New perspectives on schizophrenia in later life: implications for treatment, policy, and research

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Worldwide, in the past few decades, the demographics of older people (ie, people 55 years and over) with schizophrenia have changed completely with respect to absolute numbers of people affected, the proportion of all people with the disorder, life expectancy, and residential status. The ageing schizophrenia population has created vast health-care needs and their medical comorbidity contributes to higher mortality than in the general population. Proposals to classify schizophrenia into early-onset, late-onset, and very-late-onset subtypes now should be tempered by the recognition that comorbid medical and neurological disorders can contribute to psychotic symptoms in later life. The concept of outcome has become more nuanced with an appreciation that various outcomes can occur, largely independent of each other, that need different treatment approaches. Data show that schizophrenia in later life is not a stable end-state but one of fluctuation in symptoms and level of functioning, and show that pathways to improvement and recovery exist. Several novel non-pharmacological treatment strategies have been devised that can augment the clinical options used to address the specific needs of older adults with schizophrenia.

Introduction

Worldwide, a crisis is emerging in the care of older adults with schizophrenia. People aged 55 years and older will soon represent a fourth or more of individuals with schizophrenia in many developed countries, and worldwide,[1] among mental disorders and substance-use disorders, schizophrenia now ranks third in causes of disability-adjusted life years in people aged 60 years and older.[2] The estimated expenditures per person for this population exceed those of other common medical and psychiatric disorders.[3] Older adults with schizophrenia have been largely neglected in scientific research, with about 1% of schizophrenia literature devoted to this population, and health-care systems are ill prepared to address substantial growth in this population. Moreover, knowledge about schizophrenia in later life, when it is most developed and complex, might enable greater understanding of schizophrenia. In this Review, we discuss seven evolving theoretical and clinical issues with respect to their effects on health policy, research, and the care of this population.

The changing demographics of people aged 55 and over with schizophrenia

In tandem with the rise in absolute numbers of people aged 55 and over in general, more people with schizophrenia are living longer than they did in the past. In the USA, the prevalence estimate for schizophrenia is 0·6%–1·0% in people aged between 45 and 64 years and 0·1–0·5% in people aged 65 years and older.[4] In the first quarter of this century, the number of people with schizophrenia aged 55 years and older will double, reaching 1·1 million in 2025, or about a fourth of all people with schizophrenia.[1] Worldwide, the number of people aged 60 years and older will more than double between 2014 and 2050.[5] Thus, assuming a 0·5% prevalence of schizophrenia in people older than 60 years, the number of people in this age category with the disorder will reach about 10 million by 2050. This prediction is especially ominous because of the pronounced changes happening in traditional social structures in the wake of increased urbanisation and industrialisation, and the resultant isolation or even abandonment that elderly people face.[6–8]

Two generations of older adults are now living with schizophrenia. The so-called old-old (those aged 75 years and older) typically had many years of institutionalisation before entering the community, whereas the so-called young-old (aged 55–74 years) have had fewer hospital admissions and been exposed to recovery service models that have been more focused on consumer needs and personal autonomy. In the USA, more than 85% of older people with schizophrenia are living in a range of settings in the community.[1] People remaining in long-term hospitals or nursing homes have the most severe outcomes, compared with those in community settings, often worsen symptomatically and cognitively over time, and more closely resemble individuals described by Kraepelin[9,10] as having dementia praecox.

Early-onset, late-onset, and very-late-onset subtypes of schizophrenia in the context of comorbid medical and neurological disorders

Older schizophrenia patients consist of people who have had the disorder for a large part of their life and those with a later onset. A review[4] of studies of late-onset schizophrenia reported that around 20–25% of patients with schizophrenia had an onset of the disorder after age 40 years. A Dutch case-register study[11] reported a 1 year prevalence rate of 0·55% for schizophrenia in people older than 59 years, of whom 64% had early-onset schizophrenia. These figures suggest that the loss of individuals with early-onset (to death or recovery) could at least partly be offset by the influx of patients with a later onset.

