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Point of View

Schizophrenia – Falling Incidence and Better Outcome?

G. HARRISON and P. MASON

It has been suggested that schizophrenia is a disappearing disease. The evidence for this assertion is reviewed, and also for a parallel theory advanced in recent years that the disorder may be undergoing a benign metamorphosis in its course and outcome. It is concluded that the evidence is presently unconvincing given the methodological problems inherent in most follow-up studies; changes have taken place in clinicians' assumptions, in treatments, and in the quality of follow-up studies, rather than in the disorder itself. Nevertheless, possible time trends in the incidence and outcome of schizophrenia call for further scientific investigation.

While some radical social theorists and critics of psychiatry in the 1960s asserted that schizophrenia would disappear altogether once wrested from the hands of medical practitioners, others suggested that the process of de-institutionalisation would greatly improve social outcome and symptomatic recovery for the patient. In recent years similar assertions have been made within the sphere of academic psychiatry.

The 'disappearing schizophrenia' theory

First, it has been suggested that schizophrenia may be a 'disappearing' disease (Eagles & Whalley, 1985; Der *et al*, 1990). If proved correct, this theory would carry enormous implications, in terms of both the burden of suffering associated with the disorder and the nature and scope of future psychiatric services. There are several reasons, however, why the 'disappearing schizophrenia' theory remains highly speculative. Although ten studies have identified a fall in the number of new cases diagnosed over the past three decades, another five have failed to demonstrate a convincing decline in incidence, and a sixth does so for men only (Kendell *et al*, 1993; Harrison, 1993). Moreover, a reduction in the administrative incidence of the disorder is not necessarily commensurate with changes in its true incidence. Factors such as earlier intervention by general practitioners, closure of in-patient facilities with increased community-based provision of care, and an increase in severe mental disorder among the homeless may all contribute to a perceived decline in the number of ascertained cases.

A spurious decline may also be produced by improved quality control in the way case registers operate (for example, producing fewer false positives for first-onset cases), and by changes in the demographic structure of the population at risk (Harrison *et al*, 1991). In addition, Kendell *et al* (1993) have demonstrated conclusively that changes in diagnostic practices were responsible for at least part of the reported decline in the incidence of schizophrenia in Edinburgh. A dispassionate review of the available evidence must therefore conclude that, while there is certainly sufficient material available to warrant further investigation, the case is so far not proven.

The metamorphosis of schizophrenia

A second but no less radical theory advanced by psychiatrists in recent years parallels the 'disappearing schizophrenia' theory and may be linked to it. It has been suggested that over the second half of this century the disorder has undergone a 'benign metamorphosis' (Zubin *et al*, 1983): perhaps as a signal of its ultimate demise, the natural history of the disorder is moving toward a more favourable social and symptomatic outcome. It is important to be clear about this proposal. It does not suggest that, with the benefit of experience, our understanding of the heterogeneous nature of the longitudinal course and outcome of the disorder has broadened. Rather, it proposes that "the disorder itself has undergone a benign metamorphosis *as has occurred with some infectious diseases*" (Zubin *et al*, 1983).

Zubin suggests that the disorder has changed in two different ways: by becoming more benign in terms of overall medium to long-term outcome, and by being transformed from a persistent to an episodic condition. Lehmann (1981) has also estimated that the chances of a favourable outcome in schizophrenia are now four to five times better than they were in the early years of the century. Manfred Bleuler (1978), Shapiro & Shader (1979), Ciompi (1980) and Huber *et al* (1980), among others, describe better outcome over recent decades. Lee *et al* (1991) point to the seductive financial prize (for politicians at least) of this putative metamorphosis.

In this paper we consider the nature of the evidence suggesting that there has been change in the natural history of schizophrenia. We shall first consider some of the methodological problems inherent in follow-up studies and examine individual studies to illustrate how these may lead to unreliable conclusions. In order to merit serious attention, claims that the course and outcome of schizophrenia have actually changed over time must be based on data from at least two periods that are reasonably comparable. We therefore critically review those studies which have attempted to establish trends over time, and discuss some of the difficulties unique to this kind of exercise. In conclusion we draw together the available evidence and make recommendations for further research.

