



# A step towards predicting lithium response in patients with bipolar disorder

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## Background

Bipolar disorder is a common, recurrent and often severe mood disorder. Those suffering experience abnormally elevated moods (mania) as well as profound low moods (depression). On average, life expectancy is reduced by 8-9 years. Yet, with effective treatment all causes of mortality are reduced. Currently, lithium is viewed as the most established long-term treatment for bipolar disorder.

## The unfortunate Truth

As we lack the ability to predict which patients will respond to which medications, individual treatment regimes are often constructed through trial and error. It is rare to find one drug that will completely control all aspects of the illness - what is effective for mania might not work for depression. As a result, there is a pressing need to establish a long-term treatment that will produce an enduring response. Lithium comes closest to addressing the full spectrum of bipolar disorder with studies showing that it treats and prevents mania and depression as well as lessening suicide. However, at the level of the individual, response is not always guaranteed with up to a third of patients noticing no improvement.

## Aim

In clinical practice, not all patients respond to lithium and achieving formal ratings of response is extremely difficult. Short-term improvements are usually easy to observe. However, the long-term effects of lithium are difficult to quantify. Research which attempts to identify the characteristics of responders is hindered by this lack of identification and assessment of response. The aim is to understand the challenges of assessing response to lithium in the long-term.

## Objectives

- Critique existing methods of assessing response.
- Establish the feasibility of a life chart method using electronic patient records.

## Existing Approaches

Prospective: assessing patient's over a specified timeframe after initiating lithium. This process is labour intensive and its suitability is limited to trials or specialist centres. Still it remains unclear what, and how often, would you rate?

Retrospective: patients recall periods of illness and wellbeing before and after lithium. Although suited to clinical practice, data is often subject to recall bias and inaccuracies. There are currently two major retrospective methods used:

- Rating scales
- Life chart methods

## Retrospective rating scale

The Alda scale, Figure 1, is a two part retrospective assessment. Part A rates response to lithium on a 0-10 scale. Part B establishes the confidence with which the response is due to lithium. The output is either a total score (TS; A score minus B score) or the A score itself.

We conducted the first in-depth critique of the Alda scale, which identified crucial errors with the content and structure. For instance, nonlinearity, double counting, inconsistent terminology and unequal percentage increments.

These fundamental problems meant this scale was unable to appropriately categorise response. It is likely this scale will generate inaccurate and invalid assessments of lithium response. The rating of response obtained from this scale distorts characteristics of a responder. However, with no clear general definition of drug response, the research in this field is extremely circular. An alternate scale or method to assess lithium response is therefore of high importance.

