EFFECTIVENESS OF MOOD STABILIZER IN EUTHYMIC BPAD PATIENTS-AN ONE YEAR PROSPECTIVE OBSERVATIONAL STUDY, COMPARING LITHIUM V/S DIVALPROATE SODIUM.

Submitted

BY

DR SARAH AFREEN MBBS

Dissertation submitted to

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY, CHENNAI,

In partial fulfilment of the requirements for the degree of

DOCTOR OF MEDICINE IN PSYCHIARY

Under the guidance of

Dr. I. SYED UMMAR

Associate Professor

DEPARTMENT OF PSYCHIATRY,

PSG INSTITUTE OF MEDICAL SCIENCES AND RESEARCH

COIMBATORE – 2017

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled "**Effectiveness of mood stabilizer in euthymic BPAD patients-An one year prospective observational study, comparing lithium v/s divalproate sodium" is** a bonafide and genuine research work carried by me under the guidance of Dr. I. SYED UMMAR, Associate Professor, Department of Psychiatry, PSGIMS & R, Coimbatore.

PLACE: COIMBATORE **DR. SARAH AFREEN**

DATE:

CERTIFICATE BY THE GUIDE

This is to certify that this dissertation entitled "**Effectiveness of mood stabilizer in euthymic BPAD patients-An one year prospective observational study, comparing lithium v/s divalproate sodium."** is a bonafide work done by Dr**. SARAH AFREEN in** partial fulfilment of the requirement for the degree of M.D (PSYCHIATRY).

PLACE: COIMBATORE **Dr. I. SYED UMMAR, M.D**

DATE: **ASSOCIATE PROFESSOR**

DEPARTMENT OF PSYCHIATRY

PSGIMS&R

ENDORSEMENT BY THE HOD/ DEAN OF THE INSTITUTION

This is to certify that this dissertation "**Effectiveness of mood stabilizer in euthymic BPAD patients-An one year prospective observational study, comparing lithium v/s divalproate sodium" i**s a bonafide research work done by **Dr. SARAH AFREEN under** the guidance of Dr**. I. SYED UMMAR**, Associate Professor, Department of Psychiatry, PSGIMS&R, and Coimbatore.

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DATE:

PLACE:

ACKNOWLEDGEMENT

At the outset, I thank God for giving me the strength to perform all my duties.

It is indeed a great pleasure to recall the people who have helped me in the completion of my dissertation. Naming all the people who have helped me in achieving this goal would be impossible, yet I attempt to thank a selected few who have helped me in diverse ways.

I acknowledge and express my humble gratitude and sincere thanks to my beloved teacher and guide **Dr.I.SYED UMMAR,** M.D (Psychiatry), Associate Professor, Department of Psychiatry, PSGIMS&R, Coimbatore for his valuable suggestion, guidance, great care and attention to details that he has so willingly shown in the preparation of this dissertation.

I owe a great deal of gratitude to all my Professors, Associate Professors and Assistant Professors, Department of Psychiatry, PSGIMS&R, Coimbatore for their whole hearted support for completion of this dissertation.

I thank the Nursing staff for their valued support and care for our patients in the hospital.

My sincere thanks to all my post graduate colleagues and my friends for their whole hearted support.

Finally, I thank my patients who formed the backbone of this study, without them this study would have not been possible.

PLACE: **Dr. SARAH AFREEN**

DATE:

PSG Institute of Medical Sciences & Research
Institutional Human Ethics Committee

Recognized by The Strategic Initiative for Developing Capacity in Ethical Review (SIDCER)
POST BOX NO. 1674, PEELAMEDU, COIMBATORE 641 004, TAMIL NADU, INDIA
Phone : 91 422 - 2598822, 2570170, Fax : 91 422 - 2594400, Email : ihec@psgimsr.ac.in

To
Dr Sarah Afreen
Postgraduate
Department of Psychiatry
PSG IMS & R
Coimbatore

Ref: Project No. 14/404

Date: January 8, 2015

Dear Dr Sarah Afreen,

Institutional Human Ethics Committee, PSG IMS&R reviewed and discussed your application dated 05.12.2014 to conduct the research study entitled "*Effectiveness of mood stabilizer in euthymic BPAD patients - an one year prospective observational study, comparing lithium vs divalproate sodium in department of Psychiatry OP*" during the IHEC review held on 19.12.2014.

The following documents were reviewed and approved:

1. Project Submission form
2. Study protocol
3. Informed consent form
4. Data collection tool
5. Current CVs of Principal investigator, Co-investigators
6. Budget

The following members of the Institutional Human Ethics Committee (IHEC) were present at the meeting held on 19.12.2014 at College Council Room, PSG IMS & R between 2.00 pm am and 4.30 pm:

Sl. No.	Name of the Member of IHEC	Qualification	Area of Expertise	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
1	Mrs Y Ashraf	MPT	Physiotherapy	Female	Yes	Yes
2	Dr. S. Bhuvaneshwari (Member-Secretary, IHEC)	MD	Clinical Pharmacology	Female	Yes	Yes
3	Mr Gowpathy Velappan	BA., BL	Legal Advisor	Male	No	Yes
4	Mr P Karuppuchamy	M Phil in PSW	Social Scientist	Male	Yes	Yes
5	Mrs G Malarvizhi	M Sc	Nursing	Female	Yes	Yes
6	Mr. R. Nandakumar (Vice-Chairperson, IHEC)	BA., BL	Legal Expert	Male	No	Yes

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7	Dr. G. Rajendiran	DM	Clinician (Cardiology)	Male	Yes	Yes
8	Dr. V. Ramamurthy	Ph D	Biotechnology	Male	Yes	No
9	Mrs P Rama	M Pharm	Non-Medical (Pharmacy)	Female	Yes	Yes
10	Dr. P. Sathyan (Chairperson, IHEC)	DO, DNB	Clinician (Ophthalmology)	Male	No	Yes
11	Dr. Seetha Panicker	MD	Clinician (Obstetrics & Gyanaecology)	Female	Yes	Yes
12	Dr. S. Shanthakumari	MD	Pathology, Ethicist	Female	Yes	No
13	Dr. Sudha Ramalingam (Alternate Member-Secretary, IHEC)	MD	Public Health, Epidemiology, Genetics, Ethicist	Female	Yes	No
14	Mrs. Swasthika Soundararaj	MBA	Lay person	Female	No	Yes
15	Dr. D. Vijaya	M Sc, Ph D	Basic Medical Sciences (Biochemistry)	Female	Yes	Yes

The study is approved in its presented form. The decision was arrived at through consensus. Neither PI nor any of proposed study team members were present during the decision making of the IHEC. The IHEC functions in accordance with the ICH-GCP/ICMR/Schedule Y guidelines. The approval is valid until one year from the date of sanction. You may make a written request for renewal / extension of the validity, along with the submission of status report as decided by the IHEC.

Following points must be noted:

1. IHEC should be informed of the date of initiation of the study
2. Status report of the study should be submitted to the IHEC every 12 months
3. PI and other investigators should co-operate fully with IHEC, who will monitor the trial from time to time
4. At the time of PI's retirement/intention to leave the institute, study responsibility should be transferred to a colleague after obtaining clearance from HOD, Status report, including accounts details should be submitted to IHEC and extramural sponsors
5. In case of any new information or any SAE, which could affect any study, must be informed to IHEC and sponsors. The PI should report SAEs occurred for IHEC approved studies within 7 days of the occurrence of the SAE. If the SAE is 'Death', the IHEC Secretariat will receive the SAE reporting form within 24 hours of the occurrence
6. In the event of any protocol amendments, IHEC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b. Alteration in the budgetary status should be clearly indicated and the revised budget form should be submitted
   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval
   d. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented
   e. If there are any amendments in the trial design, these must be incorporated in the protocol, and

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other study documents. These revised documents should be submitted for approval of the IHEC and only then can they be implemented

f. Any deviation-Violation/waiver in the protocol must be informed to the IHEC within the stipulated period for review

7. Final report along with summary of findings and presentations/publications if any on closure of the study should be submitted to IHEC

Kindly note this approval is subject to ratification in the forthcoming full board review meeting of the IHEC.

Thanking You,

Yours Sincerely,

8.8.1.15

Dr S Bhuvaneshwari
Member-Secretary
Institutional Human Ethics Committee

SECRETARY
PSG IMS&R
COIMBATORE-641004.
INSTITUTIONAL HUMAN ETHICS COMMITTEE

PSG Institute of Medical Sciences & Research
Institutional Human Ethics Committee

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January 8, 2016

To
Dr Sarah Afreen
Postgraduate
Department of Psychiatry
Guide: Dr I Syed Ummar
PSG IMS & R
Coimbatore

The Institutional Human Ethics Committee, PSG IMS & R, Coimbatore -4, has reviewed your proposal on 8th January, 2016 in its expedited review meeting held at IHEC Secretariat, PSG IMS&R, between 10.00 am and 11.00 am, and discussed your request to renew the approval for the study entitled:

"Effectiveness of mood stabilizer in euthymic BPAD patients - an one year prospective observational study, comparing lithium Vs divalproate sodium in department of Psychiatry OP patients"

The following documents were received for review:

1. Request for renewal dated 01.01.2016
2. Status report

After due consideration, the Committee has decided to renew the approval for the study.

The members who attended the meeting held on at which your proposal was discussed, are listed below:

Sl. No.	Name of the Member of IHEC	Qualification	Area of Expertise	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
1	Mr R Nandakumar (Chairperson, IHEC)	BA., BL	Legal Expert	Male	No	Yes
2	Dr. S. Bhuvaneshwari (Member-Secretary, IHEC)	MD	Clinical Pharmacology	Female	Yes	Yes
3	Dr S Shanthakumari	MD	Pathology, Ethicist	Female	Yes	Yes
4	Dr Sudha Ramalingam	MD	Epidemiologist, Ethicist Alt. member-Secretary	Female	Yes	Yes
5	Dr D Vijaya	M Sc., Ph D	Basic Medical Sciences (Biochemistry)	Female	Yes	Yes

The approval is valid for one year (08.01.2016 to 07.01.2017).

This Ethics Committee is organized and operates according to Good Clinical Practice and Schedule Y requirements.

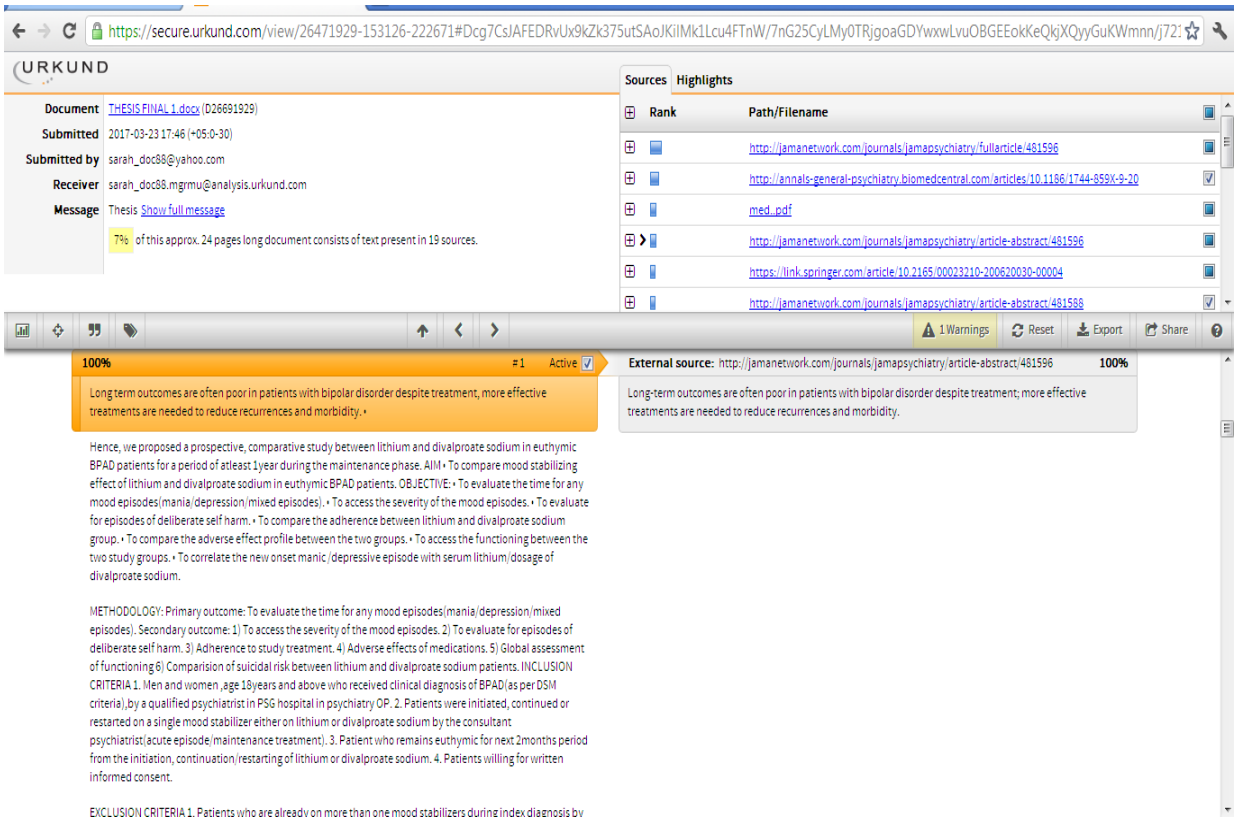
Non-adherence to the Standard Operating Procedures (SOP) of the Institutional Human Ethics Committee (IHEC) and national and international ethical guidelines shall result in withdrawal of approval (suspension or termination of the study). SOP will be revised from time to time and revisions are applicable prospectively to ongoing studies approved prior to such revisions.

Kindly note this approval is subject to ratification in the forthcoming full board review meeting of the IHEC.

Yours truly,

SECRETARY
PSG IMS&R
COIMBATORE-641004

Dr S Bhuvaneshwari
Member - Secretary
Institutional Human Ethics Committee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Long term outcomes are often poor in patients with bipolar disorder despite treatment, more effective treatments are needed to reduce recurrences and morbidity. •
Hence, we proposed a prospective, comparative study between lithium and divalproate sodium in euthymic BPAD patients for a period of atleast 1year during the maintenance phase. AIM • To compare mood stabilizing effect of lithium and divalproate sodium in euthymic BPAD patients. OBJECTIVE: • To evaluate the time for any mood episodes(mania/depression/mixed episodes). • To access the severity of the mood episodes. • To evaluate for episodes of deliberate self harm. • To compare the adherence between lithium and divalproate sodium group. • To compare the adverse effect profile between the two groups. • To access the functioning between the two study groups. • To correlate the new onset manic /depressive episode with serum lithium/dosage of divalproate sodium.
METHODOLOGY: Primary outcome: To evaluate the time for any mood episodes(mania/depression/mixed episodes). Secondary outcome: 1) To access the severity of the mood episodes. 2) To evaluate for episodes of deliberate self harm. 3) Adherence to study treatment. 4) Adverse effects of medications. 5) Global assessment of functioning 6) Comparision of suicidal risk between lithium and divalproate sodium patients. INCLUSION CRITERIA 1. Men and women ,age 18years and above who received clinical diagnosis of BPAD(as per DSM criteria),by a qualified psychiatrist in PSG hospital in psychiatry OP. 2. Patients were initiated, continued or restarted on a single mood stabilizer either on lithium or divalproate sodium by the consultant psychiatrist(acute episode/maintenance treatment). 3. Patient who remains euthymic for next 2months period from the initiation, continuation/restarting of lithium or divalproate sodium. 4. Patients willing for written informed consent.
EXCLUSION CRITERIA 1. Patients who are already on more than one mood stabilizers during index diagnosis by
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Long-term outcomes are often poor in patients with bipolar disorder despite treatment; more effective treatments are needed to reduce recurrences and morbidity.