Methodological issues

Discussion of the outcome of schizophrenia inevitably involves widely differing concepts of what is meant by 'outcome' and, indeed, what precisely is meant by 'schizophrenia'. The validity and generalisability of any individual study depends essentially upon the representativeness of the study subjects, the elimination of biases due to differential losses at follow-up and the validity of instruments used to assess outcome. Many studies fail to address the fundamental issue of what, precisely, is being measured. Patterns of course are investigated against varying backgrounds of social and medical treatment, different styles of psychiatric practice and even specially instituted rehabilitation regimes. Findings are then generalised as if the disorder unfolds independently of its social, cultural and treatment milieu. There has also been a notable lack of control or comparison groups in most of the studies which have been undertaken. The following methodological problems merit particular attention.

Diagnostic and sampling biases

Despite incorporating outcome into his diagnostic criteria, Kraepelin (1919) was too experienced as a clinician to exclude altogether the possibility of recovery. Nevertheless, his fundamental distinction between affective and schizophrenic disorders pointed to their variable long-term outcome: the former skewed in the direction of recovery and the latter in the direction of chronicity and deterioration. In contrast, Eugene Bleuler (1950) has been credited with emphasising the 'cross-sectional' rather than longitudinal features of the illness. At times, however, his emphasis upon failure of recovery was no less emphatic: "by the term 'dementia praecox' or 'schizophrenia' we designate a group of psychoses whose course is at times chronic, at times marked by intermittent attacks, and which can stop or retrograde at any stage, but does not permit a full *restituto ad integrum*" (Bleuler, 1950). Crucially, he commented that he had never discharged a schizophrenic patient from hospital in whom he "could not still see distinct signs of the disease; indeed, there are very few in whom one would have to search for such signs".

In fairness, Bleuler's views are not incompatible with the notion of 'recovery', in terms of significant social and clinical improvement. Such remarks, however, helped to perpetuate the pessimistic and gloomy notions about the longer-term course and prognosis of schizophrenia which held sway for over half a century. Writing decades after E. Bleuler, Manfred Bleuler (1978) stated "Faith in the incurability of the disease was so firmly entrenched that recoveries were misinterpreted by lines of reason that today would appear ridiculous". Indeed, Kleist (1960), Leonhard (1961), Faergeman (1963) and Langfeldt (1969) all believed that recovery almost precluded a diagnosis of schizophrenia, and re-defined patients as suffering from the cycloid psychoses, psychogenic psychoses and schizophreniform psychoses respectively.

It is probable that this 'incurability in principle' dogma seriously biased early studies of course and outcome. Evidence of chronicity was also incorporated into the later diagnostic schema of Feighner *et al* (1972), and more recently found its way into the operationalised criteria of DSM – III (American Psychiatric Association, 1980). Such diagnostic classifications, having long duration criteria, have been retrospectively applied to identify cases of 'true schizophrenia' for follow-up. The 'Iowa 500' follow-up study illustrates this point particularly well (Morrison *et al*, 1972; Tsuang & Winokur, 1974). Of the 500 patients with an original case-note diagnosis of schizophrenia, 315 were excluded on account of a failure to satisfy Feighner's strict criteria. Most were excluded because of short duration of symptoms (less than six months) or on the basis of displaying an episodic course. Fifteen patients who had other case-note diagnoses were reclassified as schizophrenic when Feighner criteria were applied at follow-up, producing a final sample of 200. At follow-up (mean duration 2.6 years), 78% of the sample remained ill or deteriorated, with only 8% recovered in the sense that they had returned to their "normal occupations". Clearly, however, the Iowa 500 were a highly selected group of patients, and their poor outcome may not be surprising.

