

Schizophrenia and Manic-Depressive Illness

Peter Cowley and Richard Jed Wyatt

Schizophrenia and manic-depressive illness constitute a tremendous health burden. They affect 2 percent of the world's population during life's most productive years, in turn straining family and other resources (Goodwin and Jamison 1990; Jablensky and others 1992). The diagnoses of schizophrenia and manic-depressive illness rely on objective criteria that can be used by trained health professionals. When broadly defined, schizophrenia can include both brief and chronic forms of the illness. Manic-depressive illness can occur in milder (bipolar II) and severe forms (bipolar I). In both forms of bipolar disorder an individual's mood, energy level, and cognition vary greatly over shorter or longer time periods. In order to limit the scope of this project, manic-depressive illness is used synonymously with bipolar I and II disorders.

Although most epidemiological studies of schizophrenia are from industrial countries, a recent World Health Organization (WHO) study provides epidemiological information from developing communities (Jablensky and others 1992). There is, however, painfully little known about manic-depressive illness in developing countries (Goodwin and Jamison 1990; Robins and Regier 1991).

The treatment of schizophrenia serves as the primary template for the cost-effectiveness calculations of how the program might work for manic-depressive illness. By showing how the cost-effectiveness template can be used for more than one mental illness, we hope that further research can be carried out on the cost-effectiveness of treating other mental illnesses, such as unipolar depression. The treatment protocol presented here has been simplified from what would be expected in the most industrialized parts of the world, making it practical and less costly, if also less exacting. Plans include a referral base (general medical practitioners, psychiatrists, families, traditional healers, and herbalists) from which individuals with such symptoms as "odd behavior," nontraditional violent outbursts, and delusional thinking can be sent to a clinic for evaluation and possible medical treatment.

The clinic will be staffed by trained auxiliary health workers and nurses; the client will visit the clinic once a month, and a trained psychiatrist will visit the clinic once a week to attend patient review sessions. Finally, the model assumes a steady-

state prevalence; therefore, it includes both old patients and new patients.

Risk Factors

There are few discernible risk factors for schizophrenia and manic-depressive illness; nonetheless, twin and adoption studies indicate that schizophrenia and manic-depressive illness have a genetic component (Gottesman and Shields 1982; Goodwin and Jamison 1990). Schizophrenia and manic-depressive illness have approximately the same incidence and prevalence in males and females (Robins and Regier 1991; Jablensky and others 1992). The peak age for developing schizophrenia and manic-depressive illness is approximately twenty; all but a few cases develop initial symptoms before age thirty-five (Goodwin and Jamison 1990; Jablensky and others 1992).

Socioeconomic class is a possible risk factor for schizophrenia, those living in poor socioeconomic conditions having high incidence and prevalence rates (Robinson and Regier 1991; Jablensky and others 1992). It is not known if the poor socioeconomic conditions in urban areas pose a risk or if persons with schizophrenia, because of their disease, migrate into these socioeconomic conditions. There is less of a "downward" social drift among persons with manic-depressive illness, which may be because manic-depressive individuals often have high energy and enthusiasm, which are correlated with social achievement (Bagley 1973).

Incidence and Prevalence: Schizophrenia

Studies done by WHO indicate that the incidence (derived from the time of the initial provider contact and interviews with family members about a patient's psychiatric history) of "broadly defined" schizophrenic patients who seek treatment is between 15 and 52 per 100,000 people (age fifteen through fifty-four), the developing world reporting the higher figures (Wig 1982; Jablensky and others 1992). "Broadly defined" schizophrenic patients include those with evidence of a psychotic state, such as nuclear schizophrenia, paranoid state,

acute paranoid reaction, alcohol- or drug-induced hallucinosis, unspecified psychosis, probable and borderline psychosis (Jablensky and others 1992).

Approximately 30 to 40 percent of individuals in the developing world who have experienced psychotic episodes feel persecuted or neglect daily tasks such as personal cleanliness (Jablensky and others 1992). If only those patients who show nuclear symptoms of schizophrenia (delusions of control, feelings of someone inserting thoughts, or auditory hallucinations) are tabulated, the incidence decreases to between 7 and 14 per 100,000 (age fifteen to fifty-four); such individuals usually show at least intermittent symptoms for the rest of their life (Jablensky and others 1992). Comparison with other annual incidence rates from developing countries is difficult because of differing diagnostic criteria. Nonetheless, other studies from Asia indicate an incidence of between 2 and 11 per 100,000 in those age fifteen and above; Beijing, China, reported an incidence of schizophrenia of 11 per 100,000 in persons age fifteen and above (Yucun and others 1981; Wig 1982).

Incidence and Prevalence: Manic-Depressive Illness

The authors of three studies in northern Europe have found an annual incidence of manic-depressive illness of between 11 and 21 per 100,000 for persons age fifteen and older who seek treatment (reviewed in Goodwin and Jamison 1990). Individuals with manic-depressive illness often present with: inflated self-esteem, distractibility, increased pleasure, decreased sleep patterns or signs of fatigue, feelings of worthlessness, or suicidal ideation. Commonly, the disease course is cyclical in nature, and the threat of a manic or depressive episode continues throughout the rest of the individual's life. It is suspected that manic-depressive illness is not as prevalent in developing countries as it is in industrial ones (Goodwin and Jamison 1990).

Morbidity and Mortality: Schizophrenia

It has been reported that the course of schizophrenia is less severe in developing countries (Jablensky and Sartorius 1988). The differing disease course patterns for suboptimally treated patients from developing and industrial countries are shown in table 28-1. Data in this table indicate that patients from developing countries are more likely to have a brief psychosis.

World Health Organization research indicates that several factors are associated with a good prognosis (being female, married, and having an acute onset); however, these prognostic indicators and the presence or absence of effective treatment do not completely explain the differences in outcome between patients from the developing and industrial worlds (Jablensky and others 1992; Leff and others 1992). The better prognosis for schizophrenic patients from the developing world may be influenced by the use of a broad case definition or differing demands posed by the particular society (Wyatt and Stevens 1987; Jablensky and Sartorius 1988).