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ABSTRACT

BACKGROUND:

Bipolar affective disorder patients, a major mental illness continues to be a distressing disorder. Lithium carbonate and divalproate sodium remains FDA approved. Studies on its long term outcome, adherence to medication, adverse effects remains less.

OBJECTIVE:

- To evaluate the time for any mood episodes(mania/depression/mixed episodes).
- To access the severity of the mood episodes.
- To evaluate for episodes of deliberate self harm.
- To compare the adherence between lithium and divalproate sodium group.
- To compare the adverse effect profile between the two groups.
- To access the functioning between the two study groups.
- To correlate the new onset manic /depressive episode with serum lithium/dosage of divalproate sodium.

METHODOLOGY:

We recruited 52 patients each on lithium and Divalproate arm, who qualified for inclusion & exclusion criteria. These patients were followed up for one year in psychiatry OP (initial evaluation 3^{rd} ,later 6^{th} ,9^{th} ,12^{th} month periodic evaluation).

Socio-demographic details, severity of mood disorders, adherence of medications, adverse effects and functioning were accessed.

RESULTS:

The socio-demographic variables did not differ between the two groups. The confounding variables (age of onset, number of episodes, previous hospitalisations, polarity of previous episodes, use of psychotrophics) did not differ between the two groups.

The duration of mood stabiliser was for a longer period in lithium group.

Patients on lithium, on prolonged follow up had less frequent & less severe manic episode, less suicidal risk(trending towards significance).

CONCLUSION:

There was no difference in terms of frequency of depressive episode, adherence, adverse effects and global functioning between the two groups. But lithium group patients had lesser manic episodes, less severe episodes and low suicidal risk , favouring Lithium to be a better mood stabilizer.

INTRODUCTION

- BPAD is one of the most disabling mental illness affecting most productive period of life at the age 15-45years.[1]Lithium carbonate is a gold standard treatment for past five decades. It has a narrow therapeutic index and significant adverse effects[2].
- Anticonvulsants (divalproate sodium, carbamazapine & oxcarbazapine), proposed as an alternative, as more adverse effect profile and there comparative efficacy with lithium is uncertain.[3-8]
- Lithium Carbonate being a gold standard mood stabilizer is a superior agent to reduce the risk of relapse and to prevent suicidal behaviours[(2-7).]In view of its adverse effects tolerance becomes an issue, which can interfere with adherence.[(4-7)]
- Anticonvulsants ,approved by FDA, has the next level of evidence as a mood stabilizer but there long term safety and efficacy is incomparision with Lithium remains uncertain.[(7)]
- Lithium causes multiple skin reactions the most common are acne and psoriasis.[(9)]
- The prevalence of skin reaction with lithium ranges between 3-34%.[(9)]

- A study shows high chances of discontinuation of lithium is due to adverse skin reactions.
- Randomised controlled trails have shown superiority of Divalproate sodium to placebo.[10-11]
- Divalproate sodium has been comparable with Lithium in Manic episode.[11]
- FDA approved mood stabilisers for the treatment of bipolar affective disorder are lithium, divalproate sodium, carbamazepine and lamotrigine.[17-20]
- Mood stabiliser can also be used as monotherapy which was approved by FDA.[21-22]
- Mania with two or more episodes of depression showed a good improvement with divalproate sodium than lithium.[23-24]
- Lithium and divalproate sodium showed more effect than any other mood stabiliser during acute mania phase and maintenance phase.[25-27]
- Olanzapine, risperidone, quetiapine are FDA approved atypical antipsychotics for the acute phase of mania.[17,18,20]

- Olanzapine is approved for maintenance monotherapy in bipolar patients.
- Quetiapine is used for both bipolar depression and maintenance therapy along with divalproate sodium and lithium.

REVIEW OF LITRATURE

- According to BALANCE study both lithium monotherapy and combination therapy with lithium and divalproate sodium are more likely to prevent relapse than divalproate sodium monotherapy, irrespective of baseline severity of illness and is maintained for upto 2years[12].

- Bowden et al, in his randomized placebo controlled 12months trial Lithium v/s Divalproate sodium, has shown no significant difference between the two groups in terms of time to recurrence of mood episode during maintenance therapy [10] .

- Compared to placebo, Divalproate sodium has lesser discontinuation rate[(13).]

- Even though open labelled trails favours Divalproate sodium , in reducing the frequency and intensity of further episodes, there are less comparative study with Lithium in maintenance therapy.[(14-16)]

- In a study by Martin Alda et al , Lithium was appreciated as a standard of comparison for long term treatment of BPAD[(47)] .

- Majority of the guidelines insist to continue the same drug used in acute treatment for maintenance therapy , unless side-effects profile preclude its long-term usage [48-53] .

RATIONALE:

- Long term outcomes are often poor in patients with bipolar disorder despite treatment, more effective treatments are needed to reduce recurrences and morbidity.
- Hence, we proposed a prospective, comparative study between lithium and divalproate sodium in euthymic BPAD patients for a period of atleast 1year during the maintenance phase.

AIM

- To compare mood stabilizing effect of lithium and divalproate sodium in euthymic BPAD patients.

OBJECTIVE:

- To evaluate the time for any mood episodes(mania/depression/mixed episodes).
- To access the severity of the mood episodes.
- To evaluate for episodes of deliberate self harm.
- To compare the adherence between lithium and divalproate sodium group.
- To compare the adverse effect profile between the two groups.
- To access the functioning between the two study groups.
- To correlate the new onset manic /depressive episode with serum lithium/dosage of divalproate sodium.

METHODOLOGY

Primary outcome:

To evaluate the time for any mood episodes(mania/depression/mixed episodes).

Secondary outcome:

1. To access the severity of the mood episodes.
2. To evaluate for episodes of deliberate self harm.
3. Adherence to study treatment.
4. Adverse effects of medications.
5. Global assessment of functioning
6. Comparison of suicidal risk between lithium and divalproate sodium patients.

INCLUSION CRITERIA

1. Men and women, age 18years and above who received clinical diagnosis of BPAD (as per DSM criteria),by a qualified psychiatrist in PSG hospital in psychiatry OP.
2. Patients were initiated, continued or restarted on a single mood stabilizer either on lithium or divalproate sodium by the consultant psychiatrist (acute episode/maintenance treatment).
3. Patient who remains euthymic for next 2months period from the initiation, continuation/restarting of lithium or divalproate sodium.
4. Patients willing for written informed consent.

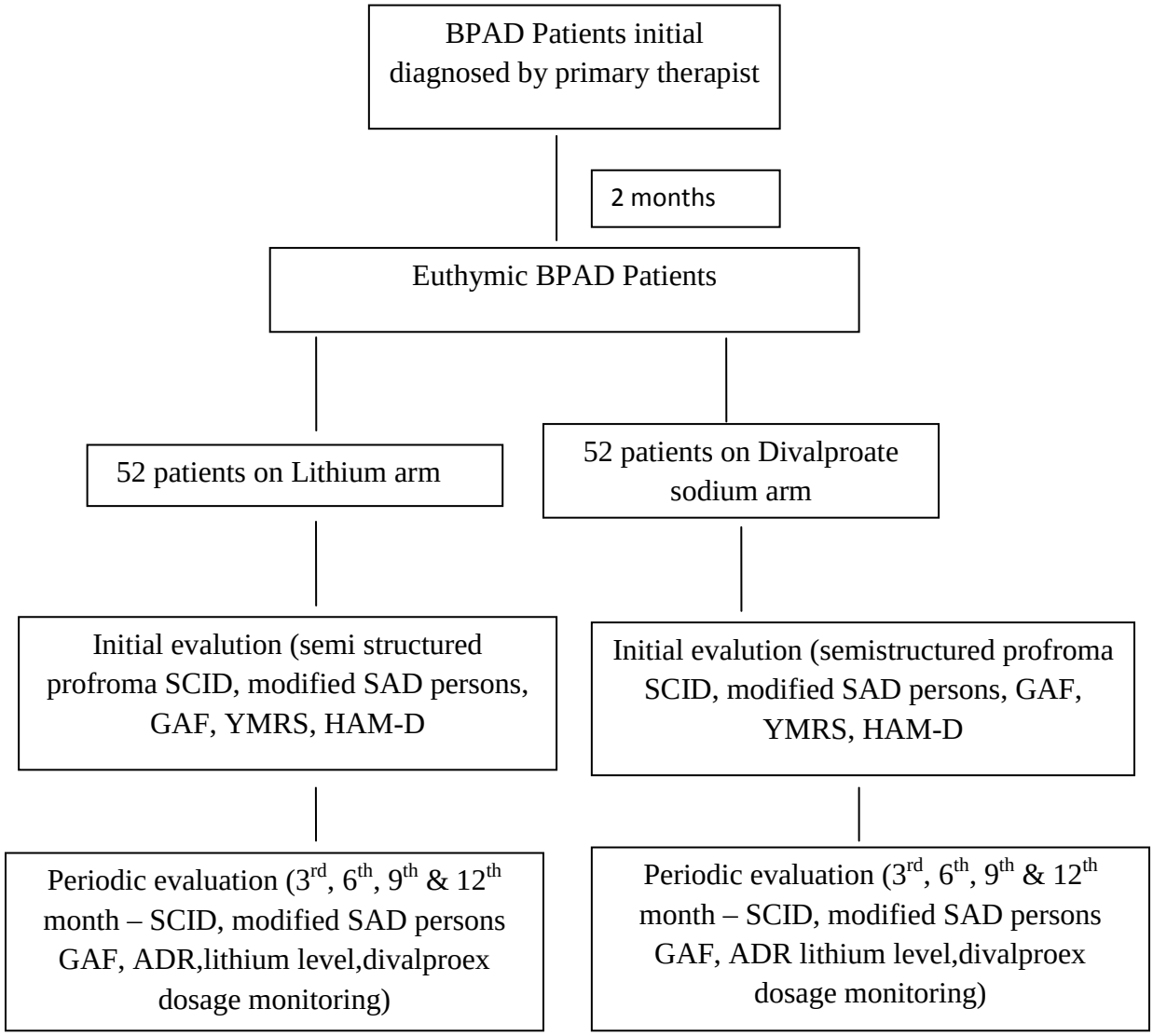
EXCLUSION CRITERIA

1. Patients who are already on more than one mood stabilizers during index diagnosis by the consultant.

2. Presence of any uncontrolled systemic disorders.

3. Patient not willing for informed consent.

FLOWCHART 1: Describing the methodology



- After recruiting the patients as per our inclusion and exclusion criteria, 52 patients who were on lithium therapy and 52 patients who were on divalproate therapy(acute episode/maintenance therapy),were prospectively followed up for 1year period in psychiatry Out Patient Department at PSG institute of medical science and research Coimbatore.

- Patients were evaluated by the investigator, following 2months of euthymic period(index evaluation).

- During follow up patients were evaluated at 3^{rd} ,6^{th},9^{th} and 12^{th} month respectively(periodic evaluation).

- No interventions are done in our study as it is an observational study.

- Patient who are missing on follow up are contacted through telephone and requested to come for follow up and assessed, if necessary.

- During initial evaluation ,a semi-structured proforma (socio-demographic details and other confounding variables) is administered. Euthymic status of the patient is ensured by applying a SCID version for mood disorder. Severity of suicidal ideas is

assessed by Modified SADPERSONS Scale. Global Assessment of Functioning, was assessed using a GAF scale.

- The dosage of the mood stabilizer could be altered by the primary therapist based on serum concentration of the drug/adverse effects, during 1year maintenance period.
- Participants who remain on the allotted treatment for 1year of study.
- Use of other psychotropics are allowed during the study trial (antipsychotics ,benzodiazepines).
- During **periodic evaluation** the following are accessed:
    1. Confounding variables.
    2. SCID-mood disorder sub-scale.
    3. YMRS.
    4. HAM-D .
    5. Modified SADPERSONS scale-to assess suicidal score.
    6. Adverse drug reaction.
    7. Global assessment of functioning (GAF)scale.
    8. Serum lithium level
    9. Dosage of divalproate sodium.

Category of Socio-demographic details:

1) The age was categorized into three groups:

   18-40years- early adulthood

   40-60years- late adulthood

   >60years- geriatric group.

2) Education level was categorized into four groups:

   Illiterate

   Upto 10^{th} std

   11^{th} -12^{th} std

   Graduates.

3) Marital status was categorized into five groups:

   Unmarried

   Married Living together

   Married and living separately

   Married- legally divorced

   Widow or widower.

Category of Confounding variables:

1) Age of onset of illness was categorized into four groups:

   Childhood<18years

   18-40years-early adulthood

   40-60years-Late adulthood

   Geriatric >60years.

2) Number of previous episodes was categorized into four groups:

No episodes,

One episode,

Two episode,

>=3 episodes.

3) Previous hospitalizations was categorized into four groups:

No hospitalization,

One hospitalization,

Two hospitalizations,

>=3 hospitalisations.

4) Polarity of episodes was categorized into seven groups:

No episode,

1Depressive episode,

1 Manic episode,

Depression=Mania,

Depression>Mania,

Mania>Depression,

>=2 Manic episodes.

5) The psychotrophics given was categorized into five groups:

No drugs,

Typical antipsychotics,

Atypical antipsychotics,

Antidepressants,

Benzodiazepines.

Category of Mood stabilizers:

The duration of use of mood stabilizer was categorized into four groups:

<6months,

6months-1year,

1year-2year,

>2years.

Rating Scales:

1) Young Mania Rating Scale(YMRS) was categorized into three groups:

No mania

Mild to Moderate

Severe

2) Hamilton depression rating scale (HAMD)was categorized into three groups:

No depression

Moderate

Severe

3) Suicidal Risk Scale(SADS) was categorized into three groups:

No risk

Moderate risk

Severe risk

4) Adverse Drug Effect(ADR) was categorized into three groups :

No drug reaction

Minimal drug reaction

More drug reaction

5) Global Assessment Functioning(GAF) was categorized from 0-3 based on scores:

Good (90-100)

Mild impairment (60-80)

Moderate impairment (50-60)

Severe impairment (<50)

6) The Time for Mania was assessed in patients which was categorized into five groups :

No episode,

<3months,

3months- 6months,

6months – 9months,

9months -12months.