Studies based upon easily accessible populations of long-stay patients, or even acute hospital admissions, are unlikely to be representative of the group of schizophrenic disorders as a whole. In an important study, Harding *et al* (1987) reported on a 20–25-year follow-up of 269 back-ward 'hopeless' cases from the Vermont State Hospital. These patients had been placed in a rehabilitation programme between 1955 and 1965. Of the total rehabilitation sample, 118 met DSM–III criteria for schizophrenia. Of these, 82 were alive and were interviewed. Surprisingly, at follow-up 68% of this 'hopeless' sample showed no further symptoms or signs of schizophrenia, and good global functioning was found in 60%. However, on closer scrutiny it appears that these 'hopeless' cases may not have been quite as hopeless as one would imagine. First, they were selected on the basis of emerging signs of clinical improvement, often being 'championed' for the rehabilitation programme after catching the attention of an interested member of staff (Chittick *et al*, 1961). Patients admitted to the programme were already working at least 30 hours per week in the hospital, and many were recruited by asking the work supervisor which patients he or she could least afford to lose (Brooks, 1959). Second, the programme was limited to those schizophrenic patients who had shown improvement as a result of neuroleptic treatments introduced in 1954 (Brooks, 1960). Third, patients referred for rehabilitation were those who, despite recovery on neuroleptics, had no family, no alternative placement, or inadequate financial resources. With appropriate social support, many would have been discharged. The rehabilitation programme itself was innovative and aggressive. To quote McGlashan (1988), this group of patients was a "remarkable cohort, perhaps unique in US psychiatry. . . These patients were provided with virtually everything that 20th-century psychiatry had to offer, all within one decade, between 1947 and 1957". It is not possible, therefore, to generalise from this particular group of patients to present-day 'back-ward' chronic patients who have failed various rehabilitation programmes and proved resistant to adequate trials of neuroleptic medication. They are simply not the same group of patients.

In another long-term follow-up study, McGlashan (1984*a*,*b*) investigated 163 schizophrenic patients who had been treated at Chestnut Lodge. This unit specialises in the long-term residential treatment of severely ill patients. Most are apparently young, chronically ill 'treatment failures'. Unsurprisingly, perhaps, the follow-up suggested a gloomy outcome, with two-thirds in the 'marginal to worse' global outcome category. In a study of young treatment failures at the Boston State Hospital (Gardos *et al*, 1982), a psychopathological outcome was found similar to the Chestnut Lodge sample, although the latter were superior in terms of living situation and employment outcome. However, given that patients from Chestnut Lodge were from social classes one and two, whereas those from Boston State Hospital were predominantly from social classes four and five, it is probable that once again the nature of the 'outcome' in these studies tells us as much about the sampling of patients admitted to the study as the disease 'processes' of schizophrenia itself.

Prevalence samples based upon consecutive admissions to hospital also tend to over-represent re-admissions as opposed to first-onset cases. In a five-year study carried out by Shepherd *et al* (1989), 49 (46%) of a sample of 107 schizophrenic patients admitted to hospital had a first admission. Twenty-two per cent of the first-admission group had no further episodes and 43% were impaired at follow-up. Among those re-admitted, only 10% had no further relapses and 60% remained impaired. Clearly, the proportions of first-contact as opposed to re-admission patients in a particular sample will have a significant effect on the reported course and outcome.

Breier *et al* (1991) have recently reported poor outcome in chronic schizophrenic patients followed up for an average of six years (range 2–12 years) after admission to a research unit in the National Institute of Mental Health. Seventy-eight per cent had a relapse in the period of follow-up, with only 3% rated as 'good outcome' on the Global Assessment Scale (GAS). However, nearly all the patients were referred to the unit "for improvement of symptom control and functional capacity", and are described as having illnesses that had continued without remission despite several treatment interventions. When interpreting their findings, the authors refer to "the long-term outcome of schizophrenia". In fact, a more accurate conclusion would point to poor outcome in treatment resistant chronic schizophrenia or, at best, in only "partially neuroleptic responsive" chronic patients (Breier *et al*, 1992). In a cogent critique of these data, Schwartz *et al* (1992) argue that the critical limitations of such studies in terms of their sampling biases should be given much greater visibility, as such studies could be employed to shape policy regarding the allocation of scarce and expensive public resources for the treatment of schizophrenia.