Table 28-1. Course of Schizophrenic Disease in Developing and Industrial Countries
(percent)

| Location | Acute | Chronic | Intermittent | Total |
|---------------------------------|-------|---------|--------------|-------------------|
| Developing regions ^a | 27.5 | 37.1 | 32.7 | 97.3 ^b |
| Industrial regions ^c | 8.5 | 63.8 | 25.3 | 98.6 ^b |

Note: Acute course: full remission, no further episodes. Chronic course: at least one subsequent psychotic episode, with incomplete remission between episodes, or continuous psychotic episodes. Intermittent: partial remission, no further episodes, or at least one subsequent episode with full remission between episodes.

a. Agra, India; Cali, Colombia; and Ibadan, Nigeria.

b. The course of illness in some patients did not fit the definition of acute, chronic, or intermittent.

c. Aarhus, Denmark; London, England; Moscow, Russia; Prague, Czechoslovakia; and Washington, D.C., United States.

Source: Leff and others 1992.

Morbidity and Mortality: Manic-Depressive Illness

Retrospective studies indicate that 0 to 55 percent of non-phylactically treated manic-depressive patients had only one episode, whereas 13 to 42 percent had two to three episodes, 8 to 40 percent had four to six episodes, and 2 to 69 percent had more than seven episodes (reviewed in Goodwin and Jamison 1990). It has been estimated that 22 percent of manic-depressive patients (mainly women) have a chronic course with virtually no normal intervals between mania and depression (Tsuang, Woolson, and Fleming 1979).

Burden of Schizophrenia

At fifteen-year follow-up, persons with schizophrenia and other categories of psychosis reported mortality rates 1.8 times greater than the general population, with 5 percent of patients adequately treated (Lin and others 1989). Approximately 8 percent of schizophrenic patients in the United States kill themselves, at an average age of thirty-one; similar rates of suicide are suspected among individuals with schizophrenia from the developing world (Roy 1986; Leff and others 1992).

Psychiatric disorders such as schizophrenia and manic-depressive illness exert a tremendous toll on the emotional and socioeconomic capabilities of both patient and caretaker. It has been reported that between 17 and 50 percent of schizophrenic patients being followed up had severe social impairment (Leff and others 1992). Other research indicates that more than 25 percent of the schizophrenic population in the United States is unable to work or perform homemaker responsibilities and that those capable of working or performing housekeeping have at least a 25 percent disability (ongoing research by Wyatt).

Burden of Manic-Depressive Illness

Untreated manic-depressive illness is reported approximately to double the yearly risk of dying, with suicide causing the

majority of the excess mortality (Goodwin and Jamison 1990). It is estimated that one in five manic-depressive patients commits suicide, often within the first five years of the disease onset (Goodwin and Jamison 1990). Suicide is suspected to be less common among manic-depressive patients in the developing world, which may be a result of lower incidence rates, differing cultural manifestations of the disease, or a cultural bias against reporting suicide (Wittkower and Rin 1965). Due to their illness, approximately 20 to 30 percent of individuals with manic-depressive illness in the United States are unable to work (ongoing research by Wyatt).

Therapeutic Strategy for Schizophrenia

Such antipsychotic medications as fluphenazine, haloperidol, and chlorpromazine reduce the length of psychotic episodes in schizophrenic patients and can prevent relapses. Within six weeks after starting treatment with antipsychotic medication, 40 to 50 percent of active and chronic schizophrenic patients experience remission (Rifkin and others 1991). In addition, maintaining patients on antipsychotic medication produces a 50 to 60 percent reduction in relapse rates (Baldessarini, Cohen, and Teicher 1990; Rifkin and others 1991).

Antipsychotic medication has been reported to cause a 50 to 60 percent decrease in the severity of illness for both acute and chronic psychotic patients as rated by standard clinical rating scales (Santos and others 1989; Baldessarini, Cohen, and Teicher 1990). Relapse rates can be further reduced by using long-acting injectable antipsychotic medications (Baldessarini, Cohen, and Teicher 1990). When a schizophrenic patient improves clinically, social outcome also improves. It has been reported that there is a 0.5 correlation between clinical and social improvement as measured by interpersonal relationships, sociability, leisure activity, and work activity (Shepard and others 1989).

Research indicates that once patients have discontinued antipsychotic medication, they tend to have a much poorer social outcome, including a decrease in work productivity and an increase in socially disruptive behavior (Johnson and others 1983). There is an apparent decline in the suicide risk among treated schizophrenic patients, compared with the risk among those who are untreated; one study indicated that 27 percent of schizophrenic patients attempted suicide when neuroleptic medication was discontinued, whereas only 11 percent attempted suicide while on medication (Johnson and others 1983).

Therapeutic Strategy for Manic-Depressive Illness

Roughly 80 to 90 percent of manic-depressive patients on lithium respond favorably, resulting in a 60 to 80 percent reduction in relapses (Goodwin and Jamison 1990). Furthermore, it has been reported that both manic and depressive episodes are 80 percent less frequent in patients treated with lithium (Holinger and Wolpert 1979; Rybakowski and others 1980). Lithium helps to decrease the duration of an episode by

reducing the intensity of mania or depression; correspondingly, there is a decreased episode frequency (Goodwin and Jamison 1990). By reducing the intensity of mania or depression, lithium also helps reduce suicide. Research has shown that 1.17 suicide attempts per patient were made before lithium and 0.18 suicide attempts per patient were made after lithium was introduced (Causemann and Muller-Oberlinghausen 1988).

Cost-Effective Schizophrenia Case Management

There is no model available regarding the cost-effectiveness of either a schizophrenia or manic-depressive outpatient medical program in the developing world. The following model is an attempt to provide estimates of the cost and effectiveness of a case management program based on a best-case scenario; it is presented in equation format with results in table 28-2.