7) The Time for Depression was assessed which was categorized into five groups:

No episode,

<3 months,

3months-6months,

6months- 9months,

9months-12months.

8) The number of follow ups was assessed and was categorized into five groups: No follow ups,

One follow up,

Two follow ups,

Three follow ups,

Four follow ups.

SAMPLE SIZE:

According to the formula to estimate sample size

$$\frac{\text{Sample size}}{d^2} = (z\alpha+z\beta)^2 * p * q * 2$$

Estimated sample size is 98 in each group.

Because of time constrain and availability of patient in our department. We thought to have sample size of 52 in each group.

RATING SCALES USED:

YMRS:

The Young Mania Rating Scale is commonest scale used in mania for rating the patients condition over past 48hours.This has 11 items, each item has scoring according to the severity of the symptoms.

Four items are scored from 0-8 and rest seven items are scored from 0-4[27,28].

HAM-D:

Hamilton depression rating scale is the commonest scale used in depression patients to assess the severity of the illness [29].

This scale is administered in patients who have no underlying organic cause.[30]

Hamilton [31-32] reported the scale was not for the diagnostic purpose but it was used to differentiate depression from other diagnosis like other affective disorders, anxiety disorders and other mental illness with varying in there sensitivity and specificity[33-38].

Modified SADPERSONS scale-to see suicidal score:

SADS PERSONS Scale consist of major 10 factors to assess the risk in adult suicide.

The scoring ranges from 0-14 which consist of age, gender and subjective related assessment is done.[39)]

Global assessment of functioning (GAF) scale:

The GAF is translated in many languages and used across the world for the assessment of the functioning.[40-43)]

GAF does not reflect the diagnosis of the patient, but needs information in many aspects which measures the overall functioning of mental illness and psychological condition.[43-45)]

It scores the degree of mental illness by rating the social, psychological and occupational functioning. [42-46)]

STATISTICAL ANALYSIS

The Data entered in excel sheet was conducted using software package used for statistical analysis (SPSS) version 20.

We compared the efficacy of lithium and divalproate sodium with the following variable such as age, gender, marital status and education status and were expressed in percentage and their association was analysed using chi square test with statistical significance of P value <=0.05.

The association of age of onset, number of previous episodes, previous hospitalisation, polarity of previous episodes, psychotrophics and duration of mood stabiliser with that of lithium and divalproate sodium was done using chi-square that with statistical significant of P value <=0.05.

Association of duration of illness ,association of time for any mood episodes, time taken for manic episode, depressive episode ,association of severity of manic episode and depressive episode ,association of suicidal risk, adherence to study, association of adverse effects , association of global assessment functioning between lithium and divalproate sodium was done using chi-square test with statistical significance of P value <0.05.

We compared the new mood episode with varying serum lithium levels, using chi-square test with statistical significant with P value <=0.05.

We compared the new mood episode with varying divalproate dosage, using chi-square test with statistical significant with P value <=0.05.

We compared the frequency with mania and depression episode, we depicted in bar diagram.

RESULTS

Table 1:

Comparison of sociodemographic variable between Lithium and Divalproate sodium group:

AGE:

		Lithium	Divalproate sodium	P value
Age	Early Adulthood	31(59.6%)	25(48.1%)	0.392
	Late Adulthood	18(34.6%)	21(40.4%)	
	Geriatric	3(5.8%)	6(11.5%)	

31 Patients on lithium had developed bipolar effective disorder in early adulthood,18 patients in late adulthood and 3 patients in the geriatric group.

25 patients on divalproate sodium had developed bipolar effective disorder in early adulthood, 21 had developed in late adulthood and 6 developed in geriatric group.

GENDER:

		Lithium	Divalproate Sodium	P Value
Gender	**Male**	32(61.5%)	39(75.0%)	0.140
	Female	20(38.5%)	13(25.0%)	

32 patients on lithium were male and 20 were female.

39 patients on divalproate sodium were male and 13 were female.

EDUCATION STATUS:

		Lithium	Divalproate sodium	P value
Education Status	**Illiterate**	7(13.5%)	14(26.9%)	0.101
	Upto 10^{th} std	27(51.9%)	20(38.5%)	
	11^{th}-12^{th}	5(9.6%)	10(19.2%)	
	Graduate	13(25.0%)	8(15.4%)	

Of the patients on lithium, 7 were illiterate, 27 had education until 10^{th} class, 5 until 12^{th} class and 13 had graduated. In the group of patients on divalproate sodium 14 were illiterate, 20 had studied upto 10^{th} class, 10 upto 12^{th} class and 8 had completed graduation.

MARITAL STATUS:

		Lithium	Divalproate sodium	P value
Marital Status	**Unmarried**	15(28.8%)	11(21.2%)	0.169
	Married, living together	32(61.5%)	26(50.0%)	
	Married, living separately	3(5.8%)	7(13.5%)	
	Married, divorced	1(1.9%)	4(7.7%)	
	Widow/widower	1(1.9%)	4(7.7%)	

Among patients on lithium 15 were unmarried, 32 were married and living together, 3 were married and living separately, 1 had divorced and 1 was a widow/widower. Among patients receiving divalproate sodium 11 were unmarried, 26 were married and living together, 7 were married and living separately, 4 were divorced and 4 were widow/widower.

There was no significant difference between the two groups in sociodemographic variables like age(P=0.392),Gender(P=0.140), Educational qualification(P=0.101) and Marital Status(P=0.169).

TABLE 2:

Impact of confounding variables on Lithium and Divalproate sodium patients:

AGE OF ONSET:

		Lithium	Divalproate sodium	P value
Age of Onset	**Early adulthood**	19(36.5%)	9(17.3%)	0.085
	Late adulthood	27(51.9%)	36(69.2%)	
	Geriatric	6(11.5%)	7(13.5%)	

The onset of bipolar disorder among patients on lithium was in early adulthood for 19 patients, late adulthood for 27 and old age for 6. The onset of bipolar disorder among those receiving divalproate sodium was in early adulthood for 9 patients, late adulthood for 36 and old age for 7.

NUMBER OF EPISODES:

		Lithium	Divalproate Sodium	P Value
Number of Episodes	**1episode**	0(0.0%)	3(5.8%)	0.145
	2episode	18(34.6%)	13(25.0%)	
	>=3episodes	34(65.4%)	36(69.2%)	

Among the patients on lithium 18 patients had 2 episodes and 34 patients had 3 or more episodes. Among the patients on divalproate sodium 3 had 1 episode, 13 had 2 episodes and 36 had 3 or more episodes.

PREVIOUS HOSPITALISATIONS:

		Lithium	Divalproate sodium	P value
Previous Hospitalisation	**No hospitalisation**	7(13.5%)	6(11.5%)	0.594
	1hospitalisation	9(17.3%)	5(9.6%)	
	2hospitalisation	15(28.8%)	19(36.5%)	
	>=3hospitalisation	20(38.5%)	22(42.3%)	

Of the patients receiving lithium, 7 had never been hospitalised for the disorder, 9 had been hospitalised once, 15 had been hospitalised twice and 20 were hospitalised thrice or more for bipolar disorder. Of the patients receiving divalproate sodium, 6 had never been hospitalised for the disorder, 5 had been hospitalised once, 19 had been hospitalised twice and 22 were hospitalised thrice or more for bipolar disorder.

POLARITY OF PREVIOUS EPISODES:

		Lithium	Divalproate sodium	P value
Polarity of previous episodes	**1depressive episode**	1(1.9%)	0(0.0%)	0.373
	1manic episode	4(7.7%)	6(11.5%)	
	Depression=mania	18(34.6%)	14(26.9%)	
	Depression>mania	11(21.2%)	7(13.5%)	
	Mania>depression	12(23.1%)	12(23.1%)	
	>=2 mania episodes	6(11.5%)	13(25.0%)	

Of the patients on lithium, 1 patient had one depressive episode, 4 had one manic episode, 6 had two or more manic episodes, 18 had depression equal to mania, 11 had predominantly depressive episodes and 12 had predominantly manic episodes. Of the patients on divalproate sodium, 6 had one manic episode, 13 had two or more manic episodes, 14 had depression equal to mania, 7 had predominantly depressive episodes and 12 had predominantly manic episodes.

PSYCHOTROPHICS:

		Lithium	Divalproate sodium	P value
Psychotrophics	**No drugs**	23(44.5%)	13(25.0%)	0.982
	Typical antipsychotics	7(13.5%)	15(28.8%)	
	Atypical antipsychotics	19(36.5%)	21(40.4%)	
	Antidepressants	2(3.8%)	2(3.8%)	
	Benzodiazepines	1(1.9%)	1(1.9%)	

Of the patients on lithium, 23 had not taken any drug before, 7 had taken typical antipsychotics, 19 had taken atypical antipsychotics, 2 had taken antidepressants and 1 had taken benzodiazepines before. Of the patients on divalproate sodium, 13 had not taken any drug before, 15had taken typical antipsychotics, 21 had taken atypical antipsychotics, 2 had taken antidepressants and 1 had taken benzodiazepines before.

DURATION OF MOOD STABILIZER:

Duration of Mood Stabilizer		**Lithium**	**Divalproate Sodium**	**P value**
	<6months	1(1.9%)	0(.0%)	**0.001**
	6months-1year	7(13.5%)	1(1.9%)	
	1-2year	5(9.6%)	20(38.5%)	
	>2years	39(75.0%)	31(59.6%)	

Among the patients receiving lithium, 1 had taken mood stabilisers for less than 6 months,7 had taken for 6-12 months, 5 had taken for 1-2 years and 39 had taken for more than 2 years. Among the patients receiving divalproate sodium, 1 had taken mood stabilisers for 6-12 months, 20 had taken for 1-2 years and 31 had taken for more than 2 years.

There is no statistical significance among the confounding variables like Age of onset (P=0.085), Number of episodes (P=0.145), Previous hospitalisations (P=0.594), polarity of episodes (P=0.373), Psychotrophics (P=0.982) Between the two groups.

The Duration of illness (P=0.001) was the only confounding variable which was significant between the two groups.

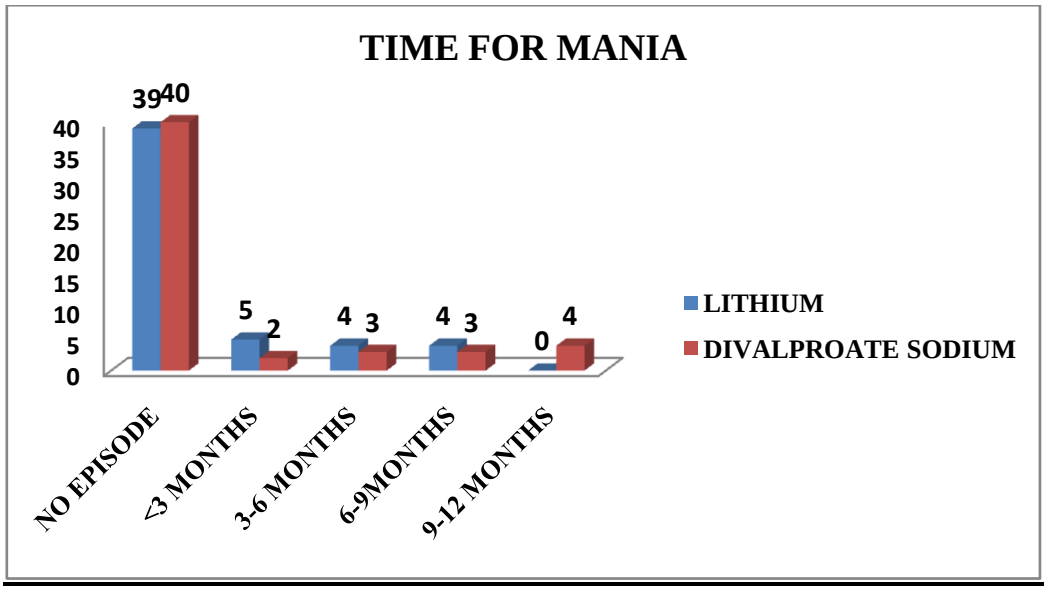
TABLE NO:3

Time for any mood episode on patients with Lithium and Divalproate sodium:

3.1TIME FOR MANIA:

Groups	TIME FOR MANIA					
	No episode	<3months	3-6months	6-9months	9-12 months	P Value
Lithium	39 (75.0%)	5 (9.6%)	4 (7.7%)	4 (7.7%)	0 (.0%)	P=0.339
Divalproate Sodium	40 (76.9%)	2 (3.8%)	3 (5.8%)	3 (5.8%)	4 (7.7%)	

FIGURE NO: 2



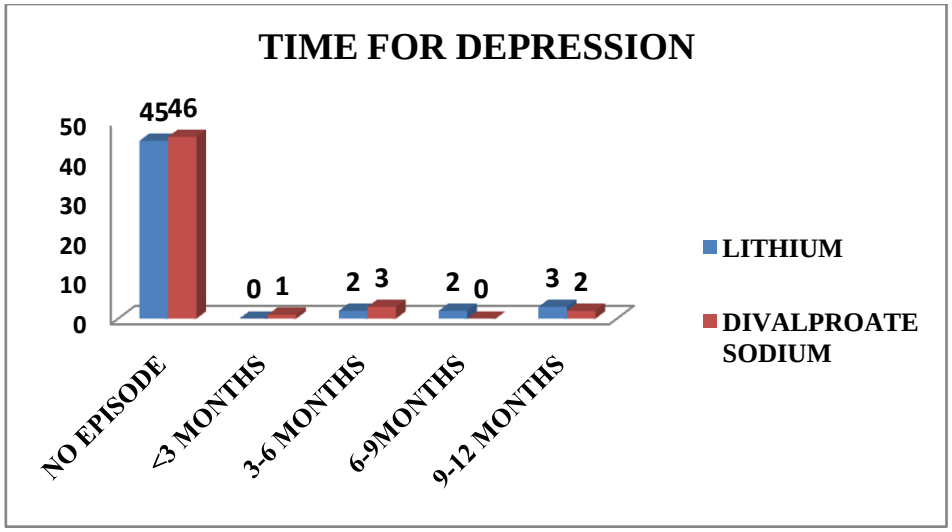
In the lithium group, 39 patients had no episodes of mania, 5 developed mania in less than 3 months, 4 developed mania between 3 to 6 months and 4 developed between 6 to 9 months. In the divalproate sodium group, 40 patients had no episodes of mania, 2 developed mania in less than 3 months, 3 developed mania between 3 to 6 months, 3 developed between 6 to 9 months and 4 developed between 9 to 12 months.

The time taken for manic episode was not statistically significant between Lithium and Divalproate sodium group(P=0.339).

