

***Multi-National Trials in the
Developing World:
Conceptualizing the Trials—
An Academic Perspective***

Ari Kiev, M.D.

President, SPRI Clinical Trials



Culture and Psychiatric Disorder

- Concepts of disease: e.g. Political dissidents and diagnoses of schizophrenia in former Soviet Union
- Definitions of normal and abnormal: e.g. Spiritistas in Puerto Rico whose auditory hallucinations are accepted as normal
- Symptomatology-pathoplastic effects of culture
- Unusual mental states, e.g. trance

Characteristics Of Mental Disorders In Developing Societies

- Special transient forms of schizophrenia, e.g. bouffee delirante aigue in Haiti,
- Frequency of hysterical disorders
- Rarity of depressive disorders
- Issues to consider:
 - Definitions are culture bound;
 - Does biology vary from culture to culture;
 - If biology is invariant, what impact does culture have and how do we set up studies to capture this?

Culture Bound Disorders

- Identify culture bound disorders and consider how to incorporate them into studies:
 - Anxiety states: koro, susto
 - OCD: shinkeishitsu
 - Hysterical disorders: latah
 - Phobic states: latah
 - Depressive reactions: the windigo psychosis
 - Dissociative states: amok, spirit possession

Defining End States In Studies

- Differences in end states in different cultures
 - chronicity and deterioration in schizophrenic patients less likely in less developed cultures.
 - Suicide less likely in depressive states
 - How to measure and assess end states to facilitate global trials in a range of societies.

Additional Practical Issues

- Taboo topics (sexual, family relationships, expressions of violence, dealing with fear and shame of serious mental illness) as relates to informed consent, accurate enquiry and reporting of side effects.
- Type of training to ensure physician cooperation with asking all relevant questions and to ensure that non-mental health professionals in some cultures understand the issues of identifying suitable patients for studies.
- Consider these factors in determining inclusion and exclusion criteria

Practical Issues: Treatment Paradigms Differ In Other Societies

- Recent experience conducting clinical trials in Ukraine
 - ICD-10 rather than DSM-IV is used.
 - Beliefs and values differ re: etiology, concepts of guilt and shame, reluctance to seek psychiatric treatment for very disturbed patients, side effects, compliance issues.
 - All diagnoses are made with reference to etiology, e.g. neurotic depression, bipolar depression and treatment approaches depend mainly on this etiology. Psychotherapy is almost exclusively used for neurotic depression .

Practical Issues: Treatment Paradigms Differ In Other Societies

- Recent experience conducting clinical trials in Ukraine,
 - Sensitivity of physician/investigators re: corrections on CRF's. Takes training to educate investigators to the importance of time lines, accountability, individual vs. committee responsibility
 - High compliance of patients once entered into studies-nevertheless low placebo response rates because patients are not symptomatic volunteers but patients in the practices of the physicians who are also the primary raters in the studies.

SPRI's Approach To Global Trials

- Evaluate differences and standardize disease diagnosis at investigator meetings-open communication on all differentiating issues
- Standardize ratings and rater training
- Evaluate cultural differences in placebo response and ensure that everyone is approaching studies from a research and not therapeutic perspective
- Maintain consistent contact throughout study to overcome wariness re: asking questions

Experience Conducting Clinical Trials In India

- Most of the mental health professionals are aware of the DSM IV criteria, variations in treatment approaches, need for standardized training.
- In India it is particularly important that mental health professionals educate non-psychiatric health care professionals about quick and reliable ways to diagnose MDD, bipolar disorders and the like since not everyone in India has access to specialized care.

Additional Issues In India

- Caregivers often believe in use of traditional medicine men, tantric healers
- Most patients with mental illness come with one or more attendants. Critical to communicate with them to ensure patient compliance
- Concomitant use of herbal-mineral medications