Whether differences exist between early-onset and late-onset schizophrenia is a matter of longstanding debate,[12,13] as is whether late-onset schizophrenia even exists.[14] In 1980, the Diagnostic and Statistical Manual of Mental Disorders

DSM III stated that schizophrenia did not have an onset after age 44 years; this age criterion was eliminated in subsequent editions.[15] In contradistinction to recent editions of the DSM[16] and International Classification of Diseases[17] that do not distinguish by age of onset, the International Late-Onset Schizophrenia Group[18] proposed that schizophrenia be termed late-onset schizophrenia for disorders that have an onset between the ages of 40 years and 60 years, and very-late-onset schizophrenia-like psychosis for onset after the age of 60 years. Unfortunately, the scientific literature has sometimes conflated these demarcations and treated people with an onset at the age of 40 or older as one group, making identification of risk factors difficult. The late-onset type that arises between the ages of 40 years and 60 years has been thought to be more akin to the early-onset subtype, although subtle differences have been noted between these two types such as a preponderance in women, a lower level of symptom severity, and less executive dysfunction in the late-onset type.[19] The very-late-onset type is distinguished by its much higher frequency of diagnosis in women than men, greater prevalence of persecutory and partition delusions, higher rates of visual, tactile and olfactory hallucinations, lower genetic load, absence of negative symptoms or formal thought disorder,[18] and possibly a higher standard mortality rate versus older people with early-onset disorder, mainly because of higher rates of comorbid illness and accidents.[20]

Cognition is a disputed domain, because a sizeable proportion of patients with very-late-onset type schizophrenia could go on to develop a type of dementia.[21] Whether this propensity to develop dementia shows a true characteristic of this subtype or suggests initial misdiagnosis is under debate. Brichant-Petitjean and colleagues[22] noted that people with late-onset disorder occupy an intermediate position between those with early-onset type and healthy controls with respect to cognitive deficits. Biological markers of schizophrenia with a later onset have been more elusive and no specific neuropathological substrate has been identified.[19] However, a study[23] reported in 2014 found raised C-reactive protein concentrations in both people with late-onset and very-late onset schizophrenia. Hahn and colleagues'[24] review of neuroimaging studies that compared early-onset and late-onset schizophrenia reported differences in eight of ten studies, but across studies these were not consistent.

Making a diagnosis of late-onset schizophrenia can be challenging. The onset of hallucinations and delusions in later life can arise de novo or be associated with mood disorders, sensory deficits, polypharmacy, substance misuse, medical disorders, or dementia.[13] For example, argyrophilic grain disease and Lewy body disease were significantly associated with late-onset schizophrenia versus controls, especially after age 65 years.[25] Moreover, about 10% of the general elderly population has a history of psychotic symptoms but very few meet criteria for a non-affective psychotic disorder.[26] Some clinicians have used cut-off scores on the Mini-Mental State Examination as a way to differentiate between late-onset schizophrenia and a dementia; however, this is not straightforward because many people with schizophrenia have cognitive deficits.[27] A pilot study by Seppalla and coauthors[28] suggests that the use of abnormal cerebrospinal fluid biomarkers can assist in differentiation of late-onset psychosis from Alzheimer's disease.

An evolving concept of outcome within a lifespan perspective

In 1974, Carpenter and coauthors[29] argued that schizophrenia is characterised by domains of pathological changes that vary between patients; over the ensuing years, outcome categories have expanded to include psychotic, mood, behavioural, and cognitive symptom categories. Conceptualisations of outcome in later life have attempted to merge the recovery and gerontological perspectives.[30] Thus, the ideal trajectory for older adults with schizophrenia can be viewed as a process in which they move from remission (symptomatic recovery), to community integration (functional recovery), to successful ageing (positive health), the latter being a more age-appropriate approach that is receiving increased attention.[31] The autonomy of outcome categories is thought to persist into later life. For example, in a study[1] of a New York City community sample of 198 adults aged 55 years and older with early-onset schizophrenia, the six clinical and social outcome categories were only slightly correlated (median value of 4% shared variance). Thus, favourable outcome in one category does not necessarily produce a favourable outcome in another category. This finding suggests that development of treatment strategies that are specific to each outcome category might be beneficial, although treating one category could have a modest effect on other categories, and approaches that combine pharmacological, social skills, and cognitive strategies seem to benefit people across several domains.[32–34]

Fluctuation of symptoms and levels of functioning in later life

Symptomatic remission

For much of the 20th century, remission was viewed as unlikely. In 1899, Kraepelin[35,36] posited rates of clinical improvement of no more than 17%. In 1980, the DSM-III[15] stated, "The most common course is one of acute exacerbations with increasing impairment between episodes." However, 7 years later, the DSM III-R[37] declared, "The residual symptoms become attenuated in the later phases of the illness." This striking change in view showed the conclusions of five catamnestic studies[38] from Europe and the USA that had followed up 1303 patients—either hospital inpatients or recently discharged patients—for 22–35 years and recorded improvement in 46–68% of people.