3.2 TIME FOR DEPRESSION:

Groups	TIME FOR DEPRESSION					P VALUE
	No episodes	<3months	3-6months	6-9months	9months-1year	
Lithium	45 (86.5%)	0 (.0%)	2 (3.8%)	2 (3.8%)	3 (5.8%)	0.240
Divalproate sodium	46 (88.5%)	1 (1.9%)	3 (5.8%)	0 (.0%)	2 (3.8%)	

FIGURE NO:3



In the lithium group, 45 patients had no episodes of depression, 2 developed depression between 3 to 6 months, 2 developed between 6 to 9 months and 3 developed between 9 to 12 months. In the divalproate sodium group, 46 patients had no episodes of depression, 1 developed depression in less than 3 months, 3 developed depression between 3 to 6 months and 2 developed between 9 to 12 months.

The time taken for depressive episode was also not statistically significant between Lithium and Divalproate sodium group (P=0.24).

TABLE NO 4:

Comparision of severity of Manic episode between Lithium and Divalproate sodium group:

YOUNG MANIA RATING SCALE-FOLLOW UP -1:

Groups	YOUNG MANIA RATING SCALE-FOLLOW UP -1			P value
	No Mania	Mild to Moderate	Severe	
Lithium	47 (90.4%)	1 (1.9%)	4 (7.7%)	0.388
Divalproate sodium	50 (96.2%)	1 (1.9%)	1 (1.9%)	

Among patients on lithium, 47 had no mania, 1 had mild to moderate mania and 4 had severe mania according to Young Mania Rating Scale, on the first follow up. Among patients on divalproate sodium, 50 had no mania, 1 had mild to moderate mania and 1 had severe mania.

YOUNG MANIA RATING SCALE-FOLLOW UP -2:

Groups	YOUNG MANIA RATING SCALE-FOLLOW UP -2			P value
	No Mania	Mild to Moderate	Severe	
Lithium	48 (92.3%)	0 (.0%)	4 (7.7%)	
Divalproate sodium	49 (94.2%)	0 (.0%)	3 (5.8%)	0.696

Among patients on lithium, 48 had no mania and 4 had severe mania according to Young Mania Rating Scale, on the second follow up. Among patients on divalproate sodium, 49 had no mania and 3 had severe mania.

YOUNG MANIA RATING SCALE-FOLLOW UP -3:

Groups	YOUNG MANIA RATING SCALE-FOLLOW UP -3			P value
	No Mania	Mild to Moderate	Severe	
Lithium	48 (92.3%)	2 (3.8%)	2 (3.8%)	0.331
Divalproate sodium	49 (94.2%)	0 (.0%)	3 (5.8%)	

Among patients on lithium, 48 had no mania, 2 had mild to moderate mania and 2 had severe mania according to Young Mania Rating Scale, on the third follow up. Among patients on divalproate sodium, 49 had no mania and 3 had severe mania.

YOUNG MANIA RATING SCALE-FOLLOW UP -4:

Groups	YOUNG MANIA RATING SCALE-FOLLOW UP -4			P value
	No Mania	Mild to Moderate	Severe	
Lithium	52 (100.0%)	0 (.0%)	0 (.0%)	
Divalproate sodium	48 (92.3%)	0 (.0%)	4 (7.7%)	**0.041**

Among patients on lithium, 52 had no mania according to Young Mania Rating Scale, on the fourth follow up. Among patients on divalproate sodium, 48 had no mania and 4 had severe mania.

Patients who are taking Divalproate sodium had more severe Manic episode at the end of 1 year (4patients v/s none – P=0.041) ,but was not significant during initial three follow ups (P=0.388,0.696,0.331).

TABLE NO 5:

Comparision of severity of depressive episode between Lithium and Divalproate sodium group:

HAMILTON DEPRESSION RATING SCALE – FOLLOW UP- 1:

Groups	HAMILTON DEPRESSION RATING SCALE – FOLLOW UP- 1			P Value
	No depression	Mild - Moderate	Severe	
Lithium	52 (100.0%)	0 (.0%)	0 (.0%)	0.315
Divalproate sodium	51 (98.1%)	1 (1.9%)	0 (.0%)	

Among patients on lithium,52 had no depression according to Hamilton Depression Rating Scale, on the first follow up. Among patients on divalproate sodium, 51 had no depression and 1 had mild to moderate depression.

HAMILTON DEPRESSION RATING SCALE – FOLLOW UP- 2:

Groups	HAMILTON DEPRESSION RATING SCALE – FOLLOW UP- 2			P Value
	No depression	Mild - Moderate	Severe	
Lithium	50 (96.2%)	1 (1.9%)	1 (1.9%)	0.842
Divalproate sodium	49 (94.2%)	1 (1.9%)	2 (3.8%)	

Among patients on lithium, 50 had no depression, 1 had mild to moderate depression and 1 had severe depression according to Hamilton Depression Rating Scale, on the second follow up. Among patients on divalproate sodium, 49 had no depression, 1 had mild to moderate depression and 2 had severe depression.

HAMILTON DEPRESSION RATING SCALE – FOLLOW UP- 3:

Groups	HAMILTON DEPRESSION RATING SCALE – FOLLOW UP- 3			P Value
	No depression	Mild - Moderate	Severe	
Lithium	50 (96.2%)	0 (.0%)	2 (3.8%)	0.153
Divalproate sodium	52 (100.0%)	0 (.0%)	0 (.0%)	

Among patients on lithium, 50 had no depression and 2 had severe depression according to Hamilton Depression Rating Scale, on the third follow up. Among patients on divalproate sodium, 52 had no depression.

HAMILTON DEPRESSION RATING SCALE – FOLLOW UP- 4:

Groups	HAMILTON DEPRESSION RATING SCALE – FOLLOW UP- 4			P Value
	No depression	Mild - Moderate	Severe	
Lithium	49 (94.2%)	0 (.0%)	3 (5.8%)	0.366
Divalproate sodium	50 (96.2%)	1 (1.9%)	1 (1.9%)	

Among patients on lithium, 49 had no depression and 3 had severe depression according to Hamilton Depression Rating Scale, on the fourth follow up.

Among patients on divalproate sodium, 50 had no depression, 1 had mild to moderate depression and had severe depression.

There was no difference in the severity of depressive episode during all four follow ups upto one year between Lithium and Divalproate sodium patients.

TABLE NO:6

To Evaluate for Suicidal risk between Lithium and Divalproate sodium group:

SUICIDAL RISK SCALE BASELINE:

	SUICIDAL RISK SCALE BASELINE			
Groups	**No risk**	**Moderate risk**	**Severe risk**	**P Value**
Lithium	37 (71.2%)	15 (28.8%)	0 (.0%)	0.671
Divalproate sodium	35 (67.3%)	17 (32.7%)	0 (.0%)	

Among patients on lithium, 37 had no suicidal risk, 15 had moderate risk according to suicidal risk scale. Among patients on divalproate sodium, 35 had no suicidal risk, 17 had moderate risk and 3 had severe risk.

SUICIDAL RISK SCALE FOLLOW UP-1:

	SUICIDAL RISK SCALE FOLLOW UP:1			
Groups	**No risk**	**Moderate risk**	**Severe risk**	**P Value**
Lithium	35 (67.3%)	14 (26.9%)	3 (5.8%)	0.173
Divalproate sodium	34 (65.4%)	18 (34.6%)	0 (.0%)	

Among patients on lithium, 35 had no suicidal risk, 14 had moderate risk and 3 had severe risk according to suicidal risk scale, on the first follow up. Among patients on divalproate sodium, 34 had no suicidal risk, 18 had moderate risk .

SUICIDAL RISK SCALE FOLLOW UP-2:

	SUICIDAL RISK SCALE FOLLOW UP:2			
Groups	**No risk**	**Moderate risk**	**Severe risk**	**P Value**
Lithium	39 (67.3%)	9 (26.9%)	4 (7.7%)	0.371
Divalproate sodium	34 (65.4%)	15 (28.8%)	3 (5.8%)	

Among patients on lithium, 39 had no suicidal risk, 9 had moderate risk and 4 had severe risk according to suicidal risk scale, on the second follow up. Among patients on divalproate sodium, 34 had no suicidal risk, 15 had moderate risk.

SUICIDAL RISK SCALE FOLLOW UP-3:

	SUICIDAL RISK SCALE FOLLOW UP:3			
Groups	**No risk**	**Moderate risk**	**Severe risk**	**P Value**
Lithium	42 (80.8%)	8 (15.4%)	2 (3.8%)	0.857
Divalproate sodium	40 (76.9%)	9 (17.3%)	3 (5.8%)	

Among patients on lithium, 42 had no suicidal risk, 8 had moderate risk and 2 had severe risk according to suicidal risk scale, on the third follow up. Among patients on divalproate sodium, 40 had no suicidal risk, 9 had moderate risk and 3 had severe risk.

SUICIDAL RISK SCALE FOLLOW UP-4:

	SUICIDAL RISK SCALE FOLLOW UP:4			
Groups	**No risk**	**Moderate risk**	**Severe risk**	**P Value**
Lithium	47 (90.4%)	3 (5.8%)	2 (3.8%)	0.073
Divalproate sodium	38 (73.1%)	9 (17.3%)	5 (9.6%)	

Among patients on lithium, 47 had no suicidal risk, 3 had moderate risk and 2 had severe risk according to suicidal risk scale, on the fourth follow up. Among patients on divalproate sodium, 38 had no suicidal risk, 9 had moderate risk and 5 had severe risk.

The severity of suicidal scale was not significant during initial and all four follow-ups,but was trending towards significance during the 12th month follow up(P=0.671,0.173,0.371,0.857,**0.073**).

TABLE NO:7

Adherence to study treatment:

Groups	NUMBER OF FOLLOW UPS					P value
	No follow ups	1 follow up	2follow up	3follow up	4follow up	
Lithium	4 (7.7%)	5 (9.6%)	8 (15.4%)	10 (19.2%)	25 (48.1%)	0.938
Divalproate sodium	5 (9.6%)	4 (7.7%)	8 (15.4%)	13 (25.0%)	22 (42.3%)	

Among 52 Lithium group patients,25 patients (48.1%) had completed all four follow ups as compared to 22 divalproate sodium goup patients (42.3%).

But the above findings were not statistically significant(P=0.938).

TABLE NO:8

Adverse effects of the treatment:

ADVERSE DRUG REACTION BASELINE:

ADVERSE DRUG REACTION BASELINE				
Groups	**No drug reaction**	**Minimal reaction**	**More reaction**	**P Value**
Lithium	28 (53.8%)	24 (46.2%)	0 (.0%)	0.303
Divalproate sodium	24 (46.2%)	26 (50.0%)	2 (3.8%)	

Among patients on lithium, 28 had no adverse drug reaction and 24 had mild <3 reactions at baseline. Among patients on divalproate sodium, 24 had no reactions, 26 had <3 reactions and 2 had >=3 reactions.

ADVERSE DRUG REACTION FOLLOW UP-1:

ADVERSE DRUG REACTION FOLLOW UP-1				
Groups	**No drug reaction**	**Minimal reaction**	**More reaction**	**P Value**
Lithium	23 (44.2%)	29 (55.8%)	0 (.0%)	0.057
Divalproate sodium	24 (46.2%)	23 (44.2%)	5 (9.6%)	

Among patients on lithium, 23 had no adverse drug reaction and 29 had <3 reactions on first follow up. Among patients on divalproate sodium, 24 had no reactions, 23 had <3 reactions and 5 had >=3 reactions.

ADVERSE DRUG REACTION FOLLOW UP-2:

ADVERSE DRUG REACTION FOLLOW UP-2				
Groups	**No drug reaction**	**Minimal reaction**	**More reaction**	**P Value**
Lithium	27 (51.9%)	25 (48.1%)	0 (.0%)	0.361
Divalproate sodium	26 (50.0%)	24 (46.2%)	2 (3.8%)	

Among patients on lithium, 27 had no adverse drug reaction and 25 had <3 reactions on second follow up. Among patients on divalproate sodium, 26 had no reactions, 24 had <3 reactions and 2 had >=3 reactions.

ADVERSE DRUG REACTION FOLLOW UP-3:

ADVERSE DRUG REACTION FOLLOW UP-3				
Groups	**No drug reaction**	**Minimal reaction**	**More reaction**	**P Value**
Lithium	30 (57.7%)	22 (42.3%)	0 (.0%)	0.312
Divalproate sodium	35 (67.3%)	16 (30.8%)	1 (1.9%)	

Among patients on lithium, 30 had no adverse drug reaction and 22 had <3 reactions on third follow up. Among patients on divalproate sodium, 35 had no reactions, 16 had <3 reactions and 1 had >=3 reactions.

ADVERSE DRUG REACTION FOLLOW UP-4:

ADVERSE DRUG REACTION FOLLOW UP-4				
Groups	**No drug reaction**	**Minimal reaction**	**More reaction**	**P Value**
Lithium	42 (80.8%)	10 (19.2%)	0 (.0%)	0.340
Divalproate sodium	39 (75.0%)	11 (21.2%)	2 (3.8%)	

Among patients on lithium, 42 had no adverse drug reaction and 10 had <3 reactions on fourth follow up. Among patients on divalproate sodium, 39 had no reactions, 11 had <3 reactions and 2 had >=3 reactions.

The adverse drug effect (catagorised as nausea, diarrhea, tremors,weight gain, sedation, polydipsia, polyuria, tachycardia, alopecia, any major skin lesions , hypothyroid symptoms, signs of renal dysfunction) profile was the same between Lithium and Divalproate sodium group during all four visits except during initial follow up(3months) in which Lithium group was better than Divalproate sodium group (five patients on Divalproate sodium group had >=3 adverse drug reaction compared to none in the Lithium group).

The above result was not statistically significant.

TABLE NO:9

Global Assessment Functioning :

GLOBAL ASSESSMENT FUNCTIONING - BASELINE:

Groups		Global Assessment Functioning – BASELINE			P Value
	Good	Mild impairment in functioning	Moderate impairment in functioning	Severe impairment	
Lithium	51 (98.1%)	1 (1.9%)	0 (.0%)	0 (.0%)	0.315
Divalproate sodium	52 (100.0%)	0 (.0%)	0 (.0%)	0 (.0%)	

Global assessment functioning among patients on lithium was good in 51 and mildly impaired in 1 at baseline. Among patients on divalproate sodium, all 52 patients had good functioning.

GLOBAL ASSESSMENT FUNCTIONING FOLLOW UP-1:

Global assessment functioning follow up-1					P Value
Groups	**Good**	**Mild impairment in functioning**	**Moderate impairment in functioning**	**Severe impairment**	
Lithium	46 (88.5%)	2 (3.8%)	3 (5.8%)	1 (1.9%)	0.553
Divalproate sodium	49 (94.2%)	2 (3.8%)	1 (1.9%)	0 (.0%)	

Global assessment functioning among patients on lithium was good in 46, mildly impaired in 2, moderately impaired in 3 and severely impaired in 1 patient, on first follow up. Among patients on divalproate sodium, 49 had good functioning, 2 had mild impairment and 1 had moderate impairment.

