IVI INNOVATION AND VALUE INITIATIVE

IVI Major Depressive Disorder Model: Draft Protocol & Areas for Input

December 15, 2021 **1:00-2:00 PM ET**

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Agenda

- Objectives for IVI's Major Depressive Disorder (MDD) Model
- Draft Model Protocol Development Process
- Targeted Literature Review
- Model Structure and Inputs
- Key Areas for Feedback
- Q&A

Our Ask of You

Review and Submit Comments by January 18, 2022

Share with Your Colleagues

Share the Recorded Webinar with your colleagues

The Innovation and Value Initiative (IVI) is holding a public comment period on the draft protocol for its economic model of major depressive disorder (MDD) treatments. We are seeking feedback from a broad range of stakeholders from Dec. 14, 2021 – Jan. 18, 2022. This open-source model seeks to incorporate multiple perspectives, data sources, and outcomes relevant to diverse stakeholders. You can learn more https://www.thevalueinitiative.org/ivi-mdd-value-model/.

There are two ways to comment:

1) Submit via email to: public.comment@thevalueinitiative.org
2) Respond to survey: https://www.surveymonkey.com/r/PNY7PPF

Thank you!

Major Depressive Disorder Value Assessment Model Advisory Group

The multi-stakeholder Advisory Group provides guidance and insight into its research and model development efforts.

Comprised of clinicians, patients, researchers, payers, purchasers, health economists and industry actors, these experts review and provide input to the development of IVI project goals, the scope of the major depressive disorder (MDD) model and its component projects, and advise on key informants, expert panelists and researchers and patients that should be included throughout the initiative.

https://www.thevalueinitiative.org/wp-content/uploads/2020/11/2020-11-20.MDD-Advisory-Group.pdf

Speakers

Rick Chapman, PhD

Chief Science Officer

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Jordana Schmier, MA

Director, Real World Evidence

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Richard Xie, PhD

HEOR Research Manager

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Objectives for IVI's MDD Model

Objectives of the MDD Model

To build a **flexible**, **open-source**, and **patient-centric** model that will:

Advance the science and practice of health technology assessment (HTA) in the U.S. context

Facilitate multi-stakeholder conversations

Inform decision needs of multiple stakeholders in the health care system, including employers, payers, and clinicians

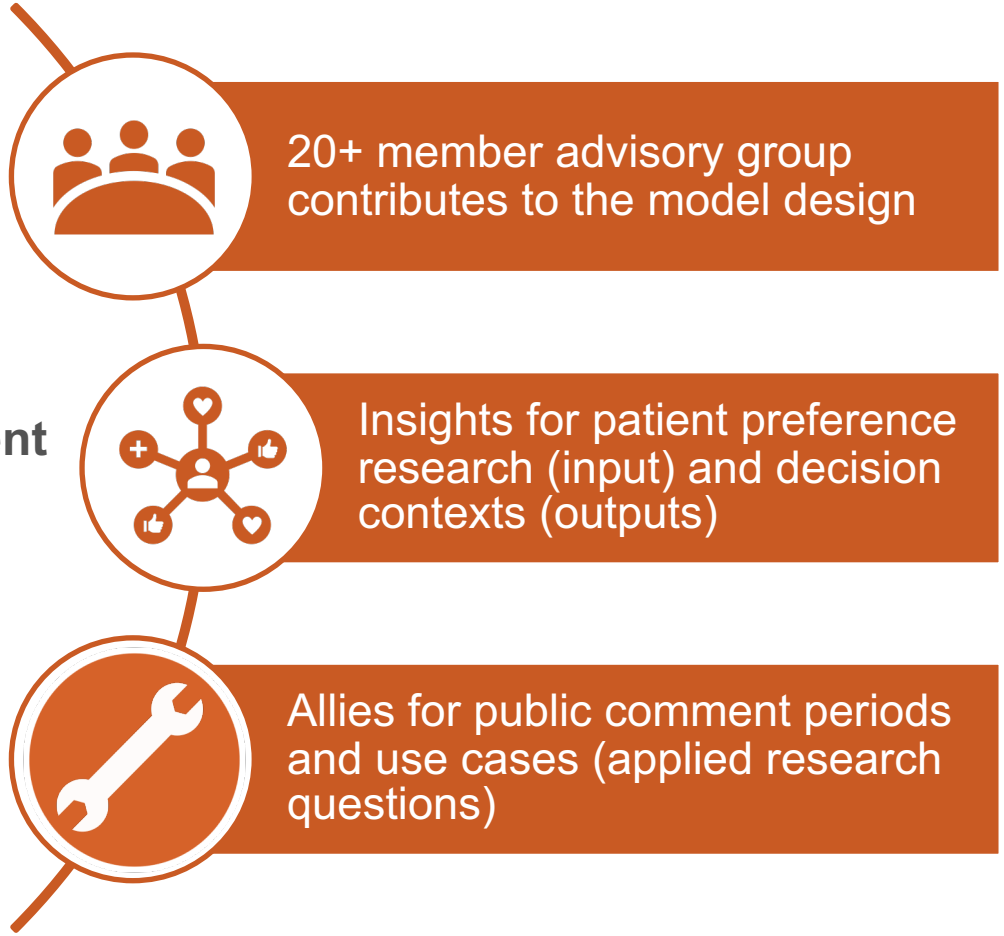
Draft Model Protocol Development Process