The annual cost of a medication treatment program for individuals with schizophrenia per million population age fifteen and above is the sum of:

- *Estimate of treatment costs per acutely psychotic patient treated successfully ($Cost_{acute}$)*. The outpatient costs per acutely psychotic patient who responds to medication and will receive antipsychotic medication for one year is equal to: $(N_{acute} \times V) + C_{acute}$, where N_{acute} = number of outpatient visits needed per year by each acutely ill schizophrenic patient; V = cost of one outpatient visit; and C_{acute} = yearly cost of antipsychotic and anticholinergic medication for each acutely ill schizophrenic patient.
- *Estimate of treatment cost per acutely psychotic patient treated unsuccessfully ($Cost_{acute/unsucc}$)*. Because a fraction of the acutely ill psychotic patient pool who will be given antipsychotic medications for a period of up to six months will not respond, the following equation is needed: $(N_{acute/unsucc} \times V) + C_{acute/unsucc}$, where $N_{acute/unsucc}$ = the number of visits used by an acutely psychotic patient who is dropped from the program after three months because of nonresponsiveness to medication, and $C_{acute/unsucc}$ = cost of medication in acutely psychotic patients who are dropped from the program because of nonresponsiveness to medication.
- *Estimate of treatment costs per chronically ill patient served ($Cost_{chronic}$)*. The outpatient costs for patients with schizophrenia who will receive long-term antipsychotic therapy is: $(N_{chronic} \times V) + C_{chronic}$, where $N_{chronic}$ = number of outpatient visits needed per year by each chronically ill schizophrenic patient, and $C_{chronic}$ = yearly cost of medication for a chronically ill schizophrenic patient.¹
- *Estimate of treatment costs per intermittently ill patient treated ($Cost_{intermittent}$)*. The outpatient costs for patients who will receive intermittent antipsychotic medication is: $(N_{intermittent} \times V) + C_{intermittent}$, where $N_{intermittent}$ = number of outpatient visits needed per year for each intermittently ill schizophrenic patient, and $C_{intermittent}$ = yearly cost of medication for an intermittently ill schizophrenic patient.

In order to simplify the equations, the estimated number of treated patients in the treatment groups (number-schizophrenia) is: $(I_{\text{schizophrenia}} \times P \times SS) \times (PT \times E)$, where $I_{\text{schizophrenia}}$ = incidence of broadly defined schizophrenia per 1 million population age fifteen through fifty-four;² P = proportion of broadly defined acutely ill schizophrenic patients of any age ($I_{\text{schizophrenia}}$) who will fall into either an acute, a chronic, or an intermittent disease outcome; SS = multiplication factor to account for preexisting patients; PT = proportion of population of each disease outcome who will be correctly diagnosed and appropriately treated at the health center (does not include those who dropped out because of medication side-effects); and E = percentage of each pool of patients that responds to antipsychotic medication.³

- *Estimate of disability-adjusted life-years (DALYS) gained per acutely psychotic patient successfully treated (DALY_{acute})*. The number of DALYS gained per acutely ill patient successfully treated can be calculated as follows: $R \times (H_{\text{acute}} + CT_{\text{acute}} + M_{\text{acute}})$, where R = percentage reduction in patient and caretaker's disabilities and patient's excess mortality with medication; H_{acute} = acutely ill patient's quality-of-life disability; CT_{acute} = disability per acutely ill patient from his or her caretaker's reduced quality of life; and M_{acute} = acutely ill patient's yearly increase in the risk of dying.

- *Estimate of DALYS gained per chronically ill patient treated (DALY_{chronic})*. The number of DALYS gained per treated chronically ill patient treated is: $R \times (H_{\text{chronic}} + CT_{\text{chronic}} + M_{\text{chronic}})$, where H_{chronic} = chronically ill patient's disability from his or her reduced quality of life; CT_{chronic} = disability per chronically ill patient from his or her caretaker's reduced quality of life; M_{chronic} = chronically ill patient's yearly increase in the risk of dying.

- *Estimate of DALYS gained per intermittently ill patient treated (DALY_{intermittent})*. The number of DALYS gained per intermittently ill patient treated is: $R \times (H_{\text{intermittent}} + CT_{\text{intermittent}} + M_{\text{intermittent}})$, where $H_{\text{intermittent}}$ = intermittently ill patient's disability from his or her reduced quality of life; $CT_{\text{intermittent}}$ = disability per intermittently ill patient from his or her caretaker's reduced quality of life; and $M_{\text{intermittent}}$ = chronically ill schizophrenic patient's yearly increase in the risk of dying.

In table 28-2 we display the equations used in determining the cost-effectiveness of the model, and in table 28-3 we present inputs used for the schizophrenia medical treatment program.⁴ The \$223.00 per disability-adjusted life-year gained is less expensive than most of the adult chronic disease interventions, such as coronary artery bypass surgery and cancer treatment programs (Jamison, chapter 1, this collection). The program would cost approximately \$0.104 per person (age fifteen or older), not an unreasonable burden for most health care systems. Over 95 percent of the case management benefits are from reductions in the patient and caretaker's quality-of-life disability, with little contribution from averted mortality.

Manic-Depressive Illness Case Management

The cost-effectiveness of a lithium medication program can be calculated using exactly the same equations as those used for the neuroleptic medication program. The input functions for the case management program for lithium treatment of manic-depressive illness are noted in table 28-4. The manic-depressive illness medication intervention program, with total cost figures of \$268.00 per disability-adjusted life-year gained and \$0.092 per person (age eighteen and above), like the program for schizophrenic patients, is affordable compared with other adult chronic disease interventions, and it has a similar distribution of benefits, as does the schizophrenia treatment program (Jamison, chapter 1, this collection).