GLOBAL ASSESSMENT FUNCTIONING FOLLOW UP-2:

	Global assessment functioning follow up-2				P Value
Groups	**Good**	**Mild impairment in functioning**	**Moderate impairment in functioning**	**Severe impairment**	
Lithium	46 (88.5%)	1 (1.9%)	3 (5.8%)	2 (3.8%)	0.912
Divalproate sodium	46 (88.5%)	2 (3.8%)	2 (3.8%)	2 (3.8%)	

Global assessment functioning among patients on lithium was good in 46, mildly impaired in 1, moderately impaired in 3 and severely impaired in 2 patients, on second follow up. Among patients on divalproate sodium, 46 had good functioning, 2 had mild impairment, 2 had moderate impairment and 2 had severe impairment.

GLOBAL ASSESSMENT FUNCTIONING FOLLOW UP-3:

	Global assessment functioning follow up-3				P Value
Groups	**Good**	**Mild impairment in functioning**	**Moderate impairment in functioning**	**Severe impairment**	
Lithium	46 (88.5%)	2 (3.8%)	3 (5.8%)	1 (1.9%)	0.330
Divalproate sodium	49 (94.2%)	0 (.0%)	1 (1.9%)	2 (3.8%)	

Global assessment functioning among patients on lithium was good in 46, mildly impaired in 2, moderately impaired in 3 and severely impaired in 1 patients, on third follow up. Among patients on divalproate sodium, 49 had good functioning, 1 had moderate impairment and 2 had severe impairment.

GLOBAL ASSESSMENT FUNCTIONING FOLLOW UP-4:

Global assessment functioning follow up-4					P value
Groups	**Good**	**Mild impairment in functioning**	**Moderate impairment in functioning**	**Severe impairment**	0.117
Lithium	49 (94.2%)	0 (.0%)	3 (5.8%)	0 (.0%)	
Divalproate sodium	46 (88.5%)	0 (.0%)	2 (3.8%)	4 (7.7%)	

Global assessment functioning among patients on lithium was good in 49 and moderately impaired in 3patients on fourth follow up. Among patients on divalproate sodium, 46 had good functioning, 2 had moderate impairment and 4 had severe impairment.

During the initial follow ups Lithium group patients had more functional impairment than Divalproate sodium group patients(initial and 3rd follow up).

During 6th month follow up two patients in each group had severe impairment.During 9th month and 1year follow up,Divalproate sodium group had more severe functional impairment than Lithium group(1 v/s 2),(0 v/s 4) but was not statistically significant.

TABLE NO:10

Comparision of new mood episode with varying serum lithium level:

Serum lithium level	New onset mania	New onset depression
<0.8	6	4
0.8-1.2	5	3
>1.2	2	1

We also calculated the patients who developed a new manic/depressive episode with varying serum lithium level.

Six out of thirteen new episode manic patients had a lower serum lithium level likewise majority of new onset depression episode patient (four out of eight), had a lower serum lithium level.

TABLE NO:11

Comparision of new mood episode with varying dosage of divalproate sodium:

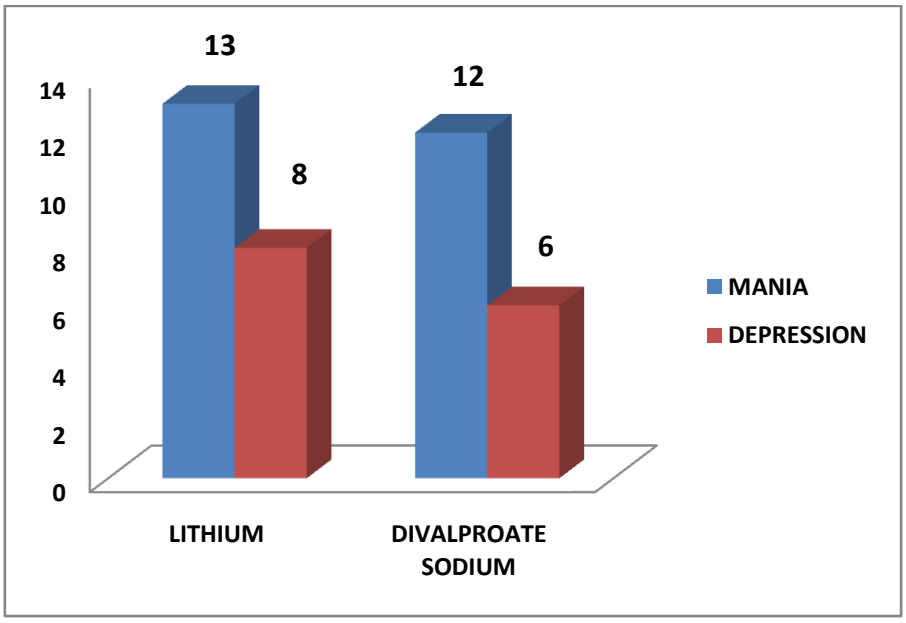
Dosage of divalproate sodium	New onset mania	New onset depression
<1gm	1	1
1gm-1.5gm	8	5
>1.5gm	3	0

Among the divalproate sodium group patients, only three out of thirteen patients who were on adequate dose (more than 1.5gm), has new onset mania (nine out of twelve patients were on inadequate dose).

None of the divalproate sodium group patients had new onset mania who are on adequate dose (all six patients who had new onset depression were on subtherapeutic dose).

FIGURE NO:4

Comparision of Frequency of Manic and Depressive episode between two groups:



Among Lithium group patients 13had Manic episode and 8 had Depressive episode. Among Divalproate sodium group patients 12 had Manic episode and 6 had Depressive episode.

In both the groups Manic episode was more common than Depressive episode.

DISCUSSION

We did a prospective study , comparing the mood stabilising effect of lithium and divalporate sodium in euthymic bipolar patients. Our study was an one year periodic prospective study done in psychiatry department at a teritiary hospital.

When we compared the sociodemographic variables (age, gender, educational status ,marital status)there was no statistical significance between the two groups.

We also considered the confounding variables namely (age of onset, number of previous episodes, previous hospitalisation, polarity of previous episodes and use of psychotrophics) ,which was also not significant between the two groups.

But the duration of mood stabiliser,(lithium group patients had more duration of treatment than divalproate sodium group patients),was statistically significant between the two groups.

The serum lithium level was less than adequate in majority of new onset manic/depressive episode patients.

Majority of the patients who developed new onset manic/depressive episode were on subtherapeutic dose of divalproate sodium.

PRIMARY OUTCOME:

Comparision of Frequency of Manic and Depressive episode between two groups:

In both lithium and divalproate sodium groups, similar number of patients had manic episode(13 v/s 12) and depressive (8 v/s 6).

The predominant mood episode was mania in both the groups. The above finding could also be because the polarity of previous episode in both the groups was predominantly mania.

B) Time for manic episode on patients with lithium and divalproate sodium:

Bipolar patients on lithium therapy had more manic episodes until first 9months of follow up but during the 1st year follow up, divalproate sodium had more manic episodes.

The above finding emphasises lithium to be a better long term mood stabiliser than divalproate sodium.

C) Time for depressive episode on patients with lithium and divalproate sodium:

There was no statistical difference between the lithium and divalproate sodium group, although lithium patient had more depressive episode than divalproate sodium patients.

SECONDARY OUTCOME:

A) The severity of mood episode in lithium and divalproate groups:

The patient who were on divalproate arm, had more severe manic episode, as the duration of follow up increased. This again emphasises lithium ,being a better antimanic agent ever during long term follow up.

The severity of depressive episodes did not differ between both the groups.

B) Comparision of suicidal risk between lithium and divalproate sodium patients:

Bipolar patients who were on lithium had lower suicidal risk than divalproate patients, especially on prolonged duration of treatment(during 1st year follow up trending towards significance).

Hence we believe if lithium group patients were had followed up for longer duration would had less new onset depressive episodes.

C) <u>Adherence to study treatment:</u>

Both lithium and divalproate sodium group patients had almost equal follow ups and hence were equally adherent to treatment.

Two patients on lithium were changed to divalproate sodium as they had severe skin reaction which affected the study adherence.

D) <u>Adverse effects of medication:</u>

Adverse effect profile did not differ during initial and periodic assessment between the two groups .

Bipolar patients on divalproate sodium had more adverse effects during initial follow ups, which was not seen during further follow up.

E) <u>Global assessment of functioning:</u>

The global functioning was better in lithium group , but was not statistically significant.

LIMITATIONS

1. Sample size was small and hence the results cannot be generalised.
2. Telephonic assessments for patients who missed follow ups, cannot be as reliable as face to face interview.
3. Our sample was convenient sample, a computer generated sampling would have been better.
4. Use of other psychotrophics (antipsychotics, benzodiazepines) were allowed. We know medication like olanzapine, risperidone and quetiapine can have a mood stabilising effect.[17,18,20]
5. Among lithium group patients, only two patients were changed to divalproate sodium in view of cutaneous side effects, which could have affected the adherence between the two groups.
6. We followed the patient, only upto 1year , which is a short duration considering the chronicity of mood disorder.
7. In our study, bipolar patients on lithium were better than divalproate sodium in preventing the manic episode which needs a longer follow up study.
8. Adherence of both the group patients were equated to the number of follow ups. Instead pill count could have been a better marker.

9. The categorisation of the dosage of divalproate sodium was arbitrary.

10. The severity of adverse drug effects were assessed only based on number of adverse effects than categorizing into simple and serious adverse effects.

CONCLUSION

1) The frequency of manic episode was better in lithium group of patients as the duration of lithium therapy increased.

2) The frequency of depressive episode was similar between the lithium and divalproate sodium groups.

3) The severity of manic episode was lesser in lithium group of patients, when treated for a longer duration.

4) Suicidal risk was lesser in lithium group patients.

5) In terms of adherence , adverse effects profile and global functioning both the groups did not differ.

6) Lithium continues to be a gold standard inspite of seven decades of dominance as a mood stabilizer agent.

7) Our study emphasis the need to treat the bipolar patients with adequate dosage.

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ANNEXURES

INFORMED CONSENT (ENGLISH)

PSG Institute of Medical Science and Research, Coimbatore
Institutional Human Ethics Committee
INFORMED CONSENT FORMAT FOR RESEARCH PROJECTS

(strike off items that are not applicable)

I, Dr Sarah Afreen am carrying out a study on the topic: Effectiveness of mood stabilizer in euthymic BPAD patients-an one year prospective observational study, comparing LITHIUM V/S DIVALPROATE SODIUM. In DEPARTMENT OF PSYCHIATRY OP patients.

(*Applicable to students only*): My / our research guide is: Dr. SYED UMMAR .I.

The justification for this study is: To study the effectiveness of mood stabilizer in euthyic BPAD patients.

The objectives of this study are:

Primary Objective: To evaluate the time for any mood episode (mania/ depression/ mixed episode).

Secondary Objective:

1. To access the severity of the mood episodes.

2. To evaluate for episodes of deliberate self harm.
3. Adherence to study treatment.
4. Adverse effects of the medication.
5. Global assessment of functioning.

Sample size: 52 per group. Total100.

S**tudy volunteers / participants** are (specify population group & age group): 18years and above.

Location: PSGIMSR

We request you to kindly cooperate with us in this study. We propose collect background information and other relevant details related to this study. We will be carrying out:

Initial interview (specify approximate duration): 20-30 minutes.

Data collected will be stored for a period of five years. We will / will not use the data as part of another study.

Interview sessions: Number of sessions: 4. Approximate **duration** of each session:

SCALES/PROFORMA USED IN OUR STUDY: 30minutes.

Clinical examination (Specify details and purpose):

Blood sample collection: Specify quantity of blood being drawn: _____ml.

No. of times it will be collected: _____.

Whether blood sample collection is part of routine procedure or for research (study) purpose:

1. Routine procedure 2. Research purpose

Specify **purpose**, discomfort likely to be felt and side effects, if any: _____

Whether blood sample collected will be stored after study period: Yes / No, it will be destroyed

Whether blood sample collected will be sold: Yes / No

Whether blood sample collected will be shared with persons from another institution: Yes / No

Medication given, if any, duration, side effects, purpose, benefits:

Whether medication given is part of routine procedure: Yes / No (If not, state reasons for giving this medication)

Whether alternatives are available for medication given: Yes / No (If not, state reasons for giving this particular medication)

Final interview (specify approximate duration):_____ mts. If **photograph** is taken, purpose:

Benefits from this study: This study may give a lead in choosing between lithium and divalproate sodium in euthymic BPAD patients. hence, may improve the outcome of the illness.

Risks involved by participating in this study: we do not predict any risk to patient as it is observational study ,as it will be decided by primary therapist.

How the **results** will be used:

If you are uncomfortable in answering any of our questions during the course of the interview / biological sample collection, **you have the right to withdraw from the interview / study at anytime.** You have the freedom to withdraw from the study at any point of time. Kindly be assured that your refusal to participate or withdrawal at any stage, if you so decide, will not result in any form of compromise or discrimination in the services offered nor would it attract any penalty. You will continue to have access to the regular services offered to a patient. You will **NOT** be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone. The information that we collect shall be used for approved research purposes only. You will be informed about any significant new findings- including adverse events, if any, – whether directly related to you or to other participants of this study, developed during the course of this research which may relate to your willingness to continue participation.

Consent: The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator/s.

Having understood the same, I hereby give my consent to them to interview me. I am affixing my signature / left thumb impression to indicate my consent and willingness to participate in this study (i.e., willingly abide by the project requirements).

Signature / Left thumb impression of the Study Volunteer / Legal Representative:

Signature of the Interviewer with date:4-12-14

Witness:

Contact number of PI:9790432213

Contact number of Ethics Committee Office: 0422 2570170 Extn.: 5818

ஒப்புதல் படிவம்

தேதி:

டாக்டர். சாரா அப்ரின் ஆகிய நான். பி.எஸ்.ஐ மருத்துவக் கல்லூரியின் மனநல மருத்துவத் துறையின் கீழ் லித்தியம் மற்றும் டைவால்ப்ரொயேட் சோடியம் ஆகிய மனயெழுச்சி நோயாளிகளுக்கான மனநிலையை நிலைப்படுத்தும் மருந்துகளின் திறனை ஒப்பிடும் ஓர் வரங்கால கண்காணிப்பு ஆய்வு மேற்கொள்ள உள்ளேன்.

ஏன் ஆய்வு வழிகாட்டி : டாக்டர். ஐ. சையத் உம்மர். உதவி பேராசிரியர்

ஆய்வின் நோக்கம் :.

1. முதன்மை நோக்கம் : மேற்கூறிய நோயின் தன்மை மீண்டும் வருவதற்குமுன்பு அதன் இடைப்பட்ட காலத்தை மதிப்பிடுதல்

மனஎழுச்சி மற்றும் மனத்தளர்ச்சி நோயின் வெளியீடுகளின் தீவிரத்தை அறிந்து கொள்வது.

சுய தீங்கு முயற்சிகளை கண்டறிவது

ஆய்வின் சிகிச்சை விதிமுறைகளை பின்பற்றுவது.

