

STAR*D – Detailed Overview

The Sequenced Treatment Alternatives to Relieve Depression (STAR* D) study is a study conducted over 6 years, funded by the National Institute of Mental Health (NIMH), including initial 4,041 participants and 2,876 “evaluable” MDD patients (i.e., after exclusion) which were then treated and followed through a pharmacological tree, comprising four treatment levels, starting with Citalopram in the first treatment level, and then either potentiation of the current patient’s medication or a switch to a different medication in the following treatment levels. The study aimed at achieving complete remission of a characterized depressive episode, and patients were encouraged to continue the study to the next treatment level if they did not achieve complete remission. Following initiation of each treatment level, participants were assessed at multiple time points (2, 4-, 6-, 9-, and 12-weeks post-treatment initiation with an optional week-14 visit). Clinical depression severity was measured at each visit by the Quick Inventory of Depressive Symptomatology (QIDS) scale, and the Hamilton-Depression Rating Scale (HDRS) at baseline and exit only. All participants provided written informed consent at enrollment, with consent and study protocols approved by institutional review boards at each participating institution.

PGRN-AMPS – Detailed Overview

The Pharmacogenomics Research Network Antidepressant Medication Pharmacogenomic Study (PGRN-AMPS) was a smaller study compared to STAR*D, which included 529 participants with nonpsychotic MDD and a HDRS score ≥ 14 who were recruited at the Mayo Clinic in Rochester, Minnesota, USA. Participants were offered an 8-week course of treatment with either Citalopram or Escitalopram and depressive symptoms were rated using QIDS and HDRS scales at initiation, with QIDS being rated at multiple time points afterward (4- and 8-week after treatment initiation). All patients provided written informed consent. The study protocol was approved by the Mayo Clinic Institutional Review Board.

Inclusion and Exclusion Criteria

Inclusion criteria for the current study were:

1. Male or female at the age of 18-75 years old
2. Indication of MDD diagnosis per DSM-5
3. Ability to read, understand and sign an informed consent document
4. Affiliated with a social security regimen

Exclusion criteria were:

1. Patient diagnosed with other major psychopathologies (i.e., schizophrenia, bipolar disorder, psychotic depression, geriatric depression)
2. Patient with a dysthymia or anxiety disorders such as social phobia and panic disorder
3. Patient requiring psychotropic medications such as second-generation antipsychotic medications, mood stabilizers, benzodiazepine, or antidepressants other than ones suggested by Predictix*
4. Patient is at substantial suicidal risk as judged by the treating physician
5. Patient has attempted suicide in the past year
6. Patient has any current unstable medical condition or surgical illness
7. Patient has history of seizure or convulsions
8. Patient has history of drug abuse or alcoholism in the last 6 months
9. Inadequate communication between the patient and the physician
10. Pregnant women lactating or parturient women**
11. Persons deprived of their liberty, hospitalized without consent or admitted to a health or social institution for purposes other than research**
12. Minors**
13. Majors under legal protection or unable to express their consent**
14. People in emergency situations who cannot express their prior consent**
15. Simultaneous participation in another clinical research or participation in another clinical research whose exclusion period is not terminated

*As this is a first pilot study, concomitant medications were not allowed. Nevertheless, only limited use of hypnotic or anxiolytic medications were allowed up to 2mg/day of (lorazepam or equivalent) for insomnia or anxiety, as per the physician discretion.

**These are vulnerable persons referred to in Articles L. 1121-5 to 8 and L. 1122-1-2 du Code de la Santé Publique.

Supplementary Table 1. Predictix Antidepressant Software Tool-Usability and Satisfaction questionnaire, intended for use by physicians ($n=2$); the answers presented here are averages of the final questionnaires' answers of two participating physicians

Measure	Average score of physicians, from 1 (disagree) to 7 (strongly agree)
Usefulness of the Predictix system	
It helps me be more effective	5.5/7
It helps me be more productive	5.5/7
It is useful	5.5/7
It saves me time when I use it	4.5/7
It meets my needs	5/7
It does everything I would expect it to do	5/7
Satisfaction from the Predictix system	
I am satisfied with it	6/7
I would recommend it to fellow physicians	5.5/7
It works the way I want it to work	5/7
I feel I need to have it	5/7
Ease of Use of the Predictix system	
It is easy to use	6/7
It is simple to use	6/7
It is user friendly	6.5/7
It requires the fewest steps possible to accomplish what I want to do with it	6/7
It is flexible	4/7
Using it is effortless	5/7
I can use it without written instructions	6/7
I don't notice any inconsistencies as I use it	5/7
I can recover from mistakes quickly and easily	4.5/7
I can use it successfully every time	5/7
Ease of Learning of the Predictix system	
I learned to use it quickly	6/7
I easily remember how to use it	6/7
I quickly became skillful with it	6.5/7

A

Currently

4. * Does the patient suffer from neuropathic pains

Select one option:

-- Select --

Clinical Questions

During the Past 6 Months

5. * Has the patient been bothered by aches and pains in different parts of their body?

Select one option:

-- Select --

6. * Has the patient been worried about having a serious illness, in a way that it interfered with activities or caused them problems?

Select one option:

-- Select --

7. * Has the patient regularly avoided doing something because they were afraid of having an anxiety attack?

Select one option:

-- Select --

B

Medication	Dosage Optimization	Important note
HIGH RATE		
Venlafaxine	++	
Mirtazapine	++	
MEDIUM RATE		
Citalopram	+++	
Duloxetine	++	
① Escitalopram	+	Possible sexual dysfunction
Fluoxetine	++	
Fluvoxamine	++	
Paroxetine	+++	
LOW RATE		
Sertraline	+	
① Bupropion	++	Reported distressing side effect
Milnacipran	++	

Supplementary Figure 1: Inputs and outputs of the Predictix system (of the version which was used in the study). (A) Screenshot of a random sample of questions from the Predictix questionnaire, completed for each patient (B) Screenshot of a Predictix report (produced for a fictional patient, of the version which was used in the study), which is sent to the physician once all the necessary information for the Predictix algorithm is inputted to the system. In the 2nd page of the report, a legend appears which states as follows: **High Rate:** High likelihood for compatibility, to be prescribed/used subject to an advice of a qualified physician, **Medium Rate:** Medium likelihood for compatibility, to be prescribed/used with caution subject to an advice of a qualified physician, **Low Rate:** Low likelihood for compatibility, to be prescribed and/or used only under strict instructions and monitoring by a qualified physician, **Dosage + :** Consider reduction of standard dose as appears in the Medication Guide, and titrate to maximum tolerated dose, **Dosage + + :** Consider administrating standard recommended dosage as appears in the Medication Guide, **Dosage + + + :** Consider increase and titration up to maximal allowed dose as appears in the Medication Guide