After the introduction of a consensus definition of remission in 2005,[39] three cross-sectional symptom

remission studies[40–42] of community dwelling older adults with schizophrenia were completed. Two North American studies[40,41] reported symptom remission rates of nearly 50% in patients with early-onset schizophrenia, whereas a catchment-area-based study[42] in the Netherlands (including some patients living in institutions and those with late-onset disorders) reported a 29% symptom remission rate. Likewise, the International Study of Schizophrenia (ISoS),[43] which assessed 18 worldwide cohorts, reported that 54% of those in the prevalence group (mean age 51 years) were symptom free or had non-disabling residual symptoms. People in developing countries generally had better outcomes than did those in developed countries.

Analysis of longitudinal follow-up data (mean 4·5 years) from the New York City community sample[1] cited previously, comprising 104 adults aged 55 years and older with early-onset schizophrenia, showed that although there was no significant decline in the proportion of patients attaining symptom remission (49% at baseline; 40% at follow-up), only 25% were in remission at both assessments, 35% were not in remission at either assessment, 25% went from remission to non-remission, and 16% went from non-remission to remission.[44] Thus, the initial pessimism that persisted for most of the 20th century (under 20% improvement), that was superseded by an optimistic view in the more recent years (50% symptom remission or improvement), might need further modification if only a fourth of patients remain persistently in symptom remission in 2012 (figure 1).The longitudinal data have also challenged the characterisation of schizophrenia in later life as a stable or quiescent end state.[45,46] Finally, if replicated, these findings show the methodological limitations of earlier cross-sectional data that reported roughly half were doing well, because it might not be the same people doing well at each point in time.

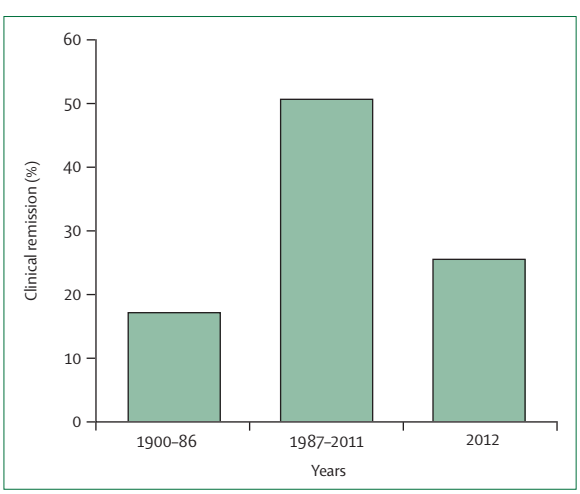

***Figure 1*: Historical trends in clinical remission of individuals with schizophrenia**
Data taken from several sources.[35,36,38–44]

Negative symptoms

Although positive symptoms could decrease in prevalence in later life,[1] negative symptoms have been thought to increase then stabilise over the course of the disorder, and might dominate as people age.[47] A multicentre study[48] showed one or more negative symptoms present in 58% of a mixed age sample. There has been a paucity of data about the prevalence of negative symptoms in older adult samples. In the 1970s and 1980s, the catamnestic studies[38] cited previously recorded deficit or negative symptoms in about 25–40% of the probands and in about 50% of persistently ill people.[49,50] ISoS[43] showed that 77% of patients had no evidence of prominent negative symptoms, although 47% of the continuously ill group had prominent negative symptoms. Likewise, 37% of a small convenience sample (n=46; aged 46 and older; mean age=62) with schizophrenia in San Diego met criteria for deficit syndrome.[51]

A cross-sectional analysis of people in the New York City study[52] noted that 40% of the schizophrenia sample met the criteria for the presence of negative symptoms, and this proportion decreased to 19% when potential secondary symptoms were excluded. Whereas a longitudinal study[53] of geriatric patients living with schizophrenia in institutions showed little movement in negative symptoms over time, results of a longitudinal follow-up (mean 4·5 years) from a subset of the New York City sample showed that 44% fluctuated between having and not having negative symptoms.[54] Thus, contrary to earlier notions of schizophrenia progressing to so-called burn-out in later life, negative symptoms do not typically dominate clinical practice; likewise, they seem to be no higher than in younger schizophrenia populations, and might fluctuate over time.

Depression

In middle-aged and older adults aged 45 years and over with schizophrenia living in the community, the prevalence of depression has ranged from 44 to 75%.[55–60] These studies did not have longitudinal data, therefore identification of the course of depression and the causal direction of associated variables was difficult to ascertain. A prospective study[61] of older adults with schizophrenia from the New York City sample showed that persistent depression (defined as the presence of syndromal or subsyndromal depression) occurred in 44% of people, 30% remained persistently non-depressed, and 26% fluctuated between depression and non-depression. The results of this study question earlier contentions that schizophrenia in later life is characterised by affective withdrawal,[45,46] whereas the fluctuations in mood, in tandem with the data regarding positive and negative symptoms described above, challenge the notion that a quiescent end-state exists.