A Path Forward: Improving Value Assessment for MDD

IVI Open-Source Value Model

- **IVI prototype model development is a laboratory:** opportunity to improve both the process and mechanics of considering value
- **Focus on MDD based on:**
  - Prevalence
  - Societal burden
  - Impact on overall health
  - Evolving treatment landscape (both pharmacologic and non-pharmacologic)
  - Broad interest from multiple stakeholder groups

Model Development is a Team Effort



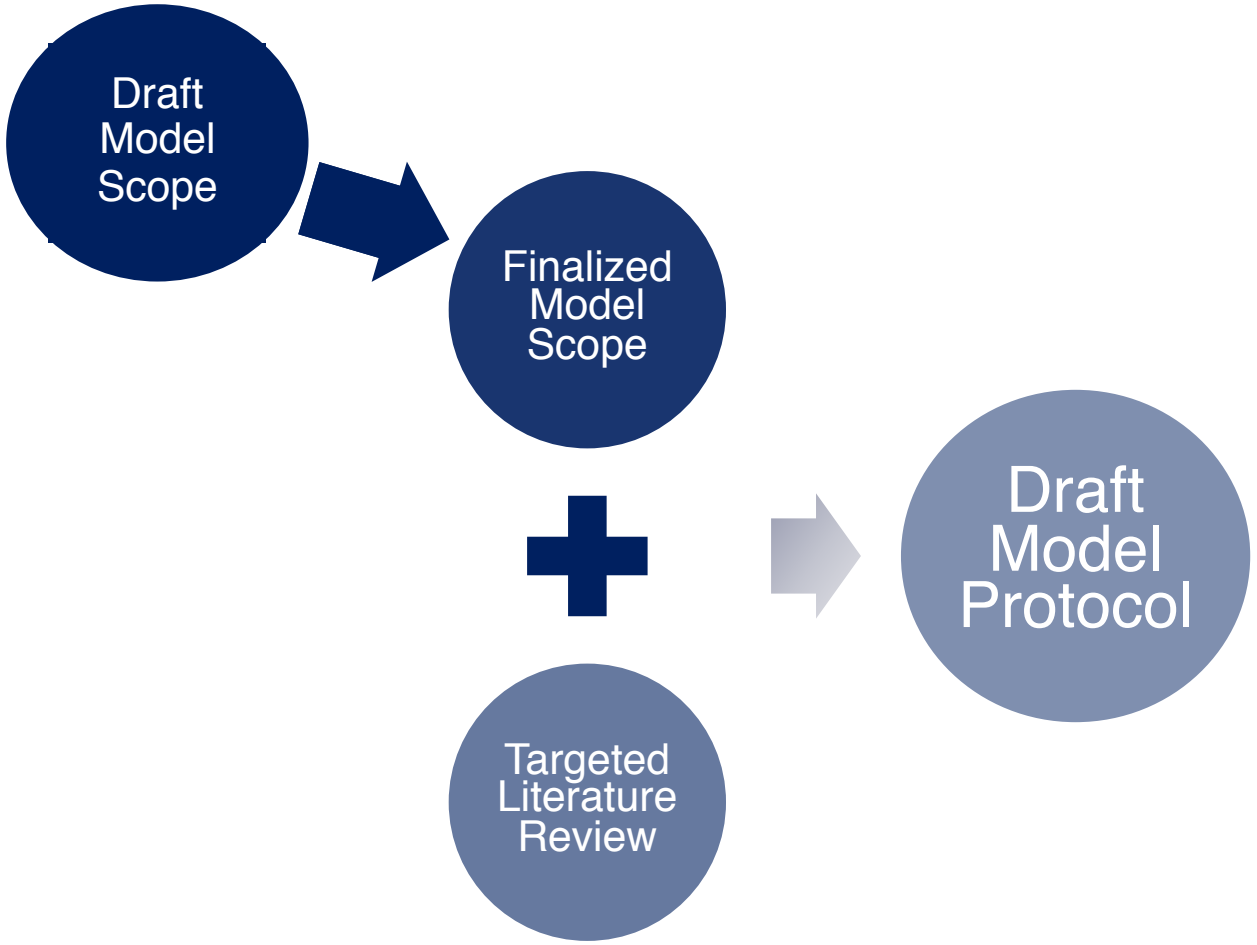
MDD Model - Health Economic Module

Specific Prioritized Research Questions

- What is the societal burden of untreated or under-treated MDD?
- How do key model outcomes vary for certain subgroups (e.g., those with prior treatment experience or lower socioeconomic status) compared with the overall population?
- What is “low-value” care in existing real-world treatment pathways?

Draft Model Protocol

Model protocol is a technical document that outlines all necessary details for model structure and analyses, including analytic approaches, assumptions, data inputs, and model outputs.



Finalized Model Scope

Dimension	Specification
Target Population	Treatment-naïve adults (age 18-64 years), diagnosed with MDD by a healthcare provider
Setting and Location	All settings of care (primary, specialty, and telehealth) in the United States
Study Perspective	Societal as base case, flexibility to customize based on specific stakeholder (e.g., employers)
Model Structure	Individual-level simulation
Comparators	Flexibility to model both treatment sequences and individual treatments, both pharmacologic and non-pharmacologic
Time Horizon	Lifetime horizon, flexibility for users to study interim time points (e.g., 1 year)
