

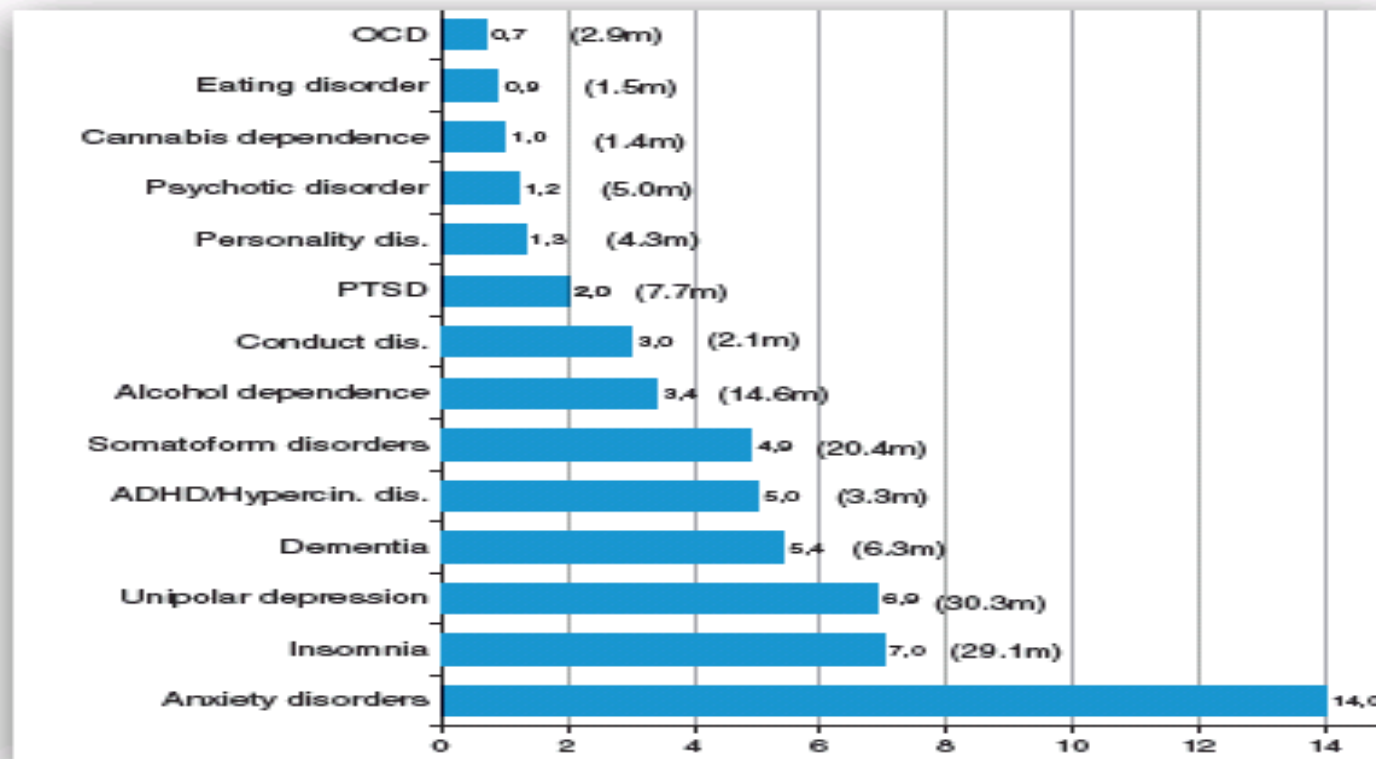
**Augmentation Strategies –
Focus on Depression,
Methodology, and Regulatory Perspective**