Cognition

Older individuals with schizophrenia show substantial cognitive deficits, both in general cognition and in specific cognitive domains.[62] By contrast, the long-term course of

cognition in schizophrenia in later life is still controversial. The debate focuses on whether the trajectory of cognitive function is static over time, in line with the supposed neurodevelopmental nature of schizophrenia, or exceeds that of healthy, age-related decline, suggesting neurodegeneration. Results of a detailed review[63] of longitudinal studies of cognitive decline published in 2012 showed that slightly more studies suggested faster cognitive decline in later life in people with schizophrenia than is expected with normal ageing, although this difference disappeared if only studies with control groups were included. Moreover, any differences in cognitive decline between early-onset and late-onset groups were inconclusive. Rajji and coauthors'[64,65] review of the scientific literature noted a heterogeneity of outcomes on the basis of residential status. First, they noted stability in community-dwelling patients, at least to the age of 65–70 years, other than the cognitive decline that is expected from normal ageing; however, an accelerated cognitive decline after age 70 years could not be ruled out.[66] Second, they noted a greater than age-normal cognitive decline in patients with long periods of institutionalisation, especially after age 65 years.[67]

Thompson and coauthors[68] recently postulated a more granular picture than previous investigations for community-dwelling middle-aged and older people with schizophrenia (aged 40–100 years). With a 3·5 year follow-up, three trajectories were identified: stable cognition in 50%; slight decline in 40%; and rapid decline in 10%. The trajectory for healthy-age peers was similar to the stable schizophrenia group. In the New York City longitudinal sample,[69] investigators recorded that nearly two-fifths of the sample improved or declined (ie, >0·5 SD change per year in the cognitive test battery) over the 4·5 year study period, with roughly equal proportions moving in each direction. Thus, the absence of a pronounced decline over time in most participants, and the substantial changes (up and down) in more than two-fifths of people, argues for the potential value of cognitive remediation programmes tailored to the needs and capabilities of ageing individuals with schizophrenia.

Longitudinal studies examining the incidence of dementia in older people with schizophrenia are scarce. The situation is confused by the amplified risk faced by people with schizophrenia due to cognitive deficits dating back to earlier in the disease course combining with a normal age-associated cognitive decline. As a result, nearly half of people with schizophrenia might meet cognitive cutoffs for mild dementia.[70] Shah and coauthors[63] found only three longitudinal studies comparing people with schizophrenia with controls; two reported an increased prevalence of dementia and one did not. None of the studies controlled for risk factors or noted the types of dementia that arose. A study[71] with data from an urban health-care system in Canada noted rates of dementia that were twice as high in elderly people with schizophrenia (mean age 70 years) than in their age peers without the disorder.

An unresolved issue is whether people with schizophrenia could be more prone to dementia because they have a higher risk of metabolic syndrome (which is a risk factor for both Alzheimer's disease and vascular dementia) than do those without the disorder.[72] However, the only available study[73] that investigated the prevalence of metabolic syndrome in older patients with schizophrenia did not report a higher prevalence than in healthy peers.

Community integration and social functioning

Almost all older people with schizophrenia are typically well behind their healthy age peers with respect to social achievements.[74] However, substantial heterogeneity is reported, ranging from individuals with severely incapacitated functioning who are socially isolated to those with near-normal functioning who are socially integrated.[74] Longitudinal data are sparse, but patients probably move along this outcome continuum; although, as suggested by the data for other outcome domains, movement might go in both directions.

Research into social function has typically used one-dimensional concepts such as marital status, social contacts and supports, residential status, occupational status, and social skills.[74] A more comprehensive measure, community integration, could be regarded as a major goal of mental health policy and is consistent with the recovery model, falling midway between clinical remission and successful ageing.[75] It can be conceptualised as a so-called normalisation of functioning in society and consists of assessments of functioning and perceived quality of life within several dimensions—ie, independence, physical, psychological, and social integration.

