

Schizophrenia: 1979–2009

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Abstract

Background: As more becomes known about the complex causation of schizophrenia, the variability of treatment response, and the effectiveness of preventive measures, treatments are likely to change. **Methods:** A standard regimen from a review article written in 1979 is examined and compared to currently recommended practice, thirty years later. **Results:** Over this period, there have been many small changes and some very significant improvements: attitudes toward families of patients have altered; patient autonomy has increased; early intervention, assertive community treatment teams, psychoeducation, and cognitive behavioral therapy have all been introduced in the last thirty years. Recovery (defined variously, but with a focus on counteracting disability and enhancing self-determination in the face of stigma), rather than symptom reduction, has become the main aim of treatment. **Conclusions:** Despite many changes, the overall health of patients with schizophrenia is poor and mortality rates are excessive. Improvement in the treatment of schizophrenia over the last thirty years is insufficient.

Key Words: Schizophrenia, Management, Antipsychotics, Morbidity, Mortality, History

Introduction

The treatment of schizophrenia changes over time as more is known about its complex causation, the variability of treatment response, and the effectiveness of preventive measures. In the last thirty years, much scientific activity has taken place in psychiatric genetics, brain imaging, therapeutic guidelines, family involvement, psychoeducation, neuroethics, early intervention, advocacy and stigma prevention, psychopharmacology, community treatment and psychiatric rehabilitation. Against those advances, I compare a 1979 regimen for comprehensive treatment of schizophrenia with current clinical recommendations.

In 1979, I wrote an article entitled “Management of the

Schizophrenic Patient” (1). The management that was described in the paper was an outgrowth of my own (fifteen years at that point) experience treating individuals with schizophrenia. Official treatment guidelines did not exist (for a history of the development of clinical guidelines, see [2]) but my views were shaped by the practice of my colleagues and the psychiatric literature that was most influential at the time (3, 4). Thirty years later, it is instructive to see what has changed.

1979 Article: “Management of the Schizophrenic Patient”

The 1979 title would be clearly unacceptable today. In the seventies and eighties, it was routine to use “schizophrenic” as a noun or an adjective referring to a person. Over time, however, “schizophrenic” has been read as pejorative. For instance, in 1992 (5), at a time when patients’ access to their own medical records was still a relatively new phenomenon, the phrase “22-year-old single, unemployed, chronic schizophrenic” in case notes was rated as offensive by all raters. This reflects the new Recovery orientation about which there will be more in the conclusion of this paper. Schizophrenia

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no longer defines a person; it may be part of one's lot in life, but it is no longer considered an identity (6).

The word "management" has also fallen into disrepute (although it remains extant in the case management literature) because it paints service users with the brush of passivity whereas, today, they expect partnership. A major change in schizophrenia treatment since thirty years ago is lessened coercion, increased patient autonomy (7).

Abstract from the 1979 Article

Schizophrenia is a continuing and relapsing disorder that begins in early adulthood and lasts indefinitely. Effective treatment, therefore, needs to be long-term and comprehensive. The physician must be able to control disabling symptoms while minimizing the side effects of neuroleptic medication. The lifetime risk remains of depression and suicide, paranoid crisis, social distress and frequent rehospitalization. It is a medical responsibility not only to look after the schizophrenic patient's health but also to coordinate social and emergency services, improve the quality of life, support the family and anticipate problems in offspring. At the same time, the physician needs to consider the welfare of the community in which the schizophrenic patient lives (1, p. 1097).

This 1979 summary statement still applies except that the word "neuroleptic" is now rarely used in North America. It was a coinage of Jean Delay's, based on the etymology "taking hold of the nerves," in line with his hope that pharmacological agents like chlorpromazine would be able to "settle the excited mind" (8). "Neuroleptic" was used for first-generation antipsychotics and was replaced with "antipsychotics" when second-generation drugs were introduced. Gründer et al. have recently proposed the use of "neuroleptic" for drugs that produce extrapyramidal symptoms and "antipsychotic" (dropping the adjective "atypical") for those that do not (9). The name change has already happened in North America, although the word "neuroleptic" does still appear in the international literature (10, 11).

The transition to the term "antipsychotic" began occurring at the same time as enthusiasm rose for preventing psychosis by intervening early, at the time of the first psychotic sign or, ideally, even earlier. In 1996, McGlashan, one of the pioneers of early intervention in the United States, was still using the term "neuroleptic" (12). The same year, McGorry in Australia, at the start of his early intervention program, was still calling the drugs he used "neuroleptics" (13). But that same year, McReadie in the United Kingdom already called them "antipsychotics" (14).