Gaps between Good and Actual Practice

Bothersome but nonlethal side effects from antipsychotic medication used to treat schizophrenia are numerous and include dry mouth, constipation, decreased libido, and tremors, all of which often can be treated by lowering the dose; tardive dyskinesia (repetitive involuntary movements) and neuroleptic malignant syndrome (high fever and blood abnormalities), which are potentially more serious, can contribute to the already serious morbidity (Baldessarini, Cohen, and Teicher 1990). Many patients who are given antipsychotic medication, particularly early in their treatment course, are also given anticholinergic and antiparkinsonian medication to prevent acute dystonic reactions (rigidity of muscle groups, especially facial), which, when they occur, are both painful and frightening (McKane and others 1987; Santos and others 1989). Compliance by the patient in taking antipsychotic medication is another important issue, and it has been estimated that as few as 50 percent of schizophrenic patients take their medication as prescribed (Wilcox, Gilian, and Hare 1965). As with all medications, describing potential side effects before they occur and making certain the diagnosis and treatment are appropriate should increase compliance.

Up to 25 percent of patients taking lithium for manic-depressive illness complain of excessive thirst, tremor, or memory problems (Goodwin and Jamison 1990). Lithium may be harmful to fetuses and can also cause decreased thyroid activity (Mannisto 1980). Toxicity due to lithium overdose can cause serious kidney damage and is often fatal (Goodwin and Jamison 1990). Noncompliance of lithium users in taking their medication ranges between 18 and 53 percent and is often thought to be connected to the denial of the disease as well as the side effects (Goodwin and Jamison 1990). Manic-depressive patients need to be monitored for suicidal ideation, particularly during the first few years of the disease, when the risk is the highest.

Ethical and legal issues regarding giving medication to patients who cannot give consent (particularly those in acute psychotic states) need to be considered in relation to local standards, and possible dispositions for aggressive patients also need to be explored. If antipsychotic medication or lithium is

Table 28-2. Derived Variables and Their Most Likely Values

| Name or symbol | Variable | Derivation | Most likely value |
|--|--|--|-------------------|
| Number-schizophrenia _{acute} | Number of acutely ill patients treated successfully | $(I_{\text{schizophrenia}} \times P_{\text{acute}} \times PT_{\text{acute}}) \times E_{\text{acute}}$ | 18 |
| Number-schizophrenia _{acute/unsucc} | Number of acutely ill patients treated unsuccessfully | $(I_{\text{schizophrenia}} \times P_{\text{acute/unsucc}} \times PT_{\text{acute/unsucc}}) \times (1 - E_{\text{acute}})$ | 15 |
| Number-schizophrenia _{chronic} | Number of chronically ill patients treated | $(I_{\text{schizophrenia}} \times P_{\text{chronic}} \times PT_{\text{chronic}}) \times E_{\text{chronic}}$ | 696 |
| Number-schizophrenia _{intermittent} | Number of intermittently ill patients treated | $(I_{\text{schizophrenia}} \times P_{\text{intermittent}} \times PT_{\text{intermittent}}) \times E_{\text{intermittent}}$ | 141 |
| Cost _{acute} | Cost per acutely ill patient treated successfully | $(N_{\text{acute}} \times V) + C_{\text{acute}}$ | \$160 |
| Cost _{acute/unsucc} | Cost per acutely ill patient treated unsuccessfully | $(N_{\text{acute/unsucc}} \times V) + C_{\text{acute/unsucc}}$ | \$63 |
| Cost _{chronic} | Cost per chronically ill patient treated | $(N_{\text{chronic}} \times V) + C_{\text{chronic}}$ | \$117 |
| Cost _{intermittent} | Cost per intermittently ill patient treated | $(N_{\text{intermittent}} \times V) + C_{\text{intermittent}}$ | \$140 |
| DALY _{acute} | Disability-adjusted life-years gained per acutely ill patient treated successfully | $R \times (H_{\text{acute}} + CT_{\text{acute}} + M_{\text{acute}})$ | 0.30 |
| DALY _{chronic} | Disability-adjusted life-years gained per chronically ill patient treated | $R \times (H_{\text{chronic}} + CT_{\text{chronic}} + M_{\text{chronic}})$ | 0.60 |
| DALY _{intermittent} | Disability-adjusted life-years gained per intermittently ill patient treated | $R \times (H_{\text{intermittent}} + CT_{\text{intermittent}} + M_{\text{intermittent}})$ | 0.30 |
| U | Total number of disability-adjusted life-years gained from case management program | $(\text{Number-schizophrenia}_{\text{acute}} \times \text{DALY}_{\text{acute}}) +$ $(\text{Number-schizophrenia}_{\text{chronic}} \times \text{DALY}_{\text{chronic}}) +$ $(\text{Number-schizophrenia}_{\text{intermittent}} \times \text{DALY}_{\text{intermittent}})$ | 465 |
| Z | Total cost of schizophrenia program | $(\text{Number-schizophrenia}_{\text{acute}} \times \text{Cost}_{\text{acute}}) +$ $(\text{Number-schizophrenia}_{\text{acute/unsucc}} \times \text{Cost}_{\text{acute/unsucc}}) +$ $(\text{Number-schizophrenia}_{\text{chronic}} \times \text{Cost}_{\text{chronic}}) +$ $(\text{Number-schizophrenia}_{\text{intermittent}} \times \text{Cost}_{\text{intermittent}})$ | \$104,999 |
| Q | Cost per disability-adjusted life-year gained | Z/U | \$223 |

Source: Authors.

