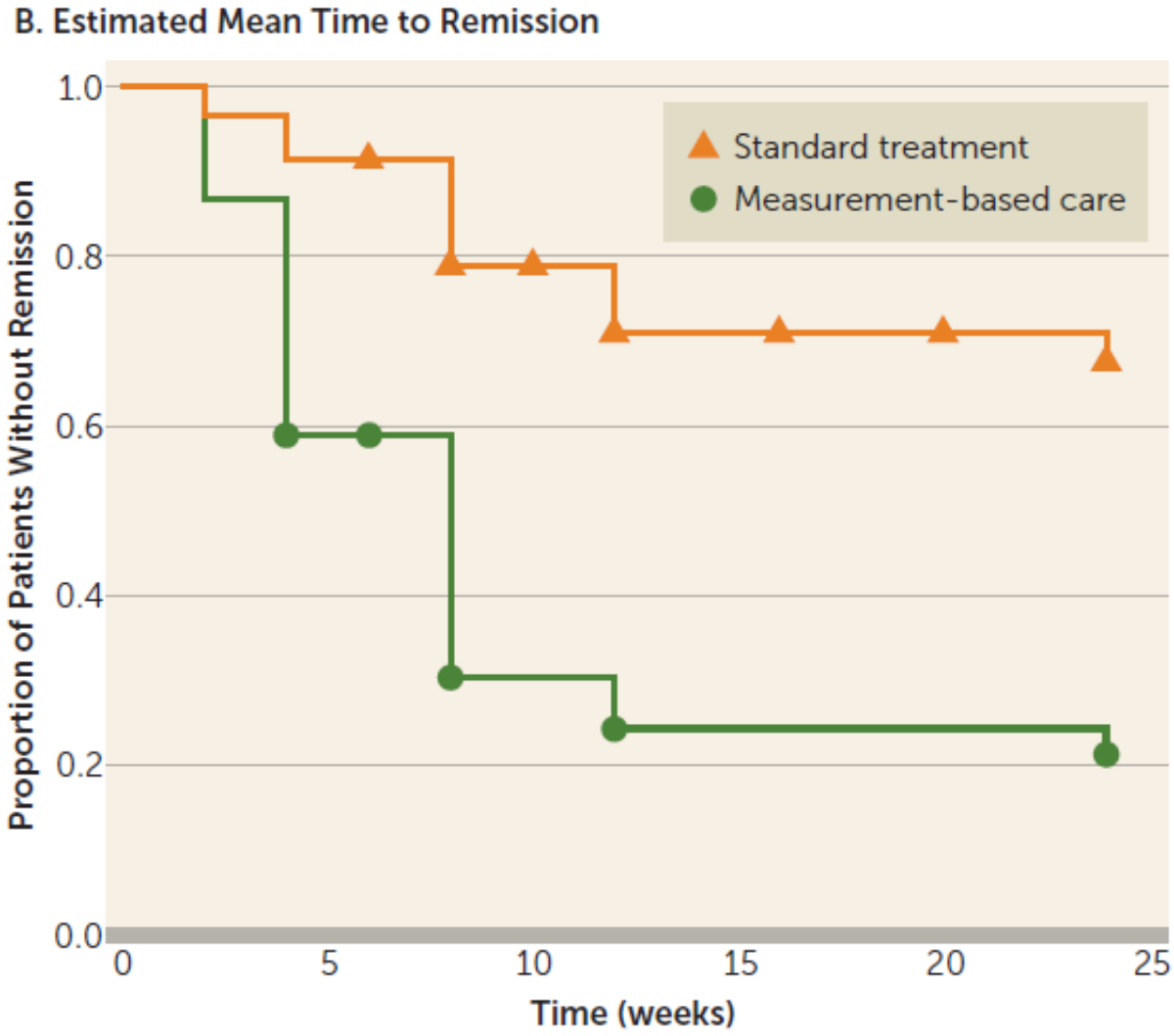
- Based on best evidence or guidelines
- Clinical experience based on large number of patients
- Keeping the course: the clinician is protected against personal biases, pressures from the patient or family
- Focus is on the patient

What we do:

Usual Care

- Based on fad “du jour”
- Little cumulative experience due to small numbers of patients receiving many different medications
- Ill-advised or ill-timed changes in treatment
- Focus is on the treatment (making decisions is exhausting)

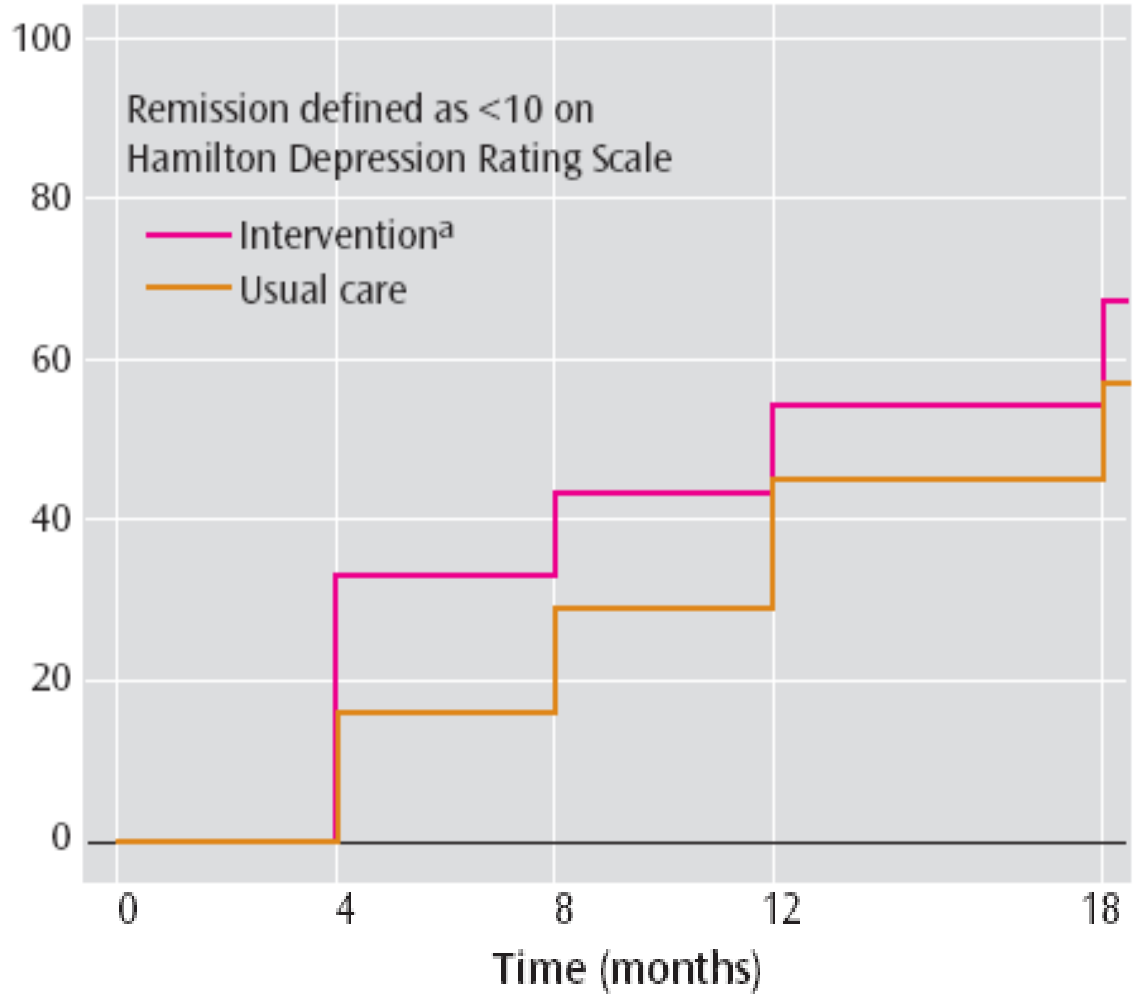
Measurement-Based Care vs. Standard Treatment While Controlling for Antidepressants



- Psychiatrists in a teaching hospital
- Adult outpatients with moderate to severe major depression
- **Pharmacotherapy restricted to paroxetine or mirtazapine <u>in both groups</u>**