Outputs	Flexibility to present a range of different economic and clinical outcomes
Key Considerations	Including productivity, adherence, delay in starting active treatments for MDD

Targeted Literature Review

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Targeted Literature Review

- Objective: Identify data sources and evidence gaps to populate model
- Why meta-analyses/reviews: Expected to find meta-analyses of response to classes of therapies
- Search strategy: ProQuest, limited to English, focused on meta-analyses and systematic reviews, searches for MDD and treatment-resistant depression (TRD)
  - TRD as proxy for 3rd and 4th line therapy
  - Limited search to 2018 and more recent to manage number of reports needing review (<500)
- Findings (n=16 included, of 455 reviewed)
  - Effectiveness report in all; safety in 2; cost and utilities not reported in meta-analyses
  - Effectiveness most often reported as effect size
  - No more than 1-2 studies reporting on each type of intervention in each population

Targeted Literature Review: Alternatives for Gaps

- As anticipated, some key model inputs were not reported in meta-analyses. In these cases, we conducted additional TLR or proposed alternative assumptions:
  - Mortality - alternatives available for all-cause mortality for MDD and incremental mortality in TRD compared to MDD
  - Costs - alternatives include top-down (using claims data and attributing portion of costs to MDD) or bottom-up methods (using guidelines or other source to estimate resources used and assigning costs)
  - Effectiveness for 3rd and 4th line therapies - plan to use findings based on TRD populations to apply to later lines of therapy
- Did not anticipate challenges with effectiveness, safety, or utility data