Table 28-3. Variables for Model of Schizophrenia Case Management

| Symbol | Variable | Value | | |
|--------|--|-------------------|---------|--------------|
| | | Acute | Chronic | Intermittent |
| P | Proportion of schizophrenic population | 0.28 | 0.37 | 0.33 |
| PT | Proportion who will receive correct treatment | 0.40 | 0.60 | 0.50 |
| SS | Steady-state factor to account for preexisting patients | 1.00 | 17.4 | 5.8 |
| N | Number of clinic visits needed per year | 30 ^a | 12 | 21 |
| V | Cost of one outpatient visit | \$2.25 | \$2.25 | \$2.25 |
| C | Yearly medication costs | \$92 ^b | \$90 | \$92 |
| E | Percentage of patients responding to medication | 0.50 | 0.60 | 0.50 |
| H | Patient's decreased quality-of-life disability | 0.40 | 0.80 | 0.40 |
| CT | Caretaker's decreased quality-of-life disability | 0.20 | 0.40 | 0.20 |
| M | Patient's yearly increase in risk of dying | 0.0035 | 0.007 | 0.0035 |
| R | Percentage reduction in patient's/caretaker's disabilities and mortality risk when patient taking medication | 50 | 50 | 50 |

Note: Total incidence (I) of schizophrenia (broadly defined) is 300 cases per million people age fifteen to fifty-four.

a. Twenty-one visits for acute patient unsuccessfully treated.

b. \$16 for acute patient unsuccessfully treated.

Source: Authors.

given by nonpsychiatrists and without serum monitoring, missed opportunities for dosage adjustment and reducing side effects will be increased. Furthermore, the use of antipsychotic medication or lithium in the developing world needs to be investigated, because medication may work better or worse in those areas. The cost-effectiveness of both programs relies heavily on community and family support. If the community does not respond, effectiveness will decrease as the costs increase because patient compliance will not be encouraged and assistance in helping the patient remain in the program (transport, jobs, housing, and so on) will be lacking.

Priorities for Control

Case management with medication is not the only alternative for these patients, but it may be the most cost-effective alternative. Psychotherapy alone has been proven to be of limited benefit compared with medical treatment, but some forms of

psychotherapy aimed at stress reduction and education about the illness together with antipsychotic medication for schizophrenia and lithium for manic-depressive illness appear to make both illnesses more manageable (Baldessarini, Cohen, and Teicher 1990).

Research on the epidemiology of schizophrenia and manic-depressive illness is of importance; of particular importance is a determination of associated disability. There are numerous rating scales which measure social activities, level of anxiety, activity, ability to perform work, self-esteem, and same and opposite gender friendship that could be used with local modification to help determine disability (Weiss and others 1985). A treatment protocol that would enable supervised primary-level health workers to identify and correctly treat psychotic and bipolar disorders needs to be developed. Research also needs to identify contact points (general practitioners, herbalists and traditional healers) that would act as bases for referral of psychiatric patients to

Table 28-4. Variables for Model of Manic-Depressive Illness Case Management

| Symbol | Variable | Value | | |
|--------|--|-------------------|---------|--------------|
| | | Acute | Chronic | Intermittent |
| P | Proportion of manic-depressive population | 0.22 | 0.55 | 0.33 |
| PT | Proportion who will receive correct treatment | 0.30 | 0.50 | 0.40 |
| SS | Steady-state factor to account for preexisting patients | 1.00 | 16.7 | 4.2 |
| N | Number of clinic visits needed per year | 30 ^a | 12 | 21 |
| V | Cost of one outpatient visit | \$2.25 | \$2.25 | \$2.25 |
| C | Yearly medication costs | \$92 ^b | \$90 | \$92 |
| E | Percentage of patients responding to medication | 70 | 60 | 70 |
| H | Patient's decreased quality-of-life disability | 0.30 | 0.60 | 0.30 |
| CT | Caretaker's decreased quality-of-life disability | 0.10 | 0.20 | 0.10 |
| M | Patient's yearly increase in risk of dying | 0.004 | 0.008 | 0.004 |
| R | Percentage reduction in patient's/caretaker's disabilities and mortality risk when patient taking medication | 60 | 60 | 60 |

Note: Incidence (I) is eighty cases per million people age eighteen and older.

a. Twenty-one visits for acute patient unsuccessfully treated.

b. \$16 for acute patient unsuccessfully treated.

Source: Authors.

a clinic-based medicine intervention program and to ensure patient compliance with the program.

Appendix 28A. Sources Used to Obtain Cost-Effectiveness Estimates

This section discusses sources for cost-effective case management of schizophrenia and manic-depressive illness.

Schizophrenia

The yearly incidence rate of broadly defined schizophrenia ($I_{\text{schizophrenia}}$) of 300 per 1 million population, age fifteen through fifty-four, is based on published results from the developing world (Jablensky and others 1992). The proportion of individuals with schizophrenia who fall into the three types of disease outcome categories (P) is derived from table 28-1 (developing world data with broad case definition of schizophrenia). P_{acute} patients are projected to need antipsychotics for only one year with no other treatment necessary, whereas $P_{\text{intermittent}}$ patients are assumed to need antipsychotics for a year's duration every third year, and P_{chronic} patients will need antipsychotics for the remainder of their lives.

The 17.4 steady-state factor for the chronic (SS_{chronic}) patient pool and the 5.8 factor for the intermittent ($SS_{\text{intermittent}}$) pool are based on a cohort calculated to remain in the program for thirty-nine years with a 5 percent yearly dropout rate.⁵ The steady-state factor of intermittently ill patients is one-third that of chronically ill ones, because they are projected to need medication only every third year. The proportions of each disease pool treated (PT), ranging from 0.40 to 0.60, are clinically based; those in the acute pool are the ones least likely to enter the program, because their illness is of shorter duration.

Thirty outpatient contacts per year (N) are needed to treat an acutely ill schizophrenic patient. This estimate is based on the assumption that the patients will need fourteen consecutive daily visits for initial stabilization, followed by weekly visits for the next six weeks, then monthly visits for the remainder of the year. The acutely ill patient who does not respond to treatment will be treated for two and a half months (twenty-one visits). The intermittently ill schizophrenic patient's course of illness would probably be known to the health center staff, making initial stabilization less time consuming; thus only twenty-one visits will be needed (seven consecutive daily visits, three weekly visits, and eleven monthly visits). The chronic pool of schizophrenic patients was projected to need outpatient visits once a month for antipsychotic medication injections each year. The \$2.25 outpatient cost per visit (V) is derived from calculations in table 28A-1 showing a hypothetical summary of capital and annual costs of health clinics and outposts that have a capacity of approximately 30,000 mental health visits per year.