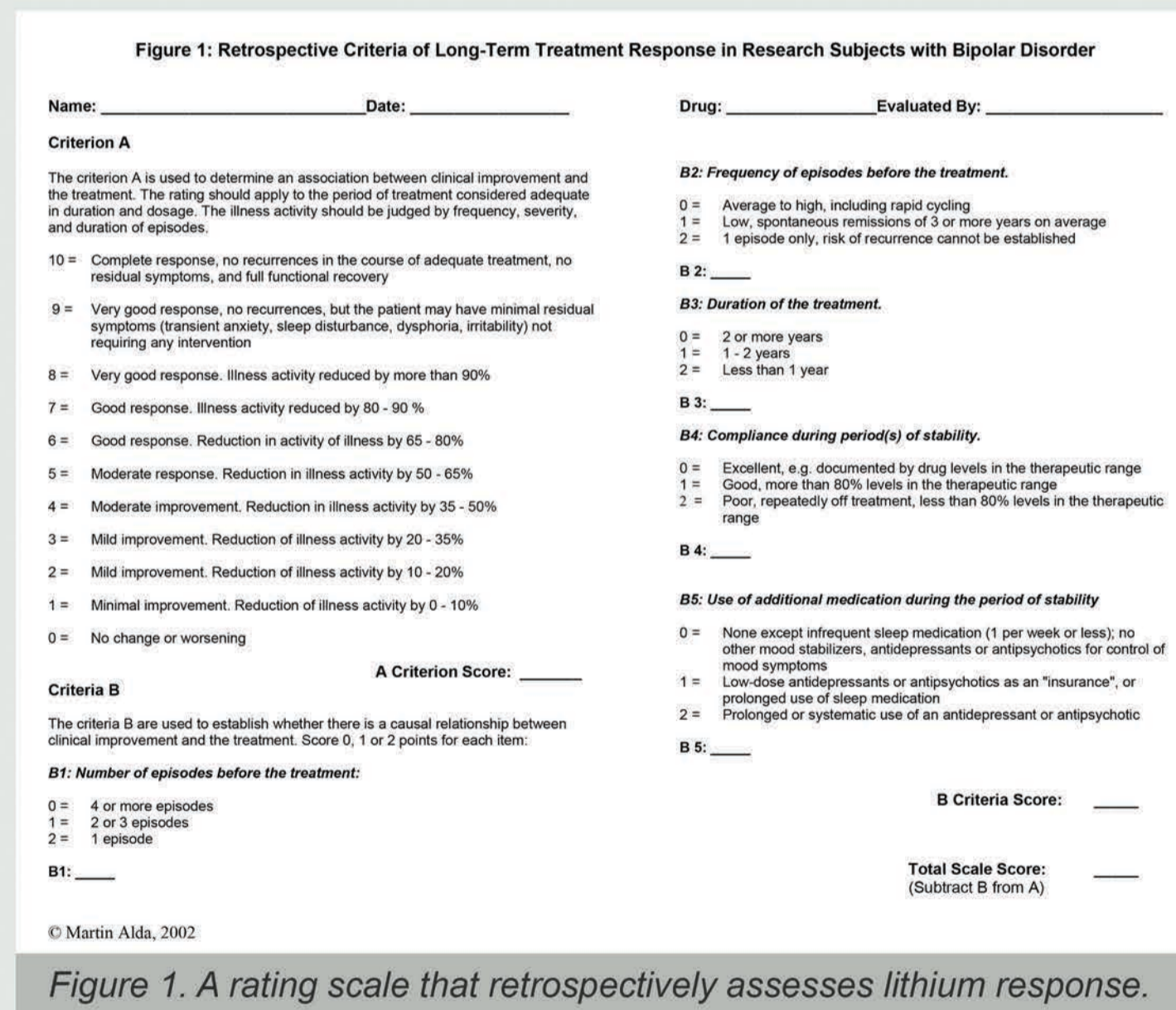


Figure 1. A rating scale that retrospectively assesses lithium response.