Co-chairs: Amir Kalali & Jill Rasmussen

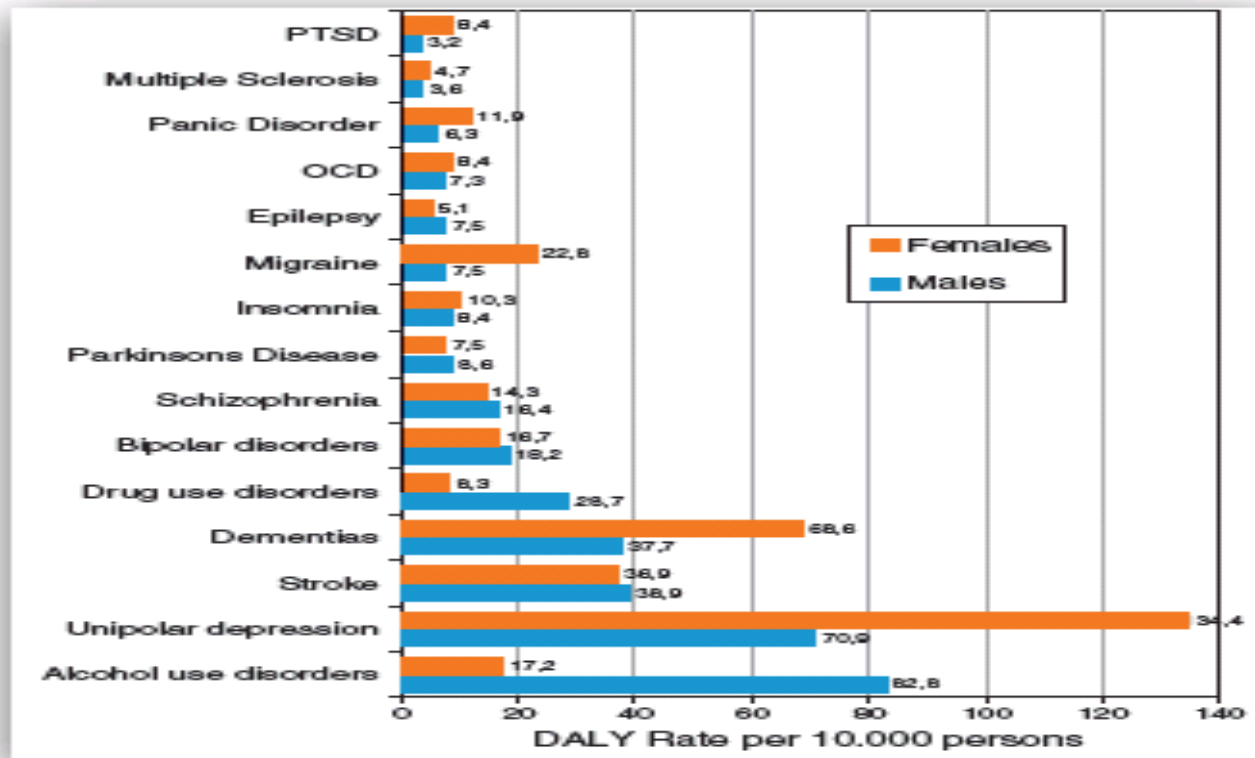
Why focus on Depression?

- **Burden of disease**
- **Only 1/3 pts remit**
- **Risk of recurrence**
- **Cost of research**
 - Need a minimum of 4 studies to have a reasonable chance of getting two studies with positive result
- **Limitations of current treatments as monotherapy**
 - Promises of improved profile and results not fulfilled
- **Unable to predict who will respond to which treatment**

Mental Disorders by Prevalence (estimated persons affected in millions)



Size and Burden of Mental Disorders and Other Disorders of the Brain in Europe 2010



Disability DALY Estimates

- **The new estimates**
 - **Confirm that disorders of the brain are the major contributor to the total EU disease burden;**
 - **Reveal that depression — in contrast to previous projections - is already now the most important single contributor to the total disease burden;**
 - **Show that there are tremendous diagnosis-specific differences, and highlight that even seemingly “less serious” disorders are associated with a substantial degree of disability**
 - **Confirm the existence of substantially different disability differences between females and males.**

Mental Health Problems the Statistics

- At least **1 in 4** people will experience a mental health problem at some point in their life and one in six adults has a mental health problem at any one time
- **1 in 10** children aged 5 –16 yrs has a mental health problem, and many continue to have mental health problems into adulthood
- Half of those with lifetime mental health problems first experience symptoms by the **age of 14 and three-quarters before their mid-20s**
- Self-harming in young people is not uncommon
 - **10–13% of 15–16-year-olds have self-harmed**
- Almost **half of all adults** will experience at least one episode of depression during their lifetime

Ref: No Health without Mental Health Feb 2011

Evidence from STAR*D

- **Four sequential levels of treatment based on Non-remission**
- **Remission rates levels 1 to 4**
 - 36.8%, 30.6%, 13.7%, 13%
 - Only 1/3 pts remitted at first treatment level
 - Only modest differences between treatments at each subsequent level
- **Although 67% pts remitted about a half relapsed over a 1 yr follow-up**
 - Increasing relapse rates at successive levels of care
 - 40.1%, 55.3%, 64.6%, 71.1%

Ref: Rush et al 2006

Conclusions from STAR*D

- **Depression difficult to treat to remission**
- **Low Sustained Remission** rates that are difficult to maintain with any treatment option or stepped treatment
- **High rates of tolerability problems**
- **Targeting monoamine neurotransmission alone appears insufficient for sustained benefit for most patients**

Ref: Shelton et al 2010

What can we do Better?

- **Most chronic diseases consider a “stepped care” model**
- **Lumping rather than splitting**
 - First vs recurrent
 - Genetics
 - Psychiatric vs physical co-morbidity
- **Alternative outcomes to mood alone:**
 - Emotion, cognition
 - LT effectiveness - function
- **What can we learn from research in other indications**

Augmentation Strategies – Methodology, and Regulatory Perspective

1:15 Introduction, Background, Concepts and Definition

- Jill Rasmussen; Amir Kalali

1:35 Antidepressant Augmentation: Acceleration & Enhancement Strategies

- Sidney Kennedy

2:00 Current Examples

- Geoffrey Dunbar, James Youakim, Erik Buntinx

2:45 Discussion / Followed by 30 min break

3:30 Regulatory Forum

FDA: Thomas Laughren

EMA - Karl Broich

4:15 Panel Discussion

Schizophrenia: Stephen Marder

Bipolar: Charles Bowden

Cognition: Richard Keefe

Discussant: Sidney Kennedy