Concepts of outcome

Widely varying concepts of outcome are used in different studies, and it is often difficult to compare

the way in which concepts are applied to patients in different centres. Questions of validity, reliability and blindness in raters have often been ignored. 'Good' outcome in one study is equivalent to only 'moderate' improvement in another. It is difficult to make meaningful comparisons between studies using such broad categories as "no further trouble of original type" (Henisz, 1966) or "pronounced improvement with defect" (Malamud & Render, 1939), or "partially productive" (Rennie, 1939). Often, no attempt has been made to discriminate between social and clinical variables, and it has only recently been recognised that rates of hospitalisation, once viewed as relatively 'hard' and reliable indicators of course type and outcome, may tell us more about patients' social support and the sophistication of local services than about the illness itself.

Completeness of follow-up

Finally, the issue of completeness of follow-up is crucial (Leff *et al*, 1992). It is possible that patients with better outcome tend to get lost in follow-up studies, just as such patients often fall out of out-patient care and distort the experience of clinicians left treating more chronic cases. On the other hand, patients with chronic paranoid symptoms may prove especially resistant to overtures from unknown research workers, and thus contribute substantially to follow-up attrition. The 11-year follow-up rate of 44% achieved by Carpenter & Strauss (1991) seriously limits the ability of such findings to be generalised, and even the major European study carried out by Ciompi (1980) re-assessed only 289 patients (18%) out of an identified sample of 1642 consecutive admissions to hospital between 1900 and 1962.

The benign metamorphosis of schizophrenia

It is clearly of little value to compare studies using different definitions of schizophrenia, having differing sampling biases, incomparable outcome categories and varying degrees of completeness of follow-up. How reliable, then, is the evidence for claims that schizophrenia is undergoing a benign metamorphosis?

The arguments which have been expounded fall broadly into two categories. The first depends upon follow-up studies which appear to meet the basic requirements of comparability. The most commonly quoted is that of Manfred Bleuler (1978) involving a life-long follow-up of 208 schizophrenic probands and affected members of their families. Diagnostic criteria were relatively stringent and clearly spelt out, and there can be little doubt about the completeness of the follow-up and the thoroughness of this major piece of work. The author personally followed up patients who entered hospital in the year 1942–43. An earlier comparison study, carried out by the same author (Bleuler, 1941), was based upon a follow-up of patients admitted to Swiss clinics in the period 1937–38, supplemented with a New York sample dated 1929–30. When comparing the 'stabilised end-state' of patients included in these two studies, 30% were recovered in both periods of follow-up, but 38% in the later sample had achieved 'mild chronic' status as opposed to only 20% in the earlier sample. In addition, only 15% of cases were designated 'severe chronic' in the later group as opposed to 30% in the earlier one. However, given sample sizes of 82 (1978) and 109 (1941) for these categories, the inferences that can be drawn are uncertain. It is notable that there was no overall change in the proportion of 'recovered' patients in the two samples, improvement being confined to movement between the 'mild' and 'severe' chronic categories. Neuroleptic treatment was introduced for the first time into the care of the later group of patients at about the middle of the 22–23-year observation period. To quote Bleuler (1978), "for many patients these drugs had their beneficial effect not only in the acute phases but also in chronic states over extended periods of time, among both the in-patients and out-patients of our clinic". Although Bleuler was circumspect in his assessment of the effectiveness of neuroleptic medication, it would seem logical to attribute most, if not all, of this modest metamorphosis in his later sample to the introduction of effective neuroleptic medication.