In a cross-sectional study[76] of the New York City sample,[1] the schizophrenia group scored lower than the older community comparison group on each of the four dimensions of the 12-item community integration scale. Older adults living in the community had roughly twice the level of high community integration (positive scores of 10 or more items) than the schizophrenia group (41% *vs* 23%). In a longitudinal study[77] of the same sample, 34% of people fluctuated between high-community and low-community integration, suggesting that later life is not a period of social stability for at least a substantial minority of people with schizophrenia, and that opportunities for improvement exist, but so do risks for decline. For middle-aged and older adults with schizophrenia who are still interested in working, Twamley and colleagues[78] showed that a manualised version of a supported employment programme was better than conventional vocational rehabilitation on attainment of competitive employment (57% *vs* 29%) or any paid work (70% *vs* 36%).

An increasing number of reports have been published about the clinical and social variables associated both cross-sectionally and longitudinally with the outcome variables just described. These studies are summarised in the table.

	Associated variables
Remission	
Cross-sectional studies	Fewer total network contacts, greater proportion of intimate partners, fewer lifetime traumatic events, higher cognitive functioning, greater adherence to psychiatric services, higher scores on measures of social functioning, and higher community integration.[30,40–42,52,58]
Longitudinal studies	Baseline remission status predicted having more total contacts at follow-up.[4] Predictors of remission at follow-up: baseline higher community integration, greater number of entitlements, fewer psychotropic medications, and lower frequency of psychiatric services.
Negative symptoms	
Cross-sectional studies	Male sex, greater use of daily living services, positive symptoms, impaired cognitive functioning, abnormal movements, lower rates of patients living independently, and fewer confidantes.[52,79–89]
Longitudinal studies	Baseline negative symptoms predict fewer social contacts at follow-up.[54] Predictors of more negative symptoms at follow-up: lower cognitive functioning, and fewer confidantes.
Depression	
Cross-sectional studies	Positive psychotic symptoms, decreased level of functioning, increased overall psychopathology, severity of general medical disorders, decreased quality of life, fewer social contacts, use of medication to cope or attempts to keep calm, and better cognition.[56–58,90]
Longitudinal studies	Baseline depression was associated with higher anxiety scores at follow-up.[61] Predictors of depression at follow up: baseline depression and a greater number of psychotropic medications.
Poorer cognition	
Cross-sectional studies	Lower daily functioning and competence, depression, positive symptoms, negative symptoms, residential status (living in institutions), older age, female sex, lower education, white skin colour, shorter duration of illness, later age of onset.[62,64,83,91,92]
Longitudinal studies	Baseline cognition predicts negative symptoms and total network size.[62,64,93] Predictors of poorer cognition at follow-up: lower baseline cognition, residential status (patients living in institutions), older age, female sex, white skin colour, shorter duration of illness, later age of onset, positive symptoms, and negative symptoms.
Community integration	
Cross-sectional studies	Female sex, higher personal income, fewer depressive symptoms, fewer negative symptoms, lower AIMS score, higher CAGE lifetime scores to detect alcoholism, and greater control of one's life.[74,76]
Longitudinal studies	Baseline community integration predicted remission, positive symptoms and general psychopathology at follow-up.[77] Predictors of community integration at follow-up: depression, cognitive functions, fewer mental health services.

AIMS=abnormal involuntary movement scale.

Table: **Summary of key outcome variables for older adults with schizophrenia and associated factors**

Pathways to improvement and recovery

A range of researchers have expressed optimism about the potential for healing in ageing people with schizophrenia. Bleuler[94] stated that: "The healthy life of schizophrenics is never extinguished". Harding[95] reported that hope—ie, the belief of the patient or of someone else that he or she could get better—was connected to the natural healing processes. Andreasen[96] noted that improvement and adaptation can arise because of brain plasticity and that our brains are in constant dynamic change, which occurs as a consequence of the impact of experience on our mental functions and states.

In a qualitative study[97] of middle-aged and older adults (aged 50–72 years) with schizophrenia undertaken by Shepherd and colleagues, participants reported that early in the course of their illness they had confusion about their diagnosis, active psychotic symptoms, and withdrawal or losses in social networks. Thereafter, nearly all participants believed that their symptoms had improved, which they attributed to increased skills in self-management of positive symptoms. However, heterogeneity in perceptions about functioning was marked: 31% of participants were in despair about the discrepancy between their present situations and life goals, 50% had accepted that they were likely to remain in supported environments, and 19% were working toward functional attainments and were optimistic about the future.

