



International Society for CNS Clinical Trials and Methodology

MAINTENANCE OF EFFECT

Introduction

Ravi Anand, MD

Difficulties in establishing long term efficacy for psychotropic drugs: common methodological issues (i)

- Despite differences in phenomenology, disease course, long-term outcome and effects of treatment (anxiolytics, antipsychotics, antidepressants, treatments for bipolar disorder), regulatory labels, drug development, and prescribing patterns are broadly similar.
- Most current terminology relating to treatment phases is based on depression research; terms used in this symposium are largely based on this work.
- Efficacy of treatments for psychiatric illnesses can be broadly divided into three phases: acute, continuation and maintenance

Difficulties in establishing long term efficacy for psychotropic drugs: common methodological issues (ii)

- Acute phase or short-term treatment
 - Control of symptoms/attainment of acceptable level of response
 - Usually 4 - 6 weeks of treatment

Difficulties in establishing long term efficacy for psychotropic drugs: common methodological issues (iii)

- Continuation treatment
 - Consolidation of response attained/conversion of partial to full remission/prevention of relapse
 - Usually ends when patients have had stable remission for 4 – 6 months
 - Conceptually understood as “recovery” or “normalization” of neurobiological function
 - Depressive episode following recovery is considered to represent a new episode of illness, i.e. recurrence
 - Relapse represents an exacerbation of the index episode

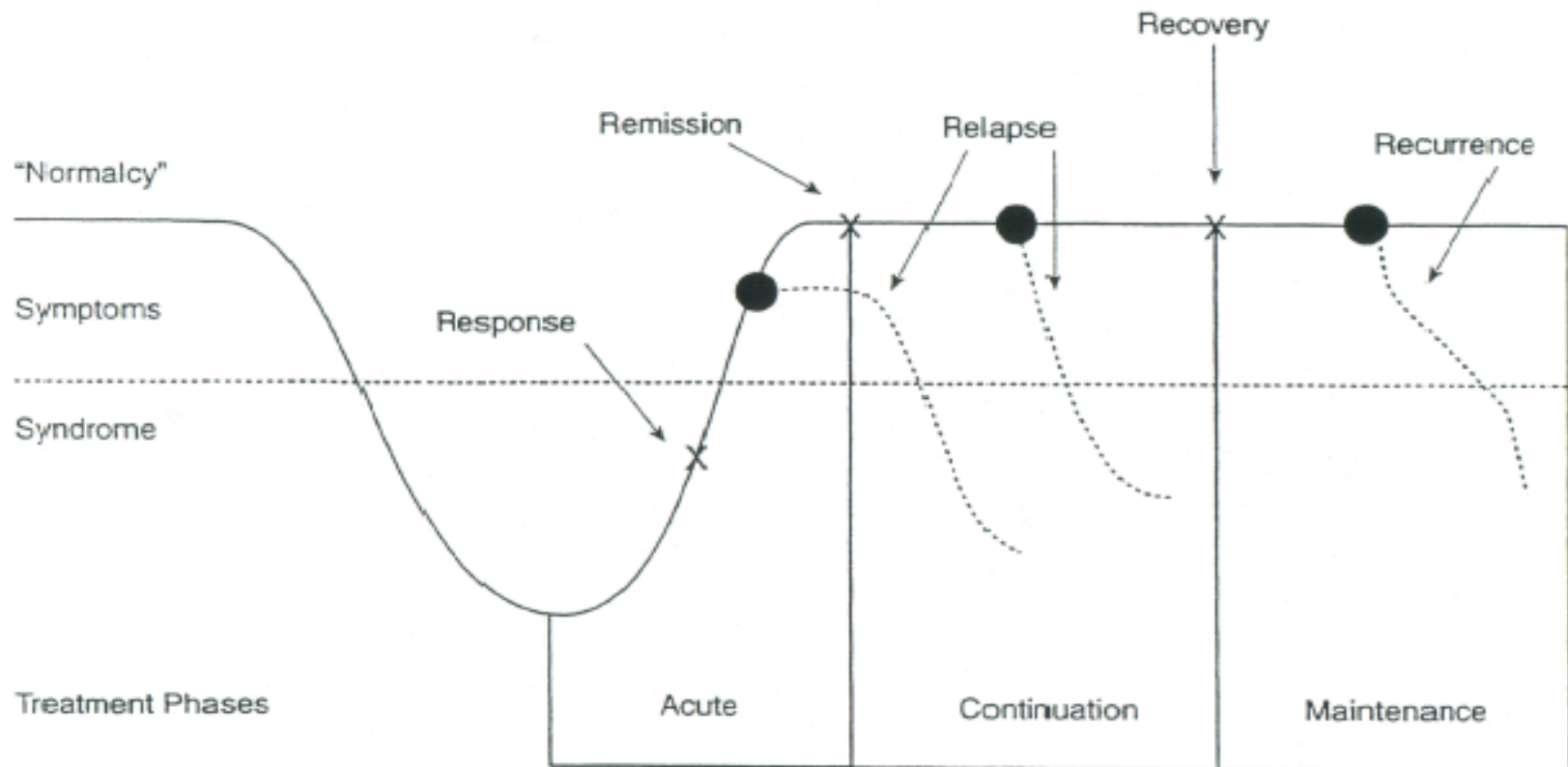
Difficulties in establishing long term efficacy for psychotropic drugs: common methodological issues (iv)

- Maintenance treatment
 - Recommended for responders who have evidence for an increased risk of recurrence, i.e., patients experiencing multiple episodes in the last few years
 - Studies have demonstrated superior outcome for patients with maintenance therapy

Regulatory Perspectives of Efficacy of Psychotropics

- Acute phase/short-term treatment
 - General satisfaction with guidelines
 - 4 – 8 week trials
 - High translatability of label for clinical practice/prescribers
- Continuation/Long-term treatment
 - Relapse prevention i.e. time to failure: the only labeling approved by FDA; not a specific claim for CHMP.
 - Well founded statistical basis; however, relevance for prescribers questionable for long-term treatment
 - Maintenance of effect: continuation of response obtained in short-term treatment over an extended period of time
 - High translatability for findings for patients/prescribers
 - Statistical analysis/basis need consideration; development of alternatives paradigms need consideration

Vocabulary of Time Course of CNS Diseases



Vocabulary of Long-Term Efficacy

- **Response**—reduction of symptoms of acute episode not necessarily complete
- **Maintenance of effect**—demonstration of the persistence of a treatment effect
- **Remission**—complete or nearly complete response of acute symptoms (implies underlying disease may still be present, but not expressed)
- **Recovery**—underlying disease has been treated and clinical symptoms absent
- **Relapse**—return of symptoms within same episode
- **Recurrence**—occurrence of new episode after an extended period of remission
- **Prophylaxis**—treatment to prevent some adverse outcome associated with disease state

Content of Symposium

- Clinical perspective of long-term efficacy
 - Mark Rapaport MD (US)
- Long-term efficacy, conceptual issues
 - Larry Alphas MD, PhD (US)
- Long-term efficacy trials in psychiatry, difficulties and solutions
 - Georges Gharabawi MD (US)
- Alternative design for long-term trials in psychiatry
 - Allan Young MD PhD (UK)
- Regulatory Perspective of long-term efficacy of treatments
 - Christina Sampaio MD (POR)
- Expert Panel Discussion
 - Michael Thase, MD (US); Ross Bullock, MA, MBBS, MRC Psych (UK)