## Retrospective life chart method

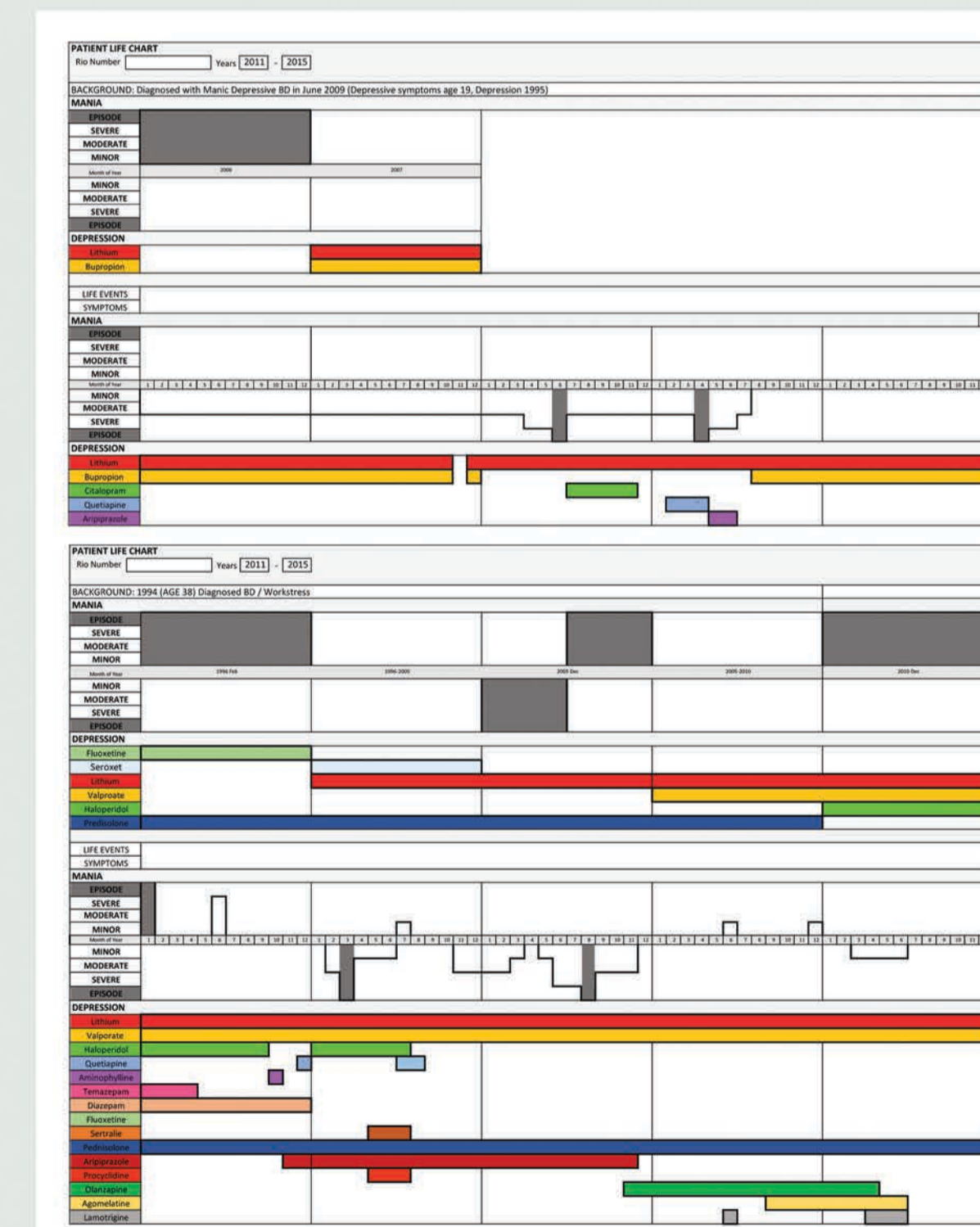


Figure 2. Bipolar disorder patient life charts. (a)

Retrospective life chart methods attempt to quantify response to lithium by charting the frequency or severity of periods of illness before and after treatment.

Common approaches include:

- Comparing number of admissions
- Comparing number of episodes
- Comparing severity of episodes
- Area under the curve (AUC) methods

In exploring the response to treatment, we chose to chart the severity of illness activity before and after lithium as shown in Figure 2 (a) and (b). Patient history records were accessed (Rio mental health system), providing background information on illness patterns. Dates (months and years) were recorded and time frames were gauged from analysing the symptoms caused by each medication. A symptom criteria was created: minor (early signs and not stable), moderate (difficulties with tasks) and severe (impact on life and an inability to cope) which were determined by reviews detailing current medications, life stressors and emotional states.

Charting illness activity was easier when relapses were documented, illustrated in Figure 2 (b), as precise times of symptom change and medication alterations were included. However, this case review demonstrated the challenges faced with objective assessments. It became evident that patient records were not sufficient in defining illness severity. Further, the onset and endings of episodes were poorly documented resulting in the need for inference. As records rarely dated back beyond 2010, illness activity was formed from clinical summaries. Thus, the information obtained from earlier years was less precise.

As AUC methods incorporate severity and duration of illness, their use in life charts is appropriate. However, impracticalities such as high sensitivity to the frequency of assessment, suggest these methods are more suitable for analysing prospectively acquired data.

## Conclusion

- Of the two methods investigated, the Alda scale is more suitable to assessing lithium response but its many faults cause a distortion in its ratings.
- It is likely a reliable definition of lithium response will only be achieved from conducting long-term prospective studies.
- Combining the use of high quality clinical notes with life chart construction may allow retrospective studies to appropriately rate the impact of lithium on a patients illness.

## References

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