Model Structure and Inputs

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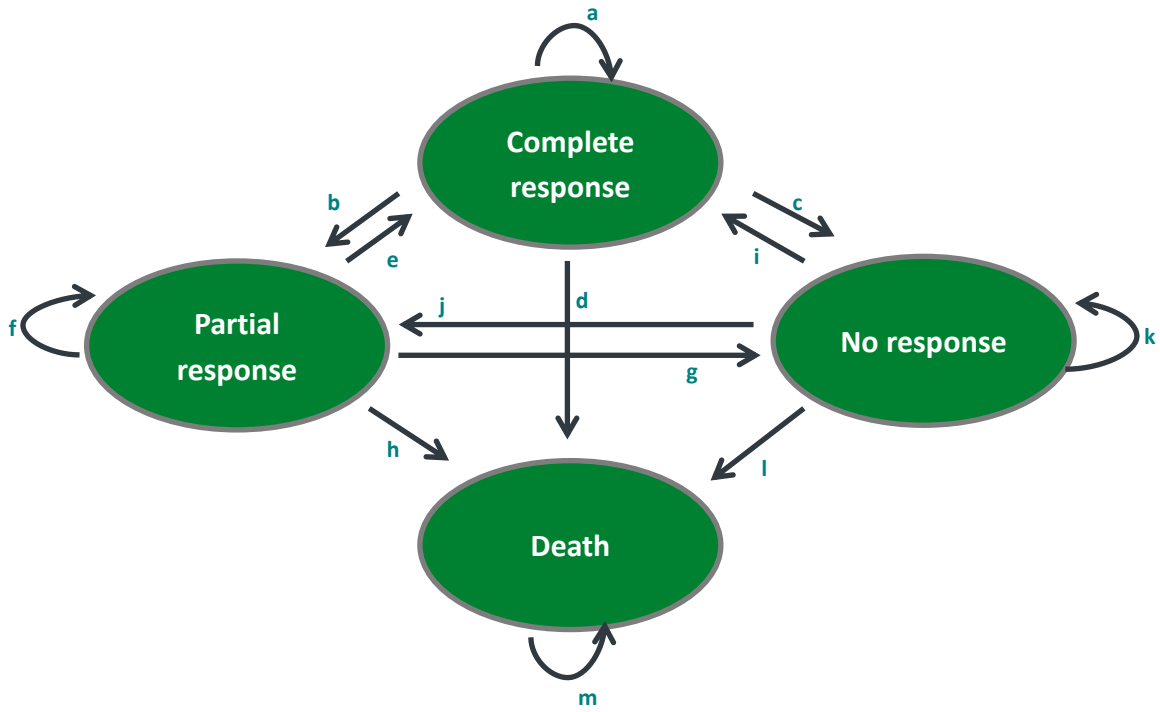
Model Structure: Microsimulation

- Why microsimulation?
  - Precedent from previous OSVP models, typically Markov with health states reflecting response
  - Interest in reflecting heterogeneity in MDD population
  - Flexibility for end users to customize insights based on their own populations
- Challenges of microsimulation
  - Simplification to limited number of health states may be perceived as glossing over important differences
  - Little or no data available yet on effectiveness by sociodemographic and economic characteristics of interest

Model Structure: Microsimulation

- Requires populating each transition, as shown
- Unique values/transition matrices would be needed for each intervention
- Can count the number of cycles in the same health state: e.g., multiple cycles in “Complete response” can constitute remission; multiple cycles in “No response” can indicate a need to start a new treatment



Defining Health States

Complete Response

- Three or more consecutive cycles of complete response => remission
- After remission, if next cycle is partial or no response, individuals can have recurrence
- After one cycle of complete response, if next cycle is partial or no response, individual is determined to have relapsed

Partial Response

- Individual can remain in partial response state indefinitely
- Can reflect inadequate response or willingness to accept partial response for manageable adverse event profile

No Response

- Health state includes treated individuals with no response and untreated individuals with continued symptoms

Questions:

Is it reasonable to assume that after two cycles of remission, individuals would switch to maintenance treatment, or should that be user-defined?