It is projected that all patients diagnosed with schizophrenia are placed on antipsychotic medication, beginning with two weeks of 2 milligrams of generic oral fluphenazine per day,

followed by injections once each month of generic long-acting fluphenazine, and that one-half of the patients need 50 milligrams of generic diphenhydramine hydrochloride to prevent dystonic side effects. The medication costs per year for the acutely or intermittently ill schizophrenic patient (C_{acute} or $C_{\text{intermittent}}$) is thus \$92 (wholesale price from survey of producers). The yearly cost of medication for the acutely ill patient who does not respond to treatment ($C_{\text{acute/nonresp}}$) is \$16 for the initial two weeks of oral medication plus two months of injectable medication. The cost of the chronically ill patient's medication (C_{chronic}) is \$90, because these patients do not need the initial stabilizing doses of fluphenazine.

The effectiveness values of antipsychotic medications (E) are derived from data that show that the decrease in relapse rates when using long-acting antipsychotic medications, in patients who show an initial response to antipsychotics, is approximately 60 percent (E_{chronic}) and that 50 percent of actively psychotic patients (or relapsing intermittently ill patients; E_{acute} or $E_{\text{intermittent}}$) will remit within six weeks after beginning antipsychotic therapy (Johnson and others 1983; Baldessarini, Cohen, and Teicher 1990; Van Putten, Marder, and Mintz 1990).

The reduction of clinical and social impairment, or quality-of-life disabilities (H), for the acute (40 percent), chronic (80 percent), and intermittent patients (40 percent) through medication is based on various clinical rating scales; the caretaker's decreased quality-of-life disability (CT) is projected to be one-half of the patient's quality-of-life disability.⁶

The yearly increase in the risk of dying (M) is from research showing that individuals with schizophrenia in Taiwan (China) had approximately a 200 percent standardized mortality ratio in a fifteen-year follow-up (Lin and others 1989). Survival statistics for Mexican males in 1980 from age twenty to sixty were then used to calculate a 0.007 yearly increase in the risk of dying (M) for the schizophrenic population (United Nations 1982).

The reductions in quality-of-life disabilities for both patient and caretaker and the reduction in excess mortality risk seen for the patient (R) from the patient's taking antipsychotic medication assume that once the patient's life improves, the caretaker's life will improve at the same rate. The reductions also assume a 60 percent clinical improvement by clinical rating scales and a published correlation between clinical and social improvement, resulting in a projected 50 percent reduction figure (Santos and others 1989; Shepard and others 1989; Baldessarini, Cohen, and Teicher 1990). The same reduction input is used for decreasing the patient's excess mortality risk and is based on research indicating a 50 percent reduction in suicide attempts with medication and an assumption that if suicidal behavior is minimized so will other dangerous behavior which causes the high mortality risk (Johnson and others 1983).

The disability associated with decreased quality of life for patient and caretaker and the increase in the risk of dying for the acute and intermittent groups (when relapsed) are projected to be one-half those of the chronic group. The reasoning

Table 28A-1. Annual Costs of Schizophrenia and Manic-Depressive Case Management Programs

| Variable | Assumptions | Cost (dollars) |
|---|---|----------------|
| <i>Operating costs</i> | | |
| Salaries: case management officers | Fifteen officers per center; \$1,000 per officer per year | 45,000 |
| Salaries: nurse practitioners | One per center; \$1,500 per nurse per year | 4,500 |
| Retirement pensions | 5 percent of salaries | 2,475 |
| Supplies | \$250 per center, not including drugs | 750 |
| Utilities | Gas, water, and electric; \$150 per center | 450 |
| In-service training | \$500 per center | 1,500 |
| Supervision | One full day each month by psychiatrist at each center; per diem and transportation | 2,000 |
| Maintenance and repair: buildings | 1.5 percent of construction price per year | 900 |
| Maintenance and repair: equipment | 15 percent of purchase price per year | 112 |
| Transportation between centers and villages | Twelve visits per year by motorcycle to each village; twenty villages per center; fifteen miles round trip; 20 cents per mile for gas | 2,160 |
| Public education | None | 2,000 |
| Contingencies | None | 3,000 |
| Total | | 64,847 |
| <i>Capital costs</i> | | |
| Buildings | Annualized with thirty-year life span; \$20,000 per center original cost | 2,000 |
| Equipment | Annualized with ten-year life span; \$250 per center | 75 |
| Vehicles | One motorcycle per center; annualized with five-year life span; \$1,000 per motorcycle | 600 |
| Total operating and capital costs | | 67,522 |
| Cost per clinic visit | 30,000 patient visits per year | 2.25 |

Note: Assumes three centers.

Source: Authors; Over 1991.

for this is straightforward: the length of a psychotic episode based on data concerning hospital stays is six months; thus, the disability of these two groups exists for only one-half of the year (Shepard and others 1989).

Manic-Depressive Illness

The incidence of manic-depressive illness ($I_{\text{manic-depressive}}$) in the developing world is projected to be 80 per 1 million people aged eighteen and older, substantially less than the 150 per million reported from the industrial world (Goodwin and Jamison 1990). The proportion of manic-depressive individuals (P) who fall into the acute (only 1 manic-depressive episode), chronic (7 episodes), and intermittent (2–7 episodes) disease categories is a derivative from research with a fifteen-year follow-up period (Goodwin and Jamison 1990).