மருந்துகளின் பக்க விளைவுகளை கண்டறிவது.

அனைத்து பிவின் செயல்பாடு திறனை மதிப்பிடுவது / பரிசோதிப்பது

ஆய்வு மேற்கொள்வதற்கான அடிப்படை

இயல்புநிலை நோயாளிகளில் மனநிலை நலைப்படுத்தும் மருந்துகளின் திறனை கண்டறியும் ஆய்வு.

பரிசோதனை எண்ணிக்கை : ஒரு குழுவிற்கு 52 நபர்கள் மொத்தம் : 100

18 வயதுக்கு மேல் இருப்பவர்கள் இதில் சேர்க்கப்படுவார்கள்.

ஆய்வு மேற்கொள்ளும் இடம் :

பி.எஸ்.ஐ மருத்துவமனை. கோயம்புத்தூர்

நேர் கானல் : 30 நிமிடங்கள் (நான்கு முறை)

ஆய்வின் பலன்கள் :

இந்த ஆய்வின் மூலம் இயல்புநிலை மனத்தளர்ச்சி மனயெழுச்சி நோயாளிகளுக்கு உகந்த மருந்தை தேர்ந்தெடுத்து அதன் மூலம் அவர்களது வாழ்க்கை தரத்தை மேற்படுத்தலாம்.

புாதகங்கள் / அபாயங்கள்

மருந்துகள் அனைத்தும் முதன்மை சிகிச்சை தேர்ந்தெடுப்பதால் இந்த கண்காணிப்பு ஆய்வின் மூலம் எந்த ஒரு பாதகமோ, அபாயமோ ஏற்படாது.

லித்தியம் ஆரம்பிக்கப்பட்ட மனதளர்ச்சி. மனஎழுச்சி நோயாளிகளை 3வது 6 வது மற்றும் 12வது மாதம் தொடர்ந்து கண்காணிக்கப்படுவர். எந்த நேரத்தில் வேண்டுமானாலும் ஆய்விலிருந்து விலகிக்கொள்ளும் உரிமை உங்களுக்கு உண்டு.

ஆய்விலிருந்து விலகிக்கொள்வதால் உங்களுக்கு அளிக்கப்படும் சிகிச்சையில் எந்த வித மாற்றமும் இருக்காது.

இந்த ஆராய்ச்சிக்காக உங்களிடம் சில கேள்விகள் கேட்கப்படும். மேலும் இந்த ஆய்வில் பங்கு கொள்வது உங்கள் சொந்த விருப்பம். இதில் எந்த விதக் கட்டாயமும் இல்லை. நீங்கள் விருப்பப்பட்டால் இந்த ஆய்வின் முடிவுகள் உங்களுக்குத் தெரியப்படுத்தப்படும்.

ஆய்வாளரின் கையொப்பம் :

தேதி :

ஆய்வுக்குட்படுபவரின் ஒப்புதல் :

நான் இந்த ஆராய்ச்சியின் நோக்கம் மற்றும் அதன் பயன்பாட்டினைப் பற்றி தெளிவாகவும். விளக்கமாகவும் தெரியப்படுத்தப்படடுள்ளேன். இந்த ஆராய்ச்சியில் பங்கு கொள்ளவும். இந்த ஆராய்ச்சியின் மருக்துவ ரீதியான குறிப்புகளை வரும் காலத்திலும் உபயோகபடபடுத்திக் கொள்ளவும் முழு மனதுடன் சம்மதிக்கிறேன்.

ஆய்வுக்குட்படுபவரின் பெயர். முகவரி :

கையொப்பம் :

தேதி :

உடனிருப்பவரின் கையொப்பம் :

தேதி :

ஆய்வாளரின் தொலைபேசி எண் : 9790432213

நெறிமுறை குழு அலுவலக தொலைபேசி எண் : 0422 – 2570170 உள்தொடர்பு எண் : 581

SOCIODEMOGRAPHIC DETAILS & CONFOUNDING VARIABLES:

Semi-structured proforma:

A.SOCIO- DEMOGRAPHIC PROFILE:

- OP no
- Age
- Sex
- Education
- Marital status
- Contact number (atleast two).

B. **Confounding variables:**

- Age of onset of illness
- Previous number of episodes
- Previous hospitalizations
- Polarity of episodes
- Serum concentration of mood stabilizer
- Dosage of mood stabilizer
- Duration of treatment with mood stabilizer
- Co-morbid substance dependence.
- Confounding psychotrophics'.
- Duration of mood stabilizer

ADVERSE DRUG REACTION

1. Nausea
2. Diarrhea
3. Tremors
4. Weight gain
5. Sedation
6. Polydipsia
7. Polyuria
8. Tachycardia
9. Alopecia
10. Any major skin lesions
11. Hypothyroid symptoms(constipation, muscle weakness, fatigue, dry skin, increased sensitivity to cold).
12. Signs of Renal dysfunction.

YMRS SCALE FOR MANIA:

Young Mania Rating Scale (YMRS)

Enter the appropriate score which best characterizes the subject for each item.

Item	*Explanation*
1. Elevated mood	0 absent 1 mildly or possibly increased on questioning 2 definite subjective elevation: optimistic, self-confident; cheerful; appropriate to content 3 elevated, inappropriate to content; humorous 4 euphoric, inappropriate laughter singing
2. Increased motor activity-energy	0 absent 1 subjectively increased 2 animated; gestures increased 3 excessive energy; hyperactive at times; restless (can be calmed) 4 motor excitement; continues hyperactivity (cannot be calmed)
3. Sexual interest	0 normal; not increased 1 mildly or possibly increased 2 definite subjective increase on questioning 3 spontaneous sexual content; elaborates on sexual matters; hypersexual by self-report 4 overt sexual acts (toward subjects, staff, or interviewer)
4. Sleep	0 reports no decrease in sleep 1 sleeping less than normal amount by up to one hour 2 sleeping less than normal by more than one hour 3 reports decreased need for sleep 4 denies need for sleep
5. Irritability	0 absent 2 subjectively increased 4 irritable at times during interview; recent episodes of anger or annoyance on ward 6 frequently irritable during interview; short, curt throughout 8 hostile, uncooperative; interview impossible
6. Speech (rate and amount)	0 no increase 2 feels talkative 4 increased rate or amount at times, verbose at times 6 push; consistently increased rate and amount; difficult to interpret 8 pressured; uninterruptible; continuous speech
7. Language-thought disorder	0 absent 1 circumstantial; mild distractibility; quick thoughts 2 distractible; loses goal of thought; changes topics frequently; racing thoughts 3 flight of ideas; tangentiality; difficult to follow; rhyming; echolalia 4 incoherent; communication impossible

8. Content	0	normal
	2	questionable plans, new interests
	4	special project(s); hyperreligious
	6	grandiose or paranoid ideas; ideas of reference
	8	delusions; hallucinations
9. Disruptive-aggressive behaviour	0	absent, cooperative
	2	sarcastic; loud at times, guarded
	4	demanding; threats on ward
	6	threatens interviewer shouting; interview difficult
	8	assaultive; destructive; interview impossible
10. Appearance	0	appropriate dress and grooming
	1	minimally unkempt
	2	poorly groomed; moderately disheveled; overdressed
	3	disheveled; partly clothed; garish make-up
	4	completely unkempt; decorated; bizarre garb
11. Insight	0	present; admits illness; agrees with need for treatment
	1	possibly ill
	2	admits behaviour change, but denies illness
	3	admits possible change in behaviour, but denies illness
	4	denies any behaviour change

Reproduced from Young RC, Biggs JT, Ziegler VE, Meyer DA. Br J Psychiatry 1978; 133:429–35 with permission from the Royal College of Psychiatrists.

HAMD SCALE FOR DEPRESSION:

THE HAMILTON RATING SCALE FOR DEPRESSION

(to be administered by a health care professional)

Patient's Name

Date of Assessment

To rate the severity of depression in patients who are already diagnosed as depressed, administer this questionnaire. The higher the score, the more severe the depression.

For each item, write the correct number on the line next to the item. (Only one response per item)

1. **DEPRESSED MOOD** (Sadness, hopeless, helpless, worthless)

_____

0= Absent
1= These feeling states indicated only on questioning
2= These feeling states spontaneously reported verbally
3= Communicates feeling states non-verbally—i.e., through facial expression, posture, voice, and tendency to weep
4= Patient reports VIRTUALLY ONLY these feeling states in his spontaneous verbal and non-verbal communication

2. **FEELINGS OF GUILT**

_____

0= Absent
1= Self reproach, feels he has let people down
2= Ideas of guilt or rumination over past errors or sinful deeds
3= Present illness is a punishment. Delusions of guilt
4= Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations

3. **SUICIDE**

_____

0= Absent
1= Feels life is not worth living
2= Wishes he were dead or any thoughts of possible death to self
3= Suicidal ideas or gesture
4= Attempts at suicide (any serious attempt rates 4)

4. **INSOMNIA EARLY**

_____ **0**= No difficulty falling asleep
1= Complains of occasional difficulty falling asleep—i.e., more than 1/2 hour
2= Complains of nightly difficulty falling asleep

5. **INSOMNIA MIDDLE**

_____ **0**= No difficulty
1= Patient complains of being restless and disturbed during the night
2= Waking during the night—any getting out of bed rates 2 (except for purposes of voiding)

Adapted from Hedlung and Vieweg, The Hamilton rating scale for depression, *Journal of Operational Psychiatry*, 1979;10(2):149-165.

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6. **INSOMNIA LATE**

_____ **0**= No difficulty
1= Waking in early hours of the morning but goes back to sleep
2= Unable to fall asleep again if he gets out of bed

7. **WORK AND ACTIVITIES**

_____ **0**= No difficulty
1= Thoughts and feelings of incapacity, fatigue or weakness related to activities; work or hobbies
2= Loss of interest in activity; hobbies or work—either directly reported by patient, or indirect in listlessness, indecision and vacillation (feels he has to push self to work or activities)
3= Decrease in actual time spent in activities or decrease in productivity
4= Stopped working because of present illness

8. **RETARDATION: PSYCHOMOTOR** (Slowness of thought and speech; impaired ability to concentrate; decreased motor activity)

_____ **0**= Normal speech and thought
1= Slight retardation at interview
2= Obvious retardation at interview
3= Interview difficult
4= Complete stupor

9. **AGITATION**

_____ **0**= None
1= Fidgetiness
2= Playing with hands, hair, etc.
3= Moving about, can't sit still
4= Hand wringing, nail biting, hair-pulling, biting of lips

10. **ANXIETY (PSYCHOLOGICAL)**

_____ **0**= No difficulty
1= Subjective tension and irritability
2= Worrying about minor matters
3= Apprehensive attitude apparent in face or speech
4= Fears expressed without questioning

11. **ANXIETY SOMATIC:** Physiological concomitants of anxiety, (i.e., effects of autonomic overactivity, "butterflies," indigestion, stomach cramps, belching, diarrhea, palpitations, hyperventilation, paresthesia, sweating, flushing, tremor, headache, urinary frequency). Avoid asking about possible medication side effects (i.e., dry mouth, constipation)

_____ **0**= Absent
1= Mild
2= Moderate
3= Severe
4= Incapacitating

12. SOMATIC SYMPTOMS (GASTROINTESTINAL)

_____
- **0**= None
- **1**= Loss of appetite but eating without encouragement from others. Food intake about normal
- **2**= Difficulty eating without urging from others. Marked reduction of appetite and food intake

13. SOMATIC SYMPTOMS GENERAL

_____
- **0**= None
- **1**= Heaviness in limbs, back or head. Backaches, headache, muscle aches. Loss of energy and fatigability
- **2**= Any clear-cut symptom rates 2

14. GENITAL SYMPTOMS (Symptoms such as: loss of libido; impaired sexual performance; menstrual disturbances)

_____
- **0**= Absent
- **1**= Mild
- **2**= Severe

15. HYPOCHONDRIASIS

_____
- **0**= Not present
- **1**= Self-absorption (bodily)
- **2**= Preoccupation with health
- **3**= Frequent complaints, requests for help, etc.
- **4**= Hypochondriacal delusions

16. LOSS OF WEIGHT

_____

A. When rating by history:
- **0**= No weight loss
- **1**= Probably weight loss associated with present illness
- **2**= Definite (according to patient) weight loss
- **3**= Not assessed

17. INSIGHT

_____
- **0**= Acknowledges being depressed and ill
- **1**= Acknowledges illness but attributes cause to bad food, climate, overwork, virus, need for rest, etc.
- **2**= Denies being ill at all

18. DIURNAL VARIATION

_____

A. Note whether symptoms are worse in morning or evening. If NO diurnal variation, mark none
- **0**= No variation
- **1**= Worse in A.M.
- **2**= Worse in P.M.

_____

B. When present, mark the severity of the variation. Mark "None" if NO variation
- **0**= None
- **1**= Mild
- **2**= Severe

19. DEPERSONALIZATION AND DEREALIZATION (Such as: Feelings of unreality; Nihilistic ideas)

_____
- **0**= Absent
- **1**= Mild
- **2**= Moderate
- **3**= Severe
- **4**= Incapacitating

20. PARANOID SYMPTOMS

_____
- **0**= None
- **1**= Suspicious
- **2**= Ideas of reference
- **3**= Delusions of reference and persecution

21. OBSESSIONAL AND COMPULSIVE SYMPTOMS

_____ **0**= Absent
1= Mild
2= Severe

Total Score _____

GLOBAL ASSESSMENT OF FUNCTIONING SCALE:

Global Assessment of Functioning (GAF) Scale

(From DSM-IV-TR, p. 34.)

Consider psychological, social, and occupational functioning on a hypothetical continuum of mental health-illness. Do not include impairment in functioning due to physical (or environmental) limitations.