Subjective reports about the improvement of coping skills noted by Shepherd and coauthors[97] have been supported by a few quantitative studies. Coping strategies entail management of specific symptoms and the ability to handle daily stressors. For example, Cohen and coauthors[98] showed that the coping styles used by older adults (aged 55 and over; mean age 62 years) with schizophrenia to deal with life stressors were similar to those used by their age peers in the community. Both groups reported use of cognitive coping strategies (eg, accept situation, keep sense of humour) most often and at equivalent levels. Likewise, one small study[99] noted that among management strategies for psychiatric symptoms, social diversion was associated with increased age. Acceptance of symptoms and fighting back against symptoms showed a positive and negative trend, respectively, with increased age. These age-associated differences in management strategies might represent an interaction of trial and error procedures unique to the disorder intertwined with lifespan changes.

Finally, changes in psychotic symptoms could have a salutary effect on resilience and the ability to cope with daily hassles. In older adults aged 55–82 years with schizophrenia in the New York City sample,[100] the proportion of people hearing pleasant or good voices was higher than the proportion reported in younger samples. The proportion of individuals obeying voices was also higher than that identified in younger groups. This finding is consistent with data that older adults in general have an affinity towards positive rather than negative information.[101] If people heard good voices, they were three and a half times more likely to obey orders than if they heard bad voices, suggesting a potentially healthy coping strategy to deal with the persistence of voices in later life.

Health-care needs, medical comorbidity, and mortality

The care of older adults with schizophrenia necessitates recognition of both the physical and psychiatric needs of this population, and the costs are among the highest of any older population, exceeding those of people with dementia, depression, and medical illness.[3,71] Notably, in a study[31] comparing so-called successful ageing in schizophrenia and community comparison groups, physical health status largely accounted for why the schizophrenia group had lower levels of successful

ageing than did the comparison group. Life expectancy is substantially shortened in people with schizophrenia. Being diagnosed with schizophrenia at age 20 years shortens life expectancy by more than 20 years.[102] The mortality risk in people with schizophrenia is two to three times higher than in the general population, and this differential mortality gap has increased in the past few decades.[103] Growing attention has been given to the high prevalence of cardiovascular disease, diabetes, and metabolic syndrome in patients with schizophrenia, that at least partly can be attributed to lifestyle factors (smoking, poor dietary habits, low levels of physical activity) and the effects of antipsychotic drugs, especially those of second generation antipsychotics.

Additionally, part of the excess morbidity and mortality in patients with schizophrenia could be inherent to the disorder itself. The search for the biological underpinning of this supposedly intrinsic propensity for accelerated physiological ageing now focuses on inflammation and oxidative stress.[104] Although people with early-onset schizophrenia who live into old age should be deemed as survivors, the difference in mortality between people with schizophrenia and their age peers persists in later life.[71,105,106] Mortality from suicides and accidents is raised in older individuals with schizophrenia; however, natural causes of death account for the largest part of the reduction in life expectancy.[105,107]

By contrast with schizophrenia at a younger age,[108] few studies have looked into the physical comorbidities of older people with schizophrenia. Hendrie and colleagues[71] reported that, compared with their age peers, older adults with schizophrenia had much higher rates of congestive heart failure, chronic obstructive pulmonary disease, and hypothyroidism, whereas they had lower cancer rates. Kredentser and coauthors[107] recorded deaths from cancer to be higher in middle-aged people aged 40–59 years with schizophrenia but not in people older than age 59 years.

Older adults with schizophrenia could be at risk for undetected or inadequately treated medical disorders that might be a result of systemic or individual factors.[109] Some investigators have found that symptoms of the disorder can contribute to diminished access to health care.[110,111] For example, one study[109] showed that positive symptoms were associated with inadequate treatment of four common medical disorders. Another investigation showed that older people with schizophrenia and comorbid medical disorders have lower compliance with non-psychotropic drugs than an age-matched comparison group.[110] A study[111] in Australia reported that, compared with age peers, people aged 50 years and older with schizophrenia had lower levels of illness management, such as understanding symptoms and taking appropriate action.

Several model programmes have combined collaborative care and case management strategies to confront the medical and psychiatric issues that patients with schizophrenia often face.[112] Collaborative strategies focus on improving communication between the mental health team and primary care providers. Case management strategies include the improvement of the patient's social and cognitive skills in conjunction with physical health enhancing strategies. Encouragement of physical activity is viewed as high priority for this population, especially as increased physical activity has been associated with higher scores on cognitive tests and lower rates of depression.[113,114] The barriers identified that reduce physical activity in mixed age samples and older people with schizophrenia include the patient's motivation, side-effects of drugs, depression, and medical disorders compounded by the low priority given to physical activity by health-care providers.[114,115]