Guo et al (2015) Am J Psych

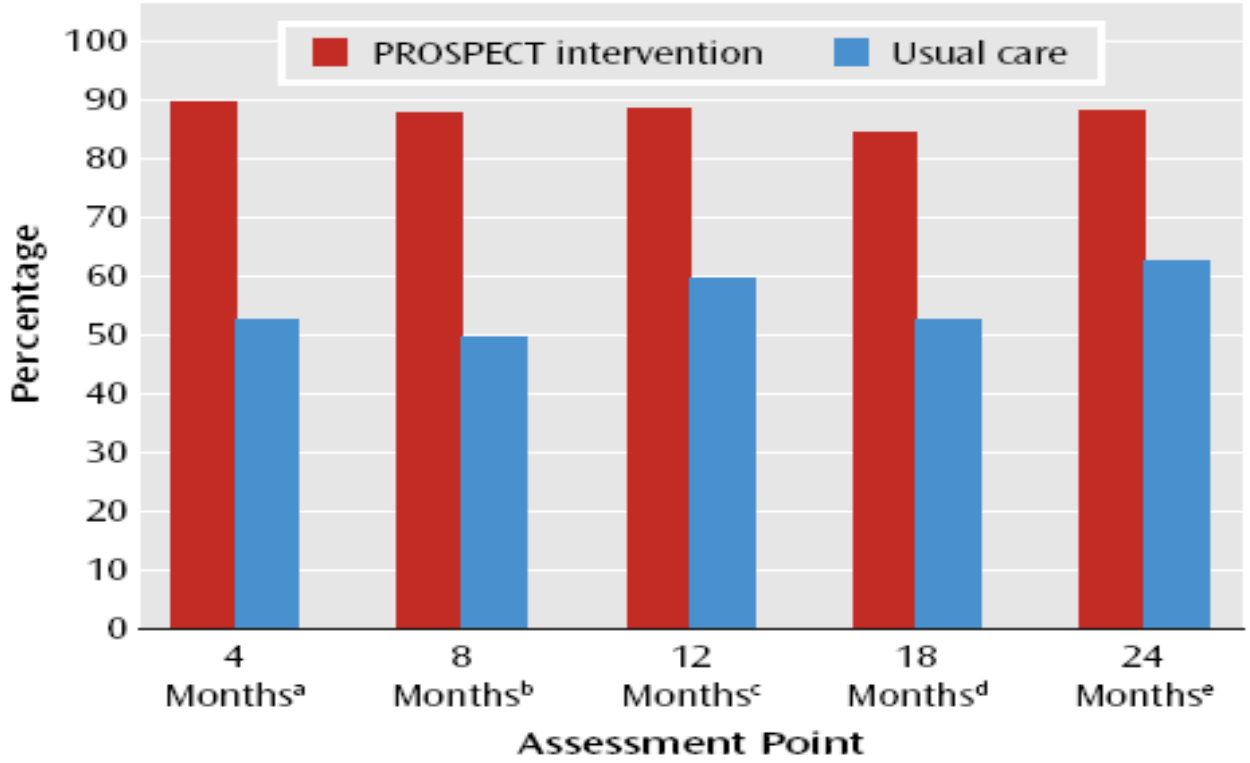
PROSPECT:
Cumulative Probability of Remission



Alexopoulos et al (2005) Am J Psych

PROSPECT:
Probability of Being Treated

FIGURE 2. Percentage of Depressed Older Primary Care Patients Who Received Treatment for Depression, by Assessment Point