For chronic manic-depressive patients the steady-state factor is 16.7 (SS_{chronic}) and is formulated much like the program for schizophrenic patients, except the cohort was followed for only thirty-four years (average age of onset: twenty-five) and the yearly dropout rate because of side effects of medication (such as tremors and gastrointestinal effects) was 5 percent. Calculations for the intermittently ill pool of manic-depressive patients use the same data, except this pool of patients will receive lithium for only one out of every four years.

The proportions of the disease category subtype population who will receive care at a health system (PT) are partially based on an assumption that a lower percentage of the manic-

depressive population than the schizophrenic population will undergo treatment because the manic-depressive disease can often be "hidden" with greater ease in society. The proportions vary between 0.30 and 0.50, with the chronic patients most likely to enter because of the length of illness.

The number of outpatient visits needed per year (N) and the cost of one outpatient visit (V) are projected to be the same for the course of each subtype of manic-depressive illness as they were for the course of the subtype pools of schizophrenia. The cost of \$92 per year for lithium (C) assumes an average daily dose of between 900 and 1,000 milligrams, which is the traditional dose of lithium for the manic-depressive patient (Goodwin and Jamison 1990; wholesale price from survey of producers). This price includes, for the acute and intermittent patient (but not for the chronic patient), a two-week 2-milligram daily dose of oral fluphenazine. As with the schizophrenia case management plan, the acutely ill manic-depressive patient unsuccessfully treated will be in the program for only two and a half months, needing twenty-one clinic visits and medication costing \$16.

Lithium has been reported to reduce relapses by 60 to 80 percent in the industrial world and it is projected that lithium will prevent relapses 6 to 60 percent (E_{chronic}) in the developing world (Rybakowski and others 1980). Lithium has also been reported to be 80 to 90 percent effective in lowering the severity of illness in acutely ill patients (E_{acute} or $E_{\text{intermittent}}$), but it is projected to be only 70 percent effective in the developing world (Goodwin and Jamison 1990).

Patient (*H*) and caretaker (*CT*) quality-of-life disabilities are clinical judgments based on clinical and social rating scales. As with the schizophrenia case management model, the acute and intermittently ill manic-depressive patient (30 percent disabled) is projected to suffer from one episode lasting half a year, resulting in both one-half the disability and one-half the mortality increase suffered by the chronically ill patient who is 60 percent disabled the entire year (Goodwin and Jamison 1990). Correspondingly, it is projected that the caretaker's quality-of-life disability is 20 percent when he or she is charged with caring for a chronically ill patient, and 10 percent when an acutely or intermittently ill patient is involved.

Research indicates that mortality rates are 2.2 times greater for manic-depressive individuals than the general population, which, if one uses the previously mentioned survival tables of Mexican males in 1980, translates into a yearly increase in the risk of dying of 0.008 for manic-depressive individuals (*M*) (United Nations 1982; Goodwin and Jamison 1990).

The patient and caretaker's projected 60 percent reduction in quality-of-life disability with lithium usage (*R*) is based on the impressions of clinicians which indicate that the intensity of manic-depressive episodes decreases significantly. The decrease in the excess mortality for the lithium-treated manic-depressive patient (*R*) is derived from published reports showing a 60 percent decrease in suicides in manic-depressive patients who are taking lithium (Goodwin and Jamison 1990). If the suicide rate decreases 60 percent, it is assumed that the generalized excess mortality will also decrease 60 percent.

Notes

An earlier version of this paper was presented at the WHO/World Bank consultation on *Interventions for Nervous System Disorders* held in Washington, D.C. on July 6-7, 1992. We wish to thank Thomas McGuire for his assistance at the consultation and later, when he reviewed this chapter.

1. In contrast to the acutely ill patient pool, there is no need for an adjustment for patients who do not respond to antipsychotics, because the treatment responses of the chronic and intermittently ill groups of patients will be known to the clinic staff.

2. Incidence reported in the WHO study (Jablensky and others 1992) was for a population of 100,000; for the present circumstances we have adjusted that figure to a population of 1 million. Incidence refers to individuals of fifteen through fifty-four years who experienced clearly psychotic symptoms, had never made contact with a helping agency in the past, and were residents of the catchment area. It was also felt that the risk for schizophrenia was negligible after age fifty-four; thus, the incidence rates are for those age fifteen and older.

3. Either of the two pools of acutely ill patients (responders and nonresponders) will not have a steady-state factor by definition. "Incidence_{schizophrenia}" is total incidence and will be the same value for each disease outcome. "Effectiveness_{acute/unsucces}" is $(1 - \text{Effectiveness}_{\text{acute}})$ because it is the pool of acute patients who are treated unsuccessfully (the response of acute patients to medication is unknown because they have never participated in the program).

4. The equations do not include an input for the number of disability-adjusted life-years gained for the acute nonresponding patient pool by definition. In addition, the inputs for this pool are different from the acute responding pool with respect to number of visits needed (number-visits) and the cost of medication (yearly cost-medication_{acute/nonres}) and are included at the

bottom of table 28-3. The same rationale applies to the manic-depressive patient treatment program (table 28-4).

5. The contributions to the total for each of the last thirty-nine years were added to this year's patient pool to give an approximate number of patients in treatment in that disease outcome category. This total number of patients treated (in that disease outcome category) divided by this year's contribution to the patient pool (in that disease outcome category) is the steady-state factor.

Because the average age of schizophrenia onset is twenty and the general life expectancy is predicted to be sixty (individuals with schizophrenia generally have a higher standardized mortality rate), a program of thirty-nine years' duration is appropriate.

6. Completely (100 percent) disabled = 1.0 disability quotient; 40 percent disabled = 0.4 disability quotient; and so on.