One phrase from the 1979 abstract, "to look after the schizophrenic patient's health," has come to take on increas-

ing importance with time. Because patients with schizophrenia live more autonomously now, they are all the more vulnerable to homelessness, serious infection, poor diet, smoking, and overuse of abusive substances. Second-generation antipsychotics place them at increased risk for weight gain, hyperglycemia, metabolic syndrome, and cardiac disorders. Because these drugs do not impede fertility to the same degree as the older agents, women with schizophrenia become pregnant more readily so that treatment can jeopardize not only their own health but also that of their fetus (15). Unless physical health is monitored carefully (16), health in this population is more compromised than it was in 1979.

Characteristics of the Patient in the Community

The illness usually begins in late adolescence; therefore, schizophrenic patients are unlikely to have completed their schooling, are interpersonally unpractised, have few firmly established links in the community and are usually vocationally untrained. Their life has been interrupted by several stays of months at a time in psychiatric wards (1, p. 1097).

That last sentence no longer applies. Already in 1979, it was being recommended that psychiatric hospitalizations be kept as short as feasible (17). By the early 1980s, most findings suggested that long admissions did not decrease subsequent hospitalization, did not clearly improve social adjustment, nor did they reduce the severity of psychopathology (18). These comparisons between the effects of long and short hospital stays have to be understood in the context of increasing economic pressures to reduce hospitalization costs (i.e., cut beds). The 1970s and 1980s were the high-point of the community care movement, a period of major expansion of community services. Even when that expansion slowed in the 1990s, hospital beds continued to be cut. For instance, an Israeli report shows that, between 2000 and 2004, the mean length of hospital stay decreased from 37.6 days to 36.4 days, in line with international practices (19). The authors of this paper comment: "particular attention needs to be devoted to planning and funding so that availability of community services matches reduction in psychiatric hospitalization" (19), a goal most communities have found difficult to achieve. A recent meta-analysis of lengths of hospital stay suggests that short stays are not associated with more frequent admission nor with discontinuity of care (20).

Antipsychotics and Side Effects

Much discussed in the 1979 paper was the burden of medication side effects:

...heightened apathy and social withdrawal, reduced motivation to exert effort, reduced libido, [they] produce a number of sensations that are unpleasant and sometimes frightening (light-headedness from orthostatic hypotension; tremulousness, restlessness and muscle stiffness from pseudoparkinsonism; blurred vision, nasal congestion, bladder and gastrointestinal disturbances from interference with parasympathetic functioning; and sunburn from skin photosensitivity, ... and cause, after several years of treatment, chronic motor dysfunctions (e.g., tardive dyskinesia) that are difficult and sometimes impossible to reverse (1, p. 1098).

To avoid some of these distressing effects, notably pseudoparkinsonism and movement disorders, newer drugs (“atypicals”) were introduced for the treatment of schizophrenia in the 1990s. Based on the chemical structure of the antidepressant imipramine, in 1958, a Swiss pharmaceutical company synthesized antidepressants with neuroleptic properties (21). One of the compounds, for which a patent was submitted in 1960, was clozapine. It produced less cataplexy than chlorpromazine on animal testing and human testing revealed no neurological side effects. In 1988, Kane et al. (22) provided the clinical evidence to show that it was an effective antipsychotic (23). Because the use of clozapine could lead (rarely) to agranulocytosis, it became a niche drug, reserved for the most ill, but other “atypicals” followed by the mid-nineties. Today, these drugs are used more than the first-generation drugs, although efficacy (except for clozapine) is not superior (24-26) and side effects are probably worse. They are metabolic (27-29) and cardiac (30) rather than neurological.

As a class, patients find the second-generation drugs more tolerable than the older ones, less productive of initial dysphoria (31). For this reason, they help adherence to treatment but, in the long run, they are potentially more toxic than older drugs.

Maintenance of Treatment

This section of the paper in 1979 emphasized the importance of continuity of treatment, a clinical preoccupation that has not changed. One of the barriers to continuity was identified as miscommunication between physician and family members:

Relatives frequently identify with the patient's misperception of the doctor as wicked or uncaring and heap blame for failure to improve on the doctor. Doctors, of course, fall into the same trap. They take at face value the patient's description of relatives as hostile or detached and do not attempt to include families in planning for the patient (1, p. 1098).

Such adversarial attitudes are far less in evidence in 2009. The relationship between physician and patient has improved, as has that between family and physician, probably because the profession is now much less prone to attribute either the cause or the exacerbation of illness to the family (32). The “schizophrenogenic mother” concept was already waning in 1979, a year after a substantive review of the work on family causation of schizophrenia was published (33). The hypothesis that high levels of criticism and hostility expressed by family members (high Expressed Emotion or EE) can lead to relapse in schizophrenia was being tested in 1979 and became very influential in the 1980s and 1990s. It is still a prominent theory of schizophrenia causation, especially outside the U.S. (34).