Code	(Note: Use intermediate codes when appropriate, e.g., 45, 68, 72.)
100 | 91	**Superior functioning in a wide range of activities, life's problems never seem to get out of hand, is sought out by others because of his or her many positive qualities. No symptoms.**
90 | 81	**Absent or minimal symptoms** (e.g., mild anxiety before an exam), **good functioning in all areas, interested and involved in a wide range of activities. socially effective, generally satisfied with life, no more than everyday problems or concerns** (e.g. an occasional argument with family members).
80 | 71	**If symptoms are present, they are transient and expectable reactions to psychosocial stressors** (e.g., difficulty concentrating after family argument); **no more than slight impairment in social, occupational or school functioning** (e.g., temporarily failing behind in schoolwork).
70 | 61	**Some mild symptoms** (e.g. depressed mood and mild insomnia) **OR some difficulty in social, occupational, or school functioning** (e.g., occasional truancy, or theft within the household), **but generally functioning pretty well, has some meaningful interpersonal relationships.**
60 | 51	**Moderate symptoms** (e.g., flat affect and circumstantial speech, occasional panic attacks) **OR moderate difficulty in social, occupational, or school functioning** (e.g.. few friends, conflicts with peers or co-workers).
50 | 41	**Serious symptoms** (e.g.. suicidal ideation, severe obsessional rituals, frequent shoplifting) **OR any serious impairment in social, occupational, or school functioning** (e.g., no friends, unable to keep a job).
40 | 31	**Some impairment in reality testing or communication** (e.g., speech is at times illogical, obscure, or irrelevant) **OR major impairment in several areas, such as work or school, family relations, judgment, thinking, or mood** (e.g., depressed man avoids friends, neglects family, and is unable to work; child frequently beats up younger children, is defiant at home, and is failing at school).
30 | 21	**Behavior is considerably influenced by delusions or hallucinations OR serious impairment in communication or judgment** (e.g., sometimes incoherent, acts grossly inappropriately, suicidal preoccupation) **OR inability to function in almost all areas** (e.g., stays in bed all day; no job, home, or friends).
20 | 11	**Some danger of hurting self or others** (e.g., suicide attempts without clear expectation of death; frequently violent; manic excitement) **OR occasionally fails to maintain minimal personal hygiene** (e.g., smears feces) **OR gross impairment in communication** (e.g., largely incoherent or mute).
10 | 1	**Persistent danger of severely hurting self or others** (e.g., recurrent violence) **OR persistent inability to maintain minimal personal hygiene OR serious suicidal act with clear expectation of death.**
0	Inadequate information.

Structured Clinical Interview for DSM-IV Axis I Disorders

Patient Edition (February 1996 FINAL)
SCID-I/P (Version 2.0)

Overview

INTERVIEW INFORMATION

Status: O In progress O Completed O Consensus reviewed

Type: O Computer O Paper

Subject ID:

Subject Initials:

Rater:

Site:

Date of Interview:

Sources of information (check all that apply):
O Subject
O Family
O Health professional/chart/referral note

Relationship to Proband:

Edited and checked by:

Date:

Recruitment Source:

DEMOGRAPHIC DATA

I'm going to be asking you about problems or difficulties you may have had, and I'll be making some notes as we go along. Do you have any questions before we begin?

Information

Gender: Date of Birth: Age:

What do you consider to be your ethnic origin?

Marital Status

What is your current marital status?

Dates of Marriage

Start Date	End Date	Comments

Children

Do you have any children? O Yes O No

Children

Gender	Age	Comments

Living Situation

With whom do you live?

Religion

What was your childhood religious affiliation, if any?

What is your current religion, if any?

FAMILY HISTORY

Were you adopted? O Yes O No

Mother

Living: O Yes O No

Brief Description (age, current location and living situation, general disposition, etc):

Occupation:

Highest Level of Education:

Religion:

# of Siblings:

Father

Living: O Yes O No

Brief Description (age, current location and living situation, general disposition, etc):

Occupation:

Highest Level of Education:

Religion:

# of Siblings:

Do you have any siblings? O Yes O No

(If yes, note genders and ages. Also indicate half of step siblings.)
Are you close to any of your siblings?

What was it like growing up in your family?
(Briefly describe home environment and relationships, including any trauma or abuse.)

Family History Form

Interviewer: "Tell me about your biological parents, children, siblings and grandparents." Ask if they have had any problems with their mood or anxiety or problems with drugs or alcohol. If adopted, ask about biological family; if not known, indicate "Adoptive Family" and answer accordingly. If deceased, note both date of death and "+" symbol in current age column.

Relation	Name	Current Age	Psychiatric Symptoms	Professional Diagnosis (list)	Psychiatric Treatment	Comments

DEVELOPMENTAL HISTORY

Where were you born and raised?
(Significant moves, health, school, friends, activities, etc.)

EDUCATION

How far did you get in school?

EVER FAILED TO COMPLETE A PROGRAM IN WHICH S/HE WAS ENROLLED: Why didn't you finish?

MILITARY HISTORY

Military Service: O Yes O No

Branch:

End of Service:

Start of Service:

Theater:

Veteran: O Yes O No

Combat: O Yes O No

Type of Discharge:

Rank at Discharge:

MOS:

Service Connected Disability: O Yes O No

Percent

Reason

WORK HISTORY

Are you working now? What is your job? How long have you been there?

[IF LESS THAN 6 MONTHS: Why did you leave your last job?]

Have you always done this kind of work? [IF NOT: What kind of work have you done?] What is the highest level job you have ever held? [Chronology of work history: (include longest job held and longest time unemployed)] How are you supporting yourself now? (If disability, list type, date and reason.)

Has there ever been a period of time when you were unable to work or go to school? (When? Why was that?)

OVERVIEW OF PRESENT ILLNESS

Have you been in any kind of treatment in the past month?

[IF CURRENTLY IN TREATMENT:
Date of admission to inpatient or outpatient facility.]

CHIEF COMPLAINT

(Description of presenting problem): [RECORD DIRECT QUOTE]

What led to your coming here? What is the major problem you have been having?

HISTORY OF PRESENT ILLNESS

Do you currently have any psychiatric symptoms or emotional problems? O Yes O No

IF YES: When did your current symptoms begin? When were you last feeling your normal self? Is this something new or a return of something you have had before? What was going on in your life when this began? (Environmental context for precipitants of present illness or exacerbation) Did anything happen or change? Since this began, when have you felt the worst? (IF MORE THAN A YEAR AGO: In the last year, when have you felt the worst?)

Have you had any other problems in the last month? What has your mood been like? How have you been spending your free time? Who do you spend time with?

How much have you been drinking (alcohol) (in the past month)? Have you been taking any drugs (in the past month)? (What about marijuana, cocaine, other street drugs?)

PAST PSYCHIATRIC HISTORY

When in your life did you first experience your symptoms? When was the first time you saw someone for emotional or psychiatric problems? (What was that for? What treatment(s) did you receive? What medications?) Were there other times when you had counseling or treatment of any kind? (What type? When?)

Age of first treatment for Depression
Age of first treatment for Mania
Age of first treatment for Hypomania
Age of first treatment for Mixed State
Age of first treatment for Psychosis/SZ

HOSPITALIZATIONS:

Have you ever been a patient in a psychiatric hospital? O Yes O No

(IF YES: When? Where? Why?)

Number of previous hospitalizations for Depression
(Do not include transfers)
Number of previous hospitalizations for Mania
Number of previous hospitalizations for Mixed State
Number of previous hospitalizations for Non-mood
Estimated lifetime total time of psychiatric hospitalization in weeks:

SUBSTANCE/ALCOHOL TREATMENT:

Have you ever had treatment for drugs or alcohol? O Yes O No

Treatment Information:

ATTENTION DEFICIT-HYPERACTIVITY DISORDER:

Have you ever been diagnosed with Attention Deficit-Hyperactivity Disorder? O Yes O No

(Include symptoms, presentation, age at diagnosis, age of first symptoms and treatment)

Medication Assessment Form

Category:	Class:	Drug Name:	Start Date:	End Date:	O Unknown

Multiple Trials:	Duration Used:	Reason Stopped:	Response Type:	Treatment Induced:

Comments
[Record side effect information whenever possible.]

MEDICAL HISTORY

Have you had any medical problems now or in the past? (What were they? How were they treated?) Were you ever in the hospital for treatment of a medical problem? (What was that for?) Have you ever had any surgeries (including outpatient)? (When? What were they for?)

O Yes O No

ALLERGIES:
Do you have any allergies? To Medications? Other?
O Yes O No

GENETIC DISORDERS:
Do you have any other genetic disorders? (What and when diagnosed?) Do you know of any genetic disorders that run in your family? (What? Who?)
O Yes O No

THYROID DISORDER:
Have you ever been treated for a thyroid disorder? (Include diagnosis, age of diagnosis, and treatment) Was this only while on Lithium?
O Yes O No

HEAD INJURY:
Have you ever had a head injury? (Did you lose consciousness? How long? How many times have you lost consciousness due to a head injury?)
O Yes O No

FEMALES ONLY:
Have you gone through menopause? (Have you ever had any serious emotional problems associated with menopause?)
O Yes O No

OTHER CURRENT PROBLEMS

MOST LIKELY CURRENT DIAGNOSIS

DIAGNOSES THAT NEED TO BE RULED OUT

GLOBAL ASSESSMENT OF FUNCTIONING
Current GAF

Module A: Depression

MAJOR AND MINOR DEPRESSIVE EPISODES

Episodes Summary

	Date of Onset	Age	Date of Offset	Duration (days)	
A - CURRENT (LAST MONTH)					O Go There
B - WORST EPISODE					O Go There
C - FIRST EPISODE					O Go There
D - ANOTHER EPISODE					O Go There
E - ANOTHER EPISODE					O Go There

Episode A: Current Depression

Date of Onset	Age	Date of Offset	Duration (days)

Depression Criteria

Now I would like to ask you some more specific questions about (TIME PERIOD FOR SUSPECTED DEPRESSIVE EPISODE).	A. Five or more of the following symptoms have been present during the same two-week period and represent a change from previous functioning; at least one of the symptoms was either (1) depressed mood or (2) loss of interest or pleasure.	
During this time, (TIME PERIOD FOR SUSPECTED DEPRESSIVE EPISODE) were you depressed or down, most of the day nearly every day? (What was that like?) IF YES: When was that? How long did it last? As long as two weeks?	(1) depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observations made by others (e.g., appears tearful). Note: in children and adolescents, can be irritable mood.	O O O O ? 1 2 3
Did you lose interest or pleasure in things you usually enjoyed? (What was that like?) IF YES: When was that? Was that nearly every day How long did it last? As long as two weeks?	(2) markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated either by subjective account or observation made by others)	O O O O ? 1 2 3

FOR ALL SUBJECTS, CONTINUE ASKING ABOUT ALL SYMPTOMS EVEN IF A(1) AND/OR (2) ARE NOT ENDORSED.

NOTE: WHEN RATING THE FOLLOWING ITEMS, CODE "1" IF CLEARLY DUE TO A GENERAL MEDICAL CONDITION, SUBSTANCE, OR TO MOOD-INCONGRUENT DELUSIONS OR HALLUCINATIONS. TO COUNT TOWARD A MAJOR DEPRESSIVE EPISODE, A SYMPTOM MUST EITHER BE NEWLY PRESENT OR MUST HAVE CLEARLY WORSENED COMPARED WITH THE PERSON'S PRE-EPISODE STATUS

I would like you to focus on the worst two week period when answering the following questions. During (TIME PERIOD OF EPISODE)

FOCUS ON WORST TWO WEEK PERIOD OF EPISODE TO DETERMINE IF FULL MAJOR DEPRESSIVE EPISODE CRITERIA ARE MET

...did you lose or gain any weight? (How much? Were you trying to lose weight?) IF NO: How was your appetite? What about compared to your usual appetite? Did you have to force yourself to eat? Eat (less/more) than usual? Was that nearly every day?	(3) significant weight loss when not dieting, or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. Note: in children, consider failure to make expected weight gains. Check if: weight loss or decreased appetite O weight gain or increased appetite O	O O O O ? 1 2 3
...how were you sleeping? (Trouble falling asleep, waking frequently, trouble staying asleep, waking too early, OR sleeping too much? How many hours a night compared to usual? Was that nearly every night?)	(4) insomnia or hypersomnia nearly every day Check if:	O O O O ? 1 2 3

insomnia O

hypersomnia O

...were you so fidgety or restless that you were unable to sit still? (Was it so bad that other people noticed it? What did they notice? Was that nearly every day?) IF NO: What about the opposite-talking more slowly than is normal for you? Was it so bad that other people noticed it? What did they notice? Was it nearly every day?	(5) psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down) Check if: psychomotor agitation O psychomotor retardation O	O O O O ? 1 2 3
...what was your energy like? (tired all the time? Nearly every day?)	(6) fatigue or loss of energy nearly every day	O O O O ? 1 2 3
...how did you feel about yourself? (Worthless? Nearly every day?) IF NO: What about feeling guilty about things you had done or not done? Nearly every day?	(7) feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick) Check if: feelings of worthlessness O excessive or inappropriate guilt O	O O O O ? 1 2 3
...did you have trouble thinking or concentrating? (What kinds of things did it interfere with? Nearly every day?) IF NO: Was it hard to make decisions about everyday things? Nearly every day?	(8) diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others) Check if: diminished ability to think O indecisiveness O	O O O O ? 1 2 3
Were things so bad you were thinking a lot about death or that you would be better off dead? What about thinking of hurting yourself? IF YES: Did you do anything to hurt yourself?	(9) recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide Check if: thoughts of own death O suicidal ideation O	O O O O ? 1 2 3

specific plan O

actual attempt O

	NUMBER OF SYMPTOMS A(1) - A(9) CODED "3"	0
	Major Depressive Episode	
	AT LEAST FIVE OF A(1) - A(9) ARE CODED "3" AND EITHER A(1) OR A(2) ARE CODED "3"	false
	Minor Depressive Episode	
	EITHER TWO,THREE, OR FOUR OF A(1) - A(9) ARE CODED "3" AND EITHER A(1) OR A(2) ARE CODED "3"	false
	SUICIDALITY IN DEPRESSION	
	FOLLOWING EPISODE A, ASK THE THREE QUESTIONS BELOW REGARDING SUICIDALITY, THEN CONTINUE ON PAGE A5 WITH REMAINDER OF EPISODE A. FOR EPISODES B-E, SKIP THIS SECTION AND GO TO NEXT PAGE (A5).	
IF UNKNOWN: Have you ever attempted suicide during a depressive episode?	Has made a suicide attempt	O O 1 3
IF YES: How many times?	Lifetime total number of suicide attempts during depression	
Do you think about suicide during most of your depressive episodes?	Determine whether suicidal ideation is present during most depressive episodes	O O O O ? 1 2 3
IF UNCLEAR: Did (DEPRESSIVE EPISODE/OWN EQUIVALENT) make it hard for you to do your work, take care of things at home, or get along with other people? IF YES, SPECIFY:	B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. NOTE: FOR SOME INDIVIDUALS WITH MILDER EPISODES, FUNCTIONING MAY APPEAR TO BE NORMAL BUT REQUIRES MARKEDLY INCREASED EFFORT.	O O O O ? 1 2 3
Just before this began, were you physically ill? Just before this began, were you drinking or taking any street drugs? IF YES: Any change in the amount you were taking? Just before this began, were you taking any medications? IF YES: Any change in the amount you were taking?	C. Not due to the direct physiological effects of a substance (e.g., a drug of abuse, medication) or to a general medical condition (e.g., hypothyroidism) IF GENERAL MEDICAL CONDITION OR SUBSTANCE MAY BE ETIOLOGICALLY ASSOCIATED WITH DEPRESSION, GO TO *GMC/SUBSTANCE* A.51, AND RETURN HERE TO MAKE RATING OF "1" OR "3."	O O O ? 1 3

IF THE EPISODE WAS PRECIPITATED BY MEDICATION TREATMENT, RECORD DETAILED INFORMATION ON THE MEDICATION ASSESSMENT FORM.

Did this begin soon after someone close to you died?