References

- Bagley, C. 1973. "Occupation Status and Symptoms of Depression." *Social Science and Medicine* 7(5):327-39.
- Baldessarini, R., B. Cohen, and M. Teicher. 1990. "Pharmacological Treatment." In S. Levy and P. Ninan, eds., *Schizophrenia Treatment*. New York: American Psychiatric Press.
- Causemann, B., and B. Müller-Oberlinghausen. 1988. "Does Lithium Prevent Suicides and Suicide Attempts?" In N. J. Birch, ed., *Lithium: Inorganic Pharmacology and Psychiatric Use*. Oxford: IRL Press.
- Goodwin, K., and K. Jamison. 1990. *Manic-Depressive Illness*. New York: Oxford University Press.
- Gottesman, I., and I. Shields. 1982. *Schizophrenia: The Epigenetic Puzzle*. Cambridge: Cambridge University Press.
- Holinger, P., and E. Wolpert. 1979. "A Ten Year Follow-Up of Lithium Use." *IMJ* 156:99-104.
- Jablensky, A., and N. Sartorius. 1988. "Is Schizophrenia Universal?" *Acta Psychiatria Scandinavica* 344(supplement):65-70.
- Jablensky, A., N. Sartorius, G. Ernberg, M. Anker, A. Korten, J. E. Cooper, R. Day, and A. Bertelsen. 1992. "Schizophrenia: Manifestations, Incidence, and Course in Different Cultures: A World Health Organization Ten-Country Study." *Psychological Medicine* 20(supplement):1-97.
- Johnson, D., G. Pastorski, J. Ludlow, K. Street, and R. Taylor. 1983. "The Discontinuance of Maintenance Neuroleptic Therapy in Chronic Schizophrenic Patients: Drug and Social Consequences." *Acta Psychiatria Scandinavica* 67:339-52.
- Leff, J., N. Sartorius, A. Jablensky, A. Korten, and G. Ernberg. 1992. "The International Pilot Study of Schizophrenia: Five-Year Follow-Up Findings." *Psychological Medicine* 22:131-45.
- Lin, T., H. Chu, H. Rin, C. Hsu, E. Yeh, and C. Chen. 1989. "Effects of Social Change on Mental Disorders in Taiwan: Observations Based on a 15-Year Follow-Up Survey." *Acta Psychiatria Scandinavica* 348(supplement):11-34.
- McKane, J., D. Robinson, D. Wiles, R. McCreadie, and G. Stirling. 1987. "Haloperidol Decanoate v. Fluphenazine Decanoate as Maintenance Therapy in Chronic Schizophrenic In-Patients." *British Journal of Psychiatry* 151:333-36.
- Mannisto, P. T. 1980. "Endocrine Side-Effects of Lithium." In F. N. Johnson, ed., *Handbook of Lithium Therapy*. Baltimore: University Park Press.
- Over, Mead. 1991. *Economics for Health Sector Analysis: Concepts and Cases*. Washington, D.C.: World Bank, Economic Development Institute.
- Rifkin, A., S. Doddi, K. Basawaraj, M. Borenstein, and M. Wachspress. 1991. "Dosage of Haloperidol for Schizophrenia." *Archives of General Psychiatry* 48:166-70.
- Robins, L., and D. Regier. 1991. *Psychiatric Disorder in America: The Epidemiologic Catchment Area Study*. New York: Free Press.

- Roy, Alec. 1986. "Depression, Attempted Suicide, and Suicide in Patients with Chronic Schizophrenia." *Clinics of North America* 2(1):193-205.
- Rybakowski, J., M. Chtopocka-Wozniak, Z. Kapelski, and W. Stryzewski. 1980. "The Relative Prophylactic Efficacy of Lithium against Mania and Depressive Recurrences in Bipolar Patients." *International Pharmacopsychiatry* 15:86-90.
- Santos, J., J. Cabranes, C. Vazquez, F. Fuentenbro, I. Almoguera, and J. Ramos. 1989. "Clinical Response and Plasma Haloperidol Levels in Chronic and Subchronic Schizophrenia." *Biological Psychiatry* 26:381-88.
- Shepard, M., D. Watt, I. Fallon, and N. Smetton. 1989. "The Natural History of Schizophrenia: A Five-Year Follow-Up Study of Outcome and Prediction in a Representative Sample of Schizophrenics." *Psychological Medicine* 15 (supplement):1-46.
- Tsuang, M., R. Woolson, and J. Fleming. 1979. "Long-Term Outcome of Major Psychoses: 1. Schizophrenia and Affective Disorders Compared with Psychiatrically Symptom-Free Surgical Conditions." *Archives of General Psychiatry* 36:1295-1301.
- United Nations. 1982. *Demographic Yearbook*. New York.
- Van Putten, T., S. Marder, and J. Mintz. 1990. "A Controlled Dose Comparison of Haloperidol in Newly Admitted Schizophrenic Patients." *Archives of General Psychiatry* 47:754-58.
- Weiss, D., K. DeWitt, N. Kaltreider, and M. Horowitz. 1985. "A Proposed Method for Measuring Change Beyond Symptoms." *Archives of General Psychiatry* 42:703-8.
- Wig, N. 1982. "Methodology of Data Collection in Field Surveys." *Acta Psychiatrica Scandinavia* 296(supplement):77-86.
- Wilcox, D., R. Gilian, and E. Hare. 1965. "Do Psychiatric Outpatients Take Their Drugs?" *British Medical Journal* 2:790-92.
- Wittkower, E., and H. Rin. 1965. "Transcultural Psychiatry." *Archives of General Psychiatry* 13:387-94.
- Wyatt, R., and J. Stevens. 1987. "Similar Incidence Worldwide of Schizophrenia: Case Not Proven." *British Journal of Psychiatry* 151:131-32.
- Yucun, S., A. Weixi, S. Liang, Y. Xiaoling, C. Yuhua, and Z. Dongfeng. 1981. "Investigation of Mental Disorders in Beijing Suburban District." *Chinese Medical Journal* 94(3):153-56.

Source: Dean T. Jamison, W. Henry Mosley, Anthony R. Measham, and Jose Luis Bobadilla (eds.). *Disease Control Priorities in Developing Countries*. New York: Oxford University Press for the World Bank. 1993.