Pharmacological studies and novel non-pharmacological therapeutic strategies

Data on the pharmacological treatment of older adults with schizophrenia are scarce. A Cochrane review[116] of antipsychotic drugs for elderly people (age more than 64 years) with schizophrenia identified only three randomised control trials (RCTs) of 252 people. One RCT assessed drugs that are no longer available. The other two studies noted no differences between risperidone and olanzapine, and olanzapine and haloperidol. Likewise, a Cochrane review[117] of antipsychotic treatment for elderly people with late-onset schizophrenia reported only one small RCT comparing two drugs and the reviewers concluded that this study provided little usable data. Open studies of typical and atypical antipsychotic agents in people with late-onset and very-late-onset schizophrenia have shown favourable results in 50% or more of participants.[18,118] No RCTs of the newer antipsychotic agents (paliperidone, iloperidone, asenapine, lurasidone) have been done in elderly people with schizophrenia, and only asenapine was studied for short-term safety.[119] One controlled study[120] suggested that citalopram can be effective for middle-aged and older adults with schizophrenia and subsyndromal depression. A consensus guideline,[121] written in 2004, provides clinicians with recommendations on the basis of experts' knowledge of various antipsychotic drugs.

Older adults are more prone to side-effects from drugs than younger people,[122] and studies have pointed to potential alternatives or complementary strategies to drugs. First, a review by Suzuki[123] suggests that some older people with schizophrenia might need little or no drug treatment. Second, because many people with schizophrenia, especially those with early-onset disorders, do not make full recoveries with drug regimens alone, a range of non-pharmacological strategies have been devised specifically for older patients. Several RCTs have shown favourable results for cognitive remediation therapy for cognitive deficits, social skills therapy for difficulties with social interaction, and cognitive behavioural therapy for problems with social relatedness, psychosis, and mood.[32,33,34,78,124–127] These programmes need to be implemented more widely to measure their

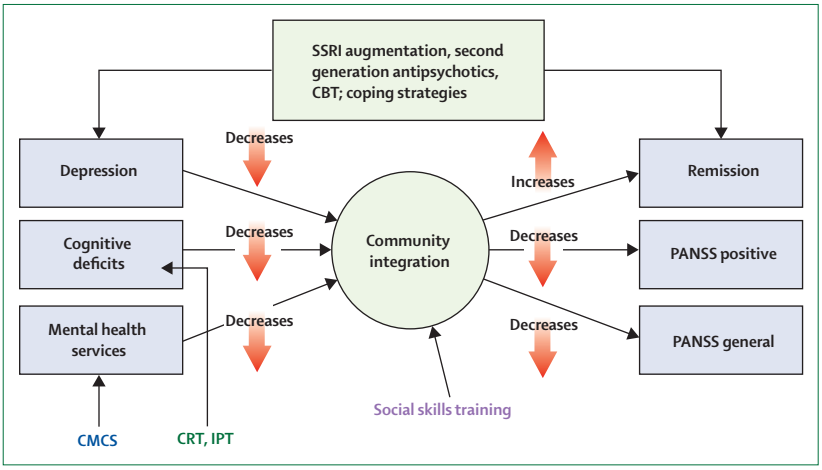

***Figure 2*: Predictors and effects of community integration, and potential intervention targets**[27,34,109–112]
CBT=cognitive behaviour therapy. CMCS=collaborative and managed care services. CRT=cognitive remediation therapy. IPT=integrated psychological therapy. PANSS=positive and negative schizophrenia scale. SSRI=selective serotonin reuptake inhibitors.

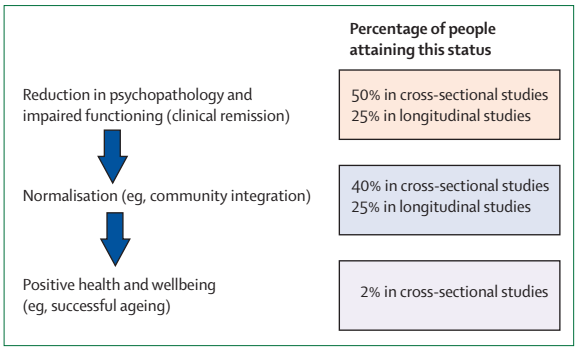

***Figure 3*: Course and outcome of schizophrenia in later life viewed within both the psychiatric recovery model and the lifecourse perspective of gerontology**
Data taken from several sources.[30,31,40–42,44,76,77]

applicability in various settings, and the development of other innovative approaches for this population should be encouraged.

Conclusions

Heterogeneity of outcome is the rule as schizophrenia progresses into later life. Despite scarce data, some findings suggest that the diversity seen in younger individuals might be even greater in older age. The relative autonomy of outcome categories persists into later life. Thus, a favourable outcome in one category does not necessarily induce a favourable outcome in another category, and treatment strategies might be needed that are targeted to specific outcome categories within the context of an ageing individual.