D. Not better accounted for by Bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms or psychomotor retardation.

O O
1 3

Major Depressive Episode

MAJOR DEPRESSIVE EPISODE CRITERIA A, B, C, AND D ARE CODED "3"

false

Minor Depressive Episode

MINOR DEPRESSIVE EPISODE CRITERIA A, B, C, AND D ARE CODED "3"

false

FIRST AND WORST DEPRESSION

IF UNCLEAR: Is this your worst episode of depression?

Worst

DETERMINE WHETHER OR NOT EACH EPISODE IS THE FIRST OR THE WORST DEPRESSION. CODE "3" FOR ONLY ONE FIRST AND ONE WORST EPISODE. THEY MAY BE THE SAME EPISODE AND MAY NOT ALWAYS BE CODED IN B OR C (I.E., D OR E MAY ACTUALLY BE EARLIER OR MORE SEVERE ONCE RECALLED).

O O
1 3

Is this the first episode?

First

O O
1 3

MIXED STATE

ASK THE FOLLOWING QUESTIONS TO DETERMINE WHETHER A MIXED STATE WAS PRESENT FOR EACH EPISODE OF DEPRESSION.

During this episode of depression did you have a week or more during which your mood changed between sadness and irritability or even elation?

O O O O
? 1 2 3

IF YES, CHECK IF:
Irritability O

Elation O

During this episode of depression did you also experience any of the following symptoms?

Over activity, such as running around, having many projects, or feeling physically agitated?

O ? O 1 O 2 O 3

More talkative than usual or feeling that your speech was pressured?

O ? O 1 O 2 O 3

Thoughts racing or jumping from topic to topic?

O ? O 1 O 2 O 3

Feeling grandiose, more important, special, or powerful?

O ? O 1 O 2 O 3

Needing less sleep or feeling energetic after little or no sleep?

O ? O 1 O 2 O 3

Attention distracted by unimportant things?

O ? O 1 O 2 O 3

Doing risky things for pleasure like excessive spending, reckless driving, sexual indiscretions, etc?

O ? O 1 O 2 O 3

	NUMBER OF "3" RESPONSES FROM MIXED STATE SECTION.	0
How long were these symptoms present?	ENTER NUMBER OF DAYS	
	CRITERIA WERE MET SIMULTANEOUSLY FOR BOTH MAJOR DEPRESSION AND MANIA. IRRITABLE MOOD PLUS FOUR SYMPTOMS, OR ELATED MOOD PLUS THREE SYMPTOMS	false
	IRRITABLE MOOD PLUS 2-3 SYMPTOMS OR ELATED MOOD PLUS 2 SYMPTOMS	false

Were your mood symptoms predominantly irritable, sad (dysphoria) or elated (euphoria)?

Predominance of:

Irritability O

Dysphoria O

Euphoria O

[PROBE IN THE SAME WAY FOR EACH CODED EPISODE]

During this episode of depression, did you have any beliefs or ideas that you later found out were not true? (Like believing that you had powers and abilities others did not have? Or that you had a special mission, perhaps from God? Or that someone was trying to harm you? How certain were you?)

Did you see or hear things other people could not see or hear?

Probe for Psychotic Symptoms per Episode:

IF DELUSIONS OR HALLUCINATIONS ARE SUSPECTED, PROBE FURTHER TO DETERMINE THE CONTENT AND WHETHER THE BELIEFS WERE HELD WITH CERTAINTY.

O O O
? 1 3

IF YES, PLEASE CHECK:

O Delusions

O Hallucinations

IF YES, DESCRIBE:

End of Episode-Specific Questions. Will Another Episode Be Coded? O Yes O No

Manic and Hypomanic Episode A (Current)

Date of Onset	Age	Date of Offset	Duration (days)

Now I'd like to ask you more specific questions about (TIME PERIOD FOR SUSPECTED MANIC OR HYPOMANIC EPISODE).

MANIC EPISODE CRITERIA

A1. (Mania and Hypomania)

During (TIME PERIOD FOR EPISODE) were you feeling so good or hyper that other people thought you were not your normal self or you were so hyper that you got into trouble? (Did anyone say you were manic? Was that more than just feeling good?)

IF NO: What about feeling so irritable that you found yourself shouting at people or starting fights or arguments? Did you find yourself shouting at people you really didn't know?

A(1) A distinct period of abnormally and persistently ("sustained" if hypomania) elevated, expansive, or irritable mood.

O O O O
? 1 2 3

What was it like?

CHECK ONE:

O elevated/expansive mood

O irritable mood

	Select if this is a manic or hypomanic episoide	O Manic O Hypomanic

A2. (Mania)

How long did that last? (As long as one week? Did you have to go to the hospital?)	A(2) Episode lasted at least one week (any duration if hospitalization is necessary, psychosis is present, or very dangerous behaviors are present)	O O 1 3

Did it last for at least two days?	Brief Mania (2 day duration required) PER KELSOE CONVENTION, BRIEF MANIA WILL BE INCLUDED IN THE MANIA ASSESSMENT, SPECIFIC PATTERNS.	O O 1 3

A2. (Hypomania)

Did it last for at least four days? What was that like?	A(2) Episode lasted throughout at least 4 days, and is clearly different from the usual non-depressed mood	O O 1 3
What was it like?	CHECK ONE:	O elevated/expansive mood O irritable mood

Did it last for at least two days?	Brief Hypomania (2 day duration required) PER KELSOE CONVENTION, BRIEF HYPOMANIA WILL BE INCLUDED IN THE HYPOMANIA ASSESSMENT	O O 1 3

FOR ALL SUBJECTS, CONTINUE ASKING ABOUT ALL SYMPTOMS, EVEN IF A(1) AND (2) ARE NOT ENDORSED

NOTE: WHEN RATING THE FOLLOWING ITEMS, CODE "1" IF CLEARLY DUE TO A GENERAL MEDICAL CONDITION, SUBSTANCE, OR TO MOOD-INCONGRUENT DELUSIONS OR HALLUCINATIONS. TO COUNT TOWARD A MANIC EPISODE, A SYMPTOM MUST EITHER BE NEWLY PRESENT OR MUST HAVE CLEARLY WORSENED COMPARED WITH THE PERSON'S PRE-EPISODE STATUS.

B. (Mania and Hypomania)

I would like you to focus on the most extreme period of feeling (OWN EQUIVALENT FOR EUPHORIA OR IRRITABILITY), when answering the following questions. During (TIME PERIOD OF EPISODE)	B. During the worst period of the mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:	
...how did you feel about yourself? (More self-confident than usual? Any special powers or abilities?)	(1) inflated self-esteem or grandiosity	O O O O ? 1 2 3

Did you need less sleep than usual? IF YES: Did you still feel rested?	(2) decreased need for sleep (e.g., feels rested after missing at least two hours of sleep) NOTE: THIS ITEM SHOULD BE PRESENTED AT EVERY CONSENSUS TO HELP ENSURE RELIABILITY.	O O O O ? 1 2 3
Were you much more talkative than usual? (Did people have trouble stopping you or understanding you? Did people have trouble getting a word in edgewise?)	(3) more talkative than usual or pressure to keep talking	O O O O ? 1 2 3
Were your thoughts racing through your head?	(4) flight of ideas or subjective experience that thoughts are racing	O O O O ? 1 2 3
Were you so easily distracted by things around you that you had trouble concentrating or staying on one track?	(5) distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)	O O O O ? 1 2 3
How did you spend your time? (Work, friends, hobbies? Were you so active that your friends or family were concerned about you?) IF NO INCREASED ACTIVITY: Were you physically restless? How bad was it?	(6) increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation Check if:	O O O O ? 1 2 3 O psychomotor agitation O increase in activity
Did you do anything that could have caused trouble for you or your family? (Buying things you didn't need? Anything sexual that was unusual for you? Reckless driving?)	(7) excessive involvement in pleasurable activities which have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)	O O O O ? 1 2 3
	NUMBER OF MANIC/HYPOMANIC SYMPTOMS IN A AND B CODED "3" (A1 AND A2 CRITERIA COUNT AS ONE). AT LEAST THREE B SYMPTOMS ARE CODED "3" (FOUR IF MOOD ONLY IRRITABLE) Note: DSM-IV Criterion C for Mania (i.e., does not meet criteria for a Mixed Episode) has been omitted from the SCID	0 false

C. (Mania)

IF UNKNOWN: At that time, did you have serious problems at home or at work (school) because you were (SYMPTOMS) or did you have to be admitted to a hospital? IF YES, SPECIFY:	C. The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.	O O 1 3

C. (Hypomania)

IF UNKNOWN: Is this very different from the way you usually are? (How were you different? At work? With friends?) IF YES, Specify:	C. The episode is associated with an unequivocal change in functioning that is uncharacteristic of the person when not symptomatic	O O 1 3

D. (Hypomania)

IF UNKNOWN: Did other people notice the change in you? (What did they say?)	D. The disturbance in mood and the change in functioning are observable by others	O O 1 3

E. (Hypomania)

IF UNKNOWN: At that time, did you have serious problems at home or at work (school) because you were (SYMPTOMS) or did you have to be admitted to a hospital?	E. The episode is not severe enough to cause marked impairment in social or occupational functioning, or to necessitate hospitalization, and there are no psychotic features	O O 1 3

D. (Mania)
F. (Hypomania)

Just before this began, were you physically ill? Just before this began, were you drinking or taking any street drugs? IF YES: Any change in the amount you were taking? Just before this began, were you taking any medications ,other than antidepressants? IF YES: Any change in the amount you were taking?	D/F. Not due to the direct physiological effects of a substance (e.g., a drug of abuse, medication) or to a general medical condition IF GENERAL MEDICAL CONDITION OR SUBSTANCE THAT CAN BE ETIOLOGICALLY ASSOCIATED WITH MANIA/HYPOMANIA, GO TO *GMC/SUBSTANCE,* A.51 AND RETURN HERE TO MAKE RATING OF "1" OR "3" Etiological general medical conditions include: degenerative neurological illnesses (e.g., Huntington's disease, multiple sclerosis), cerebrovascular disease (e.g., stroke), metabolic conditions (e.g., Vitamin B-12 deficiency, Wilson's disease), endocrine conditions (e.g., hyperthyroidism), viral or other infections, and certain cancers (e.g., cerebral neoplasms). Etiological substances include: alcohol, amphetamines, cocaine, hallucinogens, inhalants, opioids, phencyclidine, sedatives, hypnotics, and anxiolytics. Medications include psychotropic medications (e.g., anxiolytics), corticosteroids, anabolic steroids, isoniazid, antiparkinson medication (e.g., levodopa), and sympathomimetics/decongestants	O O 1 3

Were you on antidepressant treatment when this episode began?	EPISODE PRECIPITATED BY SOMATIC ANTIDEPRESSANT TREATMENT (BEGAN WITHIN TWO MONTHS OF STARTING OR CHANGING ANTIDEPRESSANT TREATMENT). CODE "3" IF APPLICABLE TO EPISODE IF YES RECORD IN MEDICATION SECTION OF OVERVIEW NOTE: FOR THE GENETICS STUDY AND IN DISTINCTION TO DSM IV, MANIC AND HYPOMANIC EPISODES THAT ARE CLEARLY PRECIPITATED BY SOMATIC ANTIDEPRESS-ANT TREATMENT (E.G., MEDICATION, ELECTROCONVULSIVE THERAPY, LIGHT THERAPY, SLEEP DEPRIVATION, HERBAL TREATMENTS) DO COUNT TOWARD A DIAGNOSIS OF BIPOLAR DISORDER	O O 1 3

IF YES, How long were you on it?	RECORD NUMBER OF WEEKS	
	MANIC EPISODE CRITERIA A, B, C AND D ARE CODED "3"	false
	HYPOMANIC EPISODE CRITERIA A, B, C, D, E, AND F ARE CODED "3"	false
	IF NO MANIC OR HYPOMANIC OR MIXED EPISODES, GO TO DYSTHYMIC DISORDER. HOWEVER, IF CODED FOR A MIXED EPISODE IN THE DEPRESSION SECTION, SKIP TO SUMMARY QUESTIONS FOR MIXED EPISODE.	
	FIRST AND WORST MANIA/HYPOMANIA:	
IF UNCLEAR: Is this your worst episode of depression?	DETERMINE WHETHER OR NOT EACH EPISODE IS THE FIRST AND/OR THE WORST MANIA/HYPOMANIA. CODE "3" FOR ONLY ONE FIRST AND ONE WORST EPISODE. THEY MAY BE THE SAME EPISODE AND MAY NOT ALWAYS BE CODED IN B OR C (I.E., D OR E MAY ACTUALLY BE EARLIER OR MORE SEVERE ONCE RECALLED).	O O 1 3
Is this the first episode?		O O 1 3

	SUICIDALITY IN MANIA	
IF UNKNOWN: Have you ever attempted suicide during a manic episode?	Has made a suicide attempt	O O O O ? 1 2 3

O Dysphoria

O Euphoria

[PROBE FOR PSYCHOTIC SYMPOTMS IN EACH CODED EPISODE. INCLUDE MIXED STATES IN NEXT SECTION]

During this episode of (MANIA) did you have any beliefs or ideas that you later found out were not true? (Like believing that you had powers and abilities others did not have? Or that you had a special mission, perhaps from God? Or that someone was trying to harm you? How certain were you?)
IF YES, DESCRIBE:

Did you see or hear things other people could not see or hear?
IF YES, DESCRIBE:

Probe for Psychotic Symptoms: Per Episode

IF DELUSIONS OR HALLUCINATIONS ARE SUSPECTED, PROBE FURTHER TO DETERMINE THE CONTENT AND WHETHER THE BELIEFS WERE HELD WITH CERTAINTY. [NOTE: IF PSYCHOTIC SYMPTOMS ARE PRESENT DURING PREVIOUSLY CODED HYPOMANIA, IT SHOULD BE RECODED AS FULL MANIA.]

O ? O 1 O 3

IF YES, PLEASE CHECK:

O Delusions

O Hallucinations

END OF EPISODE SPECIFIC QUESTIONS. CONTINUE WITH NEXT CODED EPISODE.

AFTER REVIEWING ALL NECESSARY EPISODES, CONTINUE BELOW.

MODIFIED SADSPERSONS SCALE:

MODIFIED SADPERSONS SCALE

Pnemonic		Characteristic
	Score	
S	Sex	Male
	1	
A	Age	<19 or >45
	1	
D	Depression, hopelessness	Admits to
	2	
P	Previous attempts/	
	Psychiatric care	Inpatient or out patient
	1	
E	Ethanol or drugs	History or clinical signs
	1	
R	Rational thought (loss of)	Organic brain syndrome, psychosis
	2	
S	Separated, widowed, divorced	
	1	
O	Organised, serious attempt	Or life-threatening presentation
	2	
N	No social support	
	1	
S	Stated future attempt	Or ambivalent
	2	

A score of < 5 indicates that the patient may probably be discharged
A score of 6 or more requires psychiatric consult
A score of > 9 means that the patient will require admission