All comparisons: $p < 0.0001$

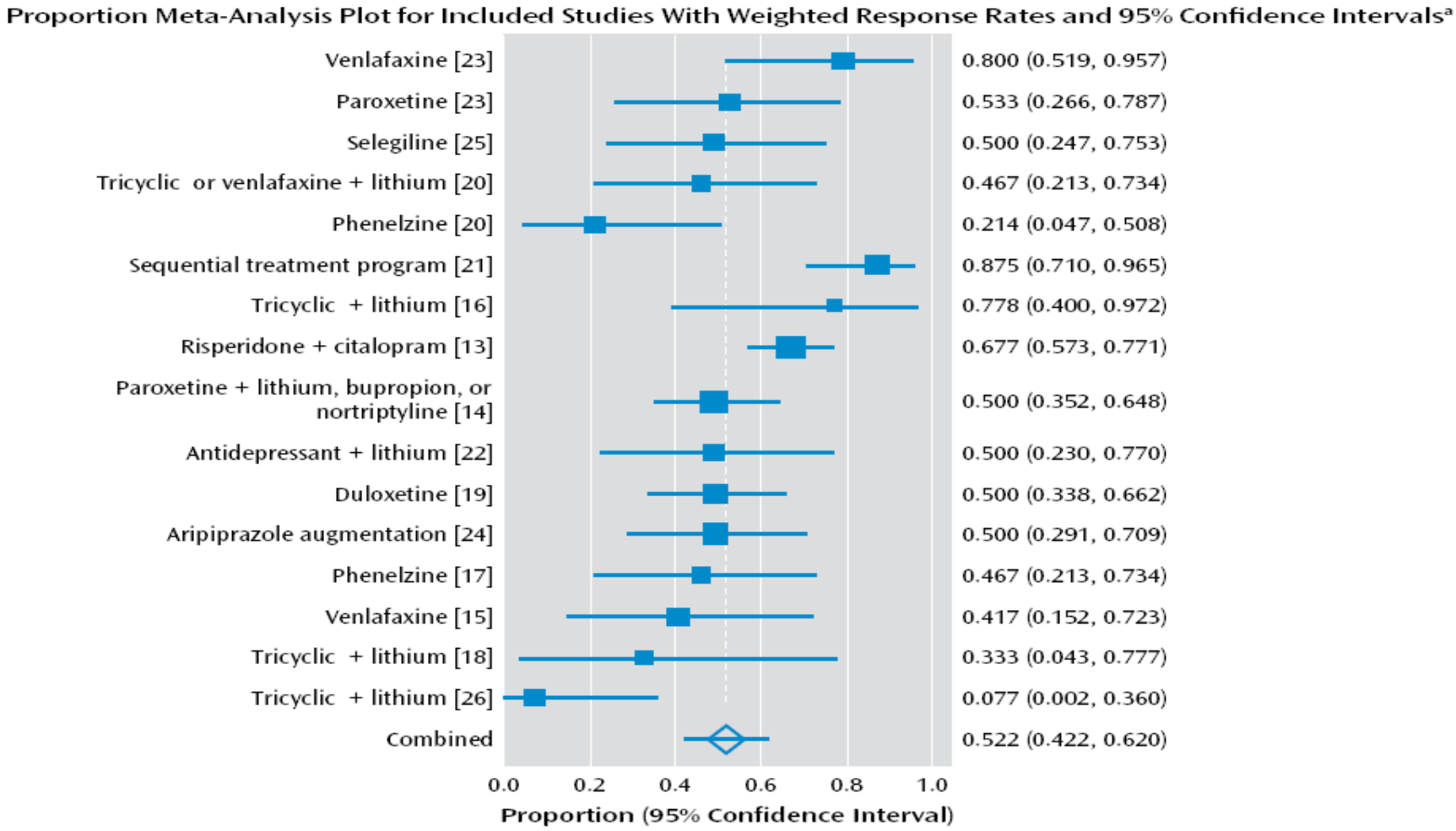
Alexopoulos et al (2009) Am J Psych

Clinical Skills Remain Essential for Successful Antidepressant Treatment

- Patients must be seen regularly
- Patients must be encouraged and supported to take dose regularly as prescribed
- Patient's personal illness model should be addressed
- It takes 2-6 weeks for beneficial effects
- Side effects occur right away (but many wear off)
- Need for continuation and maintenance treatment

Mulsant et al (2003) CNS Spectrum

Response Rates in 13 Studies of Treatment-Resistant Late-Life Depression



Cooper et al (2011) Am J Psych

Conclusions

Late-Life Depression:

- Can be effectively treated
- Requires a systematic approach
- Success requires persistence
- Do Not Give Up!