Moditen Clinics and Community Treatment Orders

1979 style “Moditen Clinics” group settings, where patients came to receive depot injections, have given way to Home Care Teams that administer injections, when needed, in the patient's home (35). The need for multidisciplinary input was already understood in 1979 and continues to be an important feature of psychiatric rehabilitation for individuals with schizophrenia (36).

A paradox of generally increasing autonomy for patients is that Community Treatment Orders (CTOs) have been introduced in many jurisdictions (they did not exist in 1979) such that specifically defined patients who do not adhere to their pre-agreed treatment plans can be legally coerced into doing so under threat of rehospitalization. CTOs emerged in the late 1980s in response to the occasional acts of violence committed by ex-psychiatric patients (37), and they remain a controversial form of treatment, although legal in 2009 in most states of the United States, Canada, the United Kingdom, Australia and New Zealand (38) and with some evidence of effectiveness (39).

Group Therapies

What seems to work is an hour-long group meeting, held at the same time every week, to which patients can come as frequently as they wish. They can come late without penalty and leave early if they wish (1, p. 1098).

The 1979 paper described extensive group intervention (support groups, problem-solving groups, psychoeducational groups, family groups, psychotherapy groups, activity groups). The emphasis was on the healing aspects of group work. The focus has now shifted so that, although many interventions continue to be offered in a group setting, the healing tends now to be attributed to the specifics of the intervention, not to the group interaction (40, 41). To a large

extent, the healing outcome looked for in group treatment (in psychoeducational groups, for instance) in 2009 is medication compliance (42), although group cognitive behavioral therapy and group cognitive enhancement therapy (43–45) have their own outcome measures. These latter treatments did not exist in 1979, whereas today they are increasingly recommended. This is especially true for cognitive behavioral therapy (46).

Symptoms and Doses

Low doses of antipsychotics were recommended in 1979 with the recommendation that higher doses be administered periodically, if needed, to forestall active psychotic symptoms:

This dose can be very low and still prevent relapse. It should be low enough that medication to counteract side effects (i.e., an anticholinergic) is not required and yet the patient experiences no side effects. For most patients this dose need be only 100 to 200 mg of chlorpromazine equivalent per day (1, p. 1099).

The literature now worries about suboptimal dosing and recommends a steady dose of medication; “compliance” is defined as following the doctor’s instructions to the letter, with no variation for periods of calm or periods of stress. In an age of increasing patient autonomy (47), this is somewhat surprising and is changing to include patient opinions (48).

In 1979, drug-free periods (drug holidays) were recommended in order to prevent tardive dyskinesia by decreasing cumulative neuroleptic exposure (49, 50):

Because of the problem of side effects “drug holidays” have been advocated. It is best if the patient is given an extended drug-free period every several months, during which he or she is extra carefully monitored (1, p. 1100).

Intermittent dosing is rarely practiced today although there are still some proponents (51, 52). Extended dosing (a pill taken every second or third day) is a different concept based on the duration of occupancy of dopamine receptors for different antipsychotics—a concept that has not widely caught on (53).

Prevention of Sequelae

Treating symptoms and minimizing side effects is just one part of the task of caring for schizophrenic patients. As in any other lifelong illness, prevention of naturally occurring sequelae is another important part of comprehensive care (1, p. 1101).

The sequelae that were seen as in need of prevention in 1979 were: suicide, rehospitalization, psychosocial crisis, discontinuity of care. Today, we would probably emphasize

homelessness, victimization, unemployment, substance abuse, physical health, and quality of life as well as suicide (54).

Family Burden

Much has been written in the psychiatric literature on the contribution of the family to the patient’s illness in terms of cause or recurrence of symptoms. Little has been written about the burden a schizophrenic person imposes on his or her family (1, p. 1102).

This is no longer the case. The burden of those who care for the person with schizophrenia at home is well recognized and is perhaps a better predictor of relapse than is Expressed Emotion in caregivers (55).

Coping with Stigma

Managing stigma is now recognized as one of the foremost challenges of those diagnosed with schizophrenia. The word, stigma, was not used in the 1979 article although there was reference to it:

Public education helps, and the present climate is much more understanding of idiosyncrasies in behaviour. The frightened responses of others elicit reactions from the patients – usually increasing fright and hostility, paranoia, withdrawal and increasingly odd behaviour (1, p. 1103).

Conclusions

Despite remarkable advances in the last thirty years in genetics, cognition, neuroimaging, and psychopharmacology, research findings have not substantially impacted on treatment. Important questions remain unanswered: whether it is possible to anticipate and, thus, prevent the development of schizophrenia in genetically predisposed individuals; whether it is possible to predict and enhance individual response to specific therapeutic strategies; and, whether drug development based on novel premises can be effective for particular domains of schizophrenia symptoms or for cognitive deficits. The challenge is to translate research findings into improved treatment.