Is it reasonable to assume that after two cycles of partial response, individuals would switch to a new treatment?

Is it reasonable to assume that after one cycle of no response to treatment, individuals would switch to a new treatment?

Following Individuals over Time

- Lifetime follow-up, unlike typical short-term models
- Individuals can switch or discontinue therapies
- User can limit which treatments are available for each line of therapy within model
- Model will follow decision rules about when individuals switch
  - Should two cycles of “no response” => initiate new treatment?
  - Should two cycles of “partial response” => initiate new treatment?
  - Does the model need multiple scenarios (i.e., one with a more aggressive and quicker time to switch and one with a passive approach and longer duration with partial response permitted)?

Defining Health States

- Characterized by response to treatment
  - “Response” is defined similarly but not identically across studies
  - Assigned counter for cycle in health state, cost of intervention, cost of other resources, utilities, indirect costs
- Inputs required to move individuals from one health state to another
  - Limited data, often at only one or two time points
  - Challenge: How to extrapolate to lifetime

Model Input Challenges and Options

- Effectiveness
  - Limited data on response and utilities from meta-analyses
  - Should key clinical trials or well-designed observational studies be used?
  - Recommendations for building transition matrices sufficient for lifetime follow-up
- Costs
  - Direct medical costs: Have proposed top-down (identify proportion of all costs attributable to MDD) or bottom-up (identify individual resources required and assign costs) approaches; either could be implemented
  - Are there any ongoing studies that are better sources than the proposed options?

Model Input Challenges and Options

- Treatment sequencing
  - Are existing assumptions about when individuals would switch to a new treatment reasonable?
- Safety
  - Are there key adverse events with sufficient impact (on utility, discontinuation/switching, or cost) that should be included?
  - How should suicide be treated?
  - Is prescribing information or real-world evidence more appropriate for the model?
- Utilities
  - Is there a preference among the existing highly variable published estimates?
  - Are there any ongoing studies that are better sources than the proposed options or that provide insight on disutility associated with side effects?

Key Areas for Feedback

Key Areas for Feedback

- We are especially seeking your feedback in the following key areas:
  - data gaps in key model assumptions and inputs, as well as potential data sources and partners to address such gaps
  - prioritization of data sources and technical approaches when multiple valid approaches exist
  - potential use cases (i.e., which specific decisions within your organization could the MDD model help inform?)

Sample Questions

- General methodological questions
  - How to identify common set of AEs for a drug class vs, specific medications
  - Efficacy inputs for 3rd or 4th line treatments
  - Long-term efficacy inputs with limited evidence from literature
- Specific questions
  - Specific input sources for suicide attempts

Use Case Examples

- What is the impact of delay in diagnosis?
- Medicaid perspective: What is the impact of effective MDD treatment strategies on the ability of Medicaid-insured individuals to regain employment and transition into private insurance?
- Employer perspective: What are the impacts of adherence programs on productivity and other outcomes? Can the model incorporate patient-defined factors that affect adherence to therapy?
- What is the long-term value of considering heterogeneous patient preferences to tailor treatments to improve likelihood of good outcomes?

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MDD Project Timeline

Draft Model Protocol

Public Comment Period
Dec 14, 2021 – Jan 18, 2022

The model protocol is a technical document that outlines all necessary details for model structure and analyses, including the analytic approaches, assumptions, data inputs, and model outputs.

Final Model Protocol

Feb 2022

The draft model protocol will be finalized based on feedback from the public and input from the multi-stakeholder advisory group.

Model Public Release

Q2 2022

The major depressive disorder (MDD) value assessment model will allow users to use the model's pre-specified inputs or their own data sources to compare treatments for MDD. All model code is open source, and we invite users to provide feedback and recommendations for improvement.

Use Case Development and Model Updates

Ongoing

IVI and interested stakeholders will use the MDD model to conduct additional research projects. IVI will update the model as new data sources become available.

Q&A

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