Achte (1967) reported similar findings to Bleuler for five-year outcome in two series of patients. The first cohort were admitted in 1950 and the second in 1960. Sample sizes were again small, with only 45 and 51 patients in the respective groups. The percentage of cases with "at least a social remission" rose from 31% in 1950 to 51% in 1960. However, the Achte study also spans the period of introduction of adequate neuroleptic medication and advances in social treatments. The relatively modest improvement in outcome reported probably reflects the impact of medication and responses to change in the social milieu, rather than any inherent change in the nature of the disorder itself. Moreover, in contrast to these two studies, Astrup & Noreik (1966) found no evidence of improving outcome in an investigation spanning a similar period. In their follow-up comparison of patients admitted between 1938 and 1950, and 1951 and 1957, the authors report that approximately 16% in both groups had a 'non-schizophrenic' (i.e. recovered) outcome. They conclude that the outcome of schizophrenia had not changed

dramatically over this period, and that the introduction of neuroleptic medication had not made a significant impact upon recovery rates. Similarly, Varga (1966) compared the case records of all psychotic patients admitted to the psychiatric department of the University of Budapest in 1910 ($n=152$) and 1960 ($n=174$). The proportion of diagnosed schizophrenic patients was similar in both samples and the re-admission rate was actually higher in the 1960 cohort.

The second line of argument in support of the metamorphosis of schizophrenia points to recent studies suggesting a marked late improvement in samples of chronic patients. It is argued that studies of such chronic 'hopeless' cases include patients closely resembling the 'dementia praecox' patients identified earlier in the century by Kraepelin and co-workers. Kraepelin (1913) reported early recoveries in only 12.6% of patients. Of these, most had subsequent relapses so the percentage of 'lasting recoveries' was 2.6%, and the percentage of patients completely recovered or suffering from only minor deficits was only 4.1%. In contrast, the study by Harding *et al* (1987) reported that dramatic improvements could be detected in up to 60% of chronic patients followed up over 20 to 25 years. Indeed, rates of recovery reported in this study are the same as, or even better than, those in cohorts including 50% or more with acute-onset cases. In the European follow-up study, Ciompi (1980) reported on a sample containing 47% of patients who had been hospitalised only once. Forty-nine per cent of the patients in Ciompi's follow-up achieved a 'mild or recovered' category of outcome, whereas a staggering 60% of the Vermont project (Harding, 1988) 'chronic hopeless' cases achieved this status. Closer scrutiny of these data reveals that a Harding *et al* 'mild or recovered' category required a GAS score of only 61, whereas Ciompi required subjects to be employed and maintaining 'normal conversation and behaviour' to be considered recovered. Nevertheless, even allowing for the considerable problems of interpretation of the Vermont data, and the unique nature of the sample, these are striking findings. These data do indeed appear to suggest that the outcome of schizophrenia may be better than many had once assumed.

We contend, however, that while outcome may prove to be better than was once assumed, this does not constitute evidence that the disease itself has changed – only our assumptions. It is not known how patients, diagnosed and followed up in the Kraepelinian era, would have progressed if admitted to a vigorous rehabilitation programme and treated with neuroleptic medication. Further, not all studies in the early part of the century reported deeply pessimistic findings. For example, Rennie (1939), in an American follow-up study between one and 26 years after admission, found 37% of patients either recovered or 'partially productive'. Stalker (1939) in the UK showed at one- to six-year follow-up that 29% were either in complete remission, in social remission, or at home, 'improved'. These outcome data are far from gloomy. The more recent World Health Organization coordinated follow-up studies (WHO, 1979; Jablensky *et al*, 1992) introduce an additional dimension: as the sampling net has been thrown wider geographically to include patients from developing countries, overall reported rates of recovery have increased dramatically. These data further challenge the traditional Kraepelinian view of course and outcome based upon the clinical experience of clinicians working in industrialised countries.