Present knowledge shows that schizophrenia in later life is not a stable end state but one of fluctuation both in symptomatology and functioning. Theoretically, patients can be positioned within a range. One end of this continuum consists of individuals in whom the negative effect of the psychotic disorder has been restricted, and who have shown resilience in the integration of their illness both emotionally and socially. If they enjoy good physical health they could come close to full recovery or to successful ageing.[128] Still, successful ageing remains elusive for most patients with schizophrenia.[31] The opposite end of the continuum consists of severely incapacitated individuals whose lives are dominated by their psychotic disorder, often requiring permanent institutional care. Although the extremes of this continuum attract most attention, most older patients with schizophrenia can be identified at some point in between these extremes, moving with time in one direction or the other. With respect to clinical care and social policy, the relative frequency of clinical transitions rather than states of quiescence could mean that more intensive, age-appropriate services will have to be allocated to serving this population than had been expected.

Although the cross-sectional and longitudinal studies reported by WHO have consistently lent more support to favourable outcomes for people with schizophrenia in developing versus developed countries, the precise reasons for these differences are unclear and controversy persists as to whether people with schizophrenia in developing countries have better outcomes than those in developed countries.[43,129,130] Nevertheless, the growing number of older people with schizophrenia in developing countries means that many more resources will have to be allocated to this group. In our scientific literature review for this report, we recorded few large-scale (ie, number of participants >100) clinical studies of older adults with schizophrenia in developing countries. Up to 80% of the population of developing countries might use traditional healers for their health care.[130] Efforts to address more systematically mental health problems have included the use of health outreach workers, non-governmental organisations, and the integration of allopathic medicine with traditional healers.[130] The striking expansion of internet services would probably allow for greater penetration of models of mental health care from high-income countries into rural areas, although new technology will have to be introduced with cultural sensitivity.

Many clinical and social variables have a proven association with the outcome variables described in this Review (table), and they represent foci for further research to assess their potential as targets for intervention. Community integration provides an example of how we might begin to approach the care of an elderly person with schizophrenia. In longitudinal research, community integration was shown to be a pivotal variable that is reduced by depressive symptoms, cognitive deficits, and (paradoxically) more mental health services.[77] Community integration helps to reduce positive symptoms and overall general psychopathology, and helps to increase overall symptom remission rates.[77] As shown in figure 2, empirically validated interventions can potentially affect each of the variables in the model.

Our Review is consistent with Jeste and colleagues'[131] characterisation of the lifecourse of schizophrenia as an exaggerated paradox of ageing: ie, people with schizophrenia typically have accelerated physical ageing, but a normal rate of cognitive ageing (in the context of mild cognitive impairment originating at the onset of the disorder), improved psychosocial function, and diminished psychotic symptoms. Although full recovery is uncommon, many older adults with schizophrenia have substantial gains in their level of wellbeing. The conceptual shift shown in figure 3 implies that ideal states exist that might be achieved under optimal circumstances, and thereby suggests possibilities for changing individual and societal conditions to attain these states.

In summary, we have identified seven emerging trends that will have important implications for health policy, research, and care of older adults with schizophrenia. Worldwide, the demographics of older people with schizophrenia have changed completely with respect to their absolute numbers, the proportion of all people with the disorder, and residential status. Proposals to classify schizophrenia into early-onset, late-onset, and very-late-onset subtypes should now be tempered by the recognition that comorbid medical and neurological disorders could contribute to psychotic symptoms in later life. The conceptualisation of outcomes in later life has become more nuanced with the recognition that various symptomatic outcomes occur, largely independent of each other, that might need different treatment methods; moreover, outcomes should incorporate a lifespan perspective with people moving along a continuum from illness to functional recovery to successful ageing. Recent outcome data have shown that schizophrenia in later life is not a quiescent or stable end-state but one of fluctuating symptoms and levels of functioning. Many pathways lead to improvement and recovery. The ageing schizophrenia population has created enormous health-care needs, and medical comorbidity contributes to higher mortality in this population. Controlled pharmacological studies are scarce, especially with newer agents, and novel non-pharmacological therapeutic strategies have not been widely disseminated.

Contributors

CIC wrote the first draft, which was reviewed by PDM. Both authors contributed to the revision of subsequent drafts. JZ contributed extensively to the scientific literature search, the summarising of relevant articles, and the completion of the manuscript for submission.

Declaration of interests

We declare no competing interests.

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