In the last year, there have been attempts to specify what facts are firmly established about this elusive illness (56–60). There are many such facts, many of them elucidated in the last three decades. During this period, there have been outstanding achievements in molecular genetics, with many chromosomal areas now thought to be harboring schizophrenia-related genes (61). There has been progress in identifying copy number variations (62), which may be of etiological significance, microRNAs in central nervous system development and function, and epigenetic mechanisms that may prove significant (63). Genetics will help to

identify subtypes of schizophrenia, such as the 22q deletion syndrome already identified, and may one day lead to more personalized treatment, but, thus far, genetics has not influenced treatment.

Important endophenotypes (intermediate phenotypes) in patients and their first-degree relatives have been identified (64) but these have not yet led to new treatments. Neuroimaging studies, unknown thirty years ago, have detected intriguing departures from the norm and progression of such changes that differs in deficit and non-deficit schizophrenia (65).

This augurs well for differentiating treatment along symptom dimensions but has not yet been sufficiently tested to be included in treatment guidelines. A wide variety of cognitive deficits have been identified in schizophrenia over the last three decades, and their evolution over time is being charted (66). This has led to a new focus on cognitive remediation, very important for vocational rehabilitation and for recovery (67).

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Cognitive remediation, early intervention during the prodromal stage and treatment of comorbid medical conditions are all being increasingly practiced but have not yet been fully integrated into treatment guidelines (68).

Most current treatment guidelines concentrate on antipsychotic drugs, their relative efficacy and recommended doses, although much remains unanswered in this area (69). A new proposed treatment modality for specific symptoms is transcranial magnetic stimulation (rTMS) for negative and positive symptoms in schizophrenia (70).

What is most new about the comprehensive care of people with schizophrenia in the last thirty years? With respect to drugs, it is the advent of clozapine for specific targets such as non-response, violence, and suicidality. An important change is the inclusion of families in treatment deliberations (71, 72).

This has come about not because of new findings but because of the growing strength of the family movement, cost issues that make families indispensable in the collaborative care of patients, and a more relational view of ethics whereby family and, at times, community, is integral to autonomous decision making. New findings (worse prognosis for longer duration of untreated psychosis) have spurred the movement toward early detection and intervention (73). The superior outcomes for early intervention probably reflect

shorter hospitalization, fewer ruptures of relationships, and fewer detours in the course of early adult life, rather than preventing psychosis from injuring the brain, as originally thought. Whatever the reason, the early intervention movement, coupled with the introduction of novel medications, has led to a welcome optimism in patients and families and professionals. The need now is to ensure that the treatments used in early intervention are safe for the long usage that is necessary in the current treatment of this illness.

The most interesting change from 1979, when the focus was on pathology, is the new focus on recovery, first coming into prominence in the late 1980s (74). The concept encompasses change that occurs over time in the patient, and change that can be brought about in the mental health system in which the patient lives. It has been described as a nonlinear process that allows for setbacks and lost ground. Recovery means not only overcoming disability but also developing mental health—i.e., feeling hopeful, renewing a sense of possibility, gaining awareness of one's potential, evolving a sense of agency and self-determination, regaining and expanding competencies and coping skills, viewing one's life as meaningful and purposeful, exercising choice, reconnecting with others and finding a place in society (filling social and vocational roles) (75). It also means working within one's community to unlock opportunities for those affected by mental illnesses, to nurture community connectedness and to eliminate stigma (76).

Before recovering psychologically, however, one needs to be physically healthy. Compared with the general population, the lifespan of persons with schizophrenia is 20% shorter, with cardiovascular disease as the leading cause of death (77). There is now an increased prevalence of the metabolic syndrome (obesity, insulin resistance, dyslipidemia, impaired glucose tolerance, and hypertension), an increased prevalence of morbidity factors such as smoking, infection, and poor nutrition, coupled with reduced access to medical care because of poverty, homelessness, unemployment, distrust of institutions, and a lack of sophistication. Currently available drugs lead to excess weight and an increased risk of associated metabolic disturbances. Patients do not yet receive adequate recognition of, monitoring of, or care for their medical illnesses. There is a critical need for psychiatrists and primary care professionals to increase awareness of, and attention to, the physical health problems of persons with mental illness. There is a critical need for safer drugs. Major advances in cognitive science, psychopharmacology, molecular genetics, and brain imaging, the expansion of community services, the reduction of stigma, and the emphasis on recovery have all improved the treatment of patients with schizophrenia, but, on balance, it is not sufficiently different from what it was thirty years ago.

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