Conclusions

We are drawn to the conclusion that there is no convincing evidence, on the basis of published research, for the proposal that there has been a benign metamorphosis in the course and outcome of schizophrenia during this century. However, possible time trends in the incidence, syndromal patterns and outcome of schizophrenia cannot be discounted and merit further epidemiological research. Few would dispute, for example, that there has been a remarkable decline in the incidence of catatonic forms of schizophrenia in industrialised countries (Morrison, 1974; Leff, 1988). This points to the potential for time trends in other syndromal subtypes of the disorder, and strengthens parallel hypotheses regarding trends in the overall incidence and patterns of course and outcome. Ideally, in relation to outcome, future descriptive analyses should be conducted on large representative and geographically defined samples in different cultural settings. Sample sizes should be large in order to confer adequate statistical power. In-depth and standardised assessments should be applied reliably to patients who are homogeneous for the stage of their illness. Multiple measures of outcome must include symptomatic and social dimensions, and reflect the course of the disorder at successive time points. Follow-up must be intensive to minimise attrition. Clearly, the logistic hurdles of such 'ideal' studies are formidable, although the WHO multicentre studies (Jablensky *et al*, 1992) offer a unique opportunity to follow up carefully defined and geographically based cohorts of patients in different cultures.

In addition to time trends in the incidence and outcome of schizophrenia, the following areas in outcome research merit special attention.

The marked differences in course and outcome between patients in developing and developed countries (WHO, 1979; Sartorius *et al*, 1986; Jablensky *et al*, 1992; Leff *et al*, 1992). The striking variation in outcome at two- and five-year follow-up requires further investigation. It is not known whether, and to what extent, this difference is sustained over long periods of time. Further descriptive analyses are required, together with the development of explanatory hypotheses which may then be tested in representative sub-samples of patients in different cultures. Investigation of the effects of high expressed emotion (EE) have been fruitful (Wig *et al*, 1987; Kuipers & Bebbington, 1988; Leff *et al*, 1990), but a crucial issue remaining to be addressed is the extent to which differences in outcome reflect the impact of different biological risk factors for schizophrenia upon the course of the illness.

The phenomenon of late recovery in chronic schizophrenia. We believe that the potential for late recovery in chronic schizophrenia was amplified in the study conducted by Harding *et al* (1987) by virtue of the unique sampling of patients and timing of the study in relation to the development of new rehabilitation techniques. The extent to which other groups of chronic patients exhibit late recovery now requires careful investigation. It is crucial to specify in what sense patients are considered to be chronic. There are chronic relapsing patterns of course, chronic continuous patterns of course; some patients are chronic in the sense of being treatment resistant, and others in the sense of displaying extensive social disability. Large sample sizes are required to produce generalisable findings in relation to this question, although small sample sizes may be quite adequate and often more reliable, providing that sampling biases are clearly presented and conclusions drawn only in relation to the specific subtype of chronic patient identified for the study. Improved understanding of the phenomenon of late recovery may reveal predictive factors early in the course of the disorder and identify therapeutic and social experiences which could be harnessed in developing further treatment strategies.

In conclusion, we suggest that it is impossible to establish whether there has been a metamorphosis in the course and outcome of the schizophrenia group of disorders over the course of the 20th century. However, as we move nearer to the 21st century, and studies approximate more closely to the epidemiological constraints outlined above, it will be possible to monitor reliably trends in the syndromal presentation, incidence and outcome of the illness. Unfortunately, recent findings of wide heterogeneity of outcome are only slowly provoking a metamorphosis in attitudes towards schizophrenia among clinicians and patients. A move away from self-fulfilling prophecies regarding the inevitable deterioration of this condition augurs well for the innovative care of patients, and should stimulate further research into modifying and preventive strategies.

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*Glynn Harrison, MD, MRCPsych, *Consultant Psychiatrist, Department of Psychiatry, University Hospital, Nottingham NG7 2UH*; Peter Mason, BMedSci, BM BS, MRCPsych, *Research Fellow, Schizophrenia Research Unit, Department of Psychiatry, University Hospital, Nottingham NG7 2UH*

*Correspondence

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