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The Syndemic Approach in Relation to Clinical Practice and Research in Psychiatry

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DEAR COLLEAGUES,

The second issue of the *Consortium Psychiatricum* journal is hot off the press! In this issue we focus on both social and clinical topics.

The editorial article raises the importance of the implementation of a syndemic approach in psychiatry. We continue to explore the organization of community psychiatry care in different countries of the world; this time we publish articles from the UK, USA and China.

Two narrative reviews relating to two essential clinical topics – depression in schizophrenia and treatment of negative symptoms in schizophrenia – are written by Russian authors. Works of contemporary experts in this field are cited, along with the works of Soviet psychiatrists that have rarely or never been mentioned previously in this international arena. Therefore, I consider these papers might also be interesting from a historical and a cultural perspective.

The paper containing case reports might also prove interesting from the perspective of the clinical description of patients, observed in Russia.

Reiterating the issues surrounding COVID-19, raised in the first issue, we publish the commentary in relation to the new ways that people are having to interact due to the pandemic. The experiences of the de-stigmatization project that is being undertaken in Moscow, is described in the information section.

We are beginning to collect papers for the thematic issues on the first episode psychosis and ICD-11 implementation aspects, that are scheduled for publication in June and September 2021 respectively. I kindly invite you to submit your manuscripts for these issues.

George P. Kostyuk,
Editor-in-Chief, Consortium Psychiatricum

The Syndemic Approach in Relation to Clinical Practice and Research in Psychiatry

Синдемический подход в психиатрии: применение в клинической практике и научных исследованиях

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ABSTRACT
The syndemic framework goes beyond the concept of comorbidity and considers how diseases interact within their wider environmental context, along with social and political factors, to mutually exacerbate negative outcomes. The syndemic approach enhances the way mental disorders are understood in terms of their aetiology, treatment and prognosis and therefore influences the direction of clinical practice, policy development and research priorities in the field of psychiatry. Using a syndemic framework to develop mental health policy globally can help address the mental health "treatment gap" in countries where resources are limited. In Russia, identified syndemics have been of particular relevance to mental disorders and further research using a syndemic framework will continue to build upon the strong background of integrated mental healthcare currently provided.

АННОТАЦИЯ
Понимание болезни с точки зрения синдемического подхода выходит за рамки концепции коморбидности и включает в себя рассмотрение болезней в более широком контексте влияния внешних факторов (включая социальные и политические факторы), которые могут взаимно усугублять негативные последствия для здоровья. Синдемический подход расширяет понимание этиологии, лечения и прогноза психических заболеваний и, следовательно, влияет на общий вектор клинической практики, научных исследований и организации психиатрической помощи. Использование синдемического подхода при планировании психиатрической помощи в мировом масштабе может помочь устранить «пробелы оказания помощи» в странах с ограниченными ресурсами. В России известные синдемии оказывают влияние на психические расстройства, использование синдемического подхода в научных исследованиях может способствовать дальнейшему укреплению интегративной психиатрической помощи, которая практикуется в настоящее время.

Keywords: *syndemic, psychiatry, research, science*

Ключевые слова: *синдемия, психиатрия, исследования, наука*

INTRODUCTION

The syndemic approach is highly relevant to both clinical practice and research in psychiatry. The ways in which mental disorders are understood in terms of their aetiology, treatment and prognosis inevitably has an influence on the direction of policy development, on clinical practice and on research priorities in the field of psychiatry. Using a syndemic approach to understand the mental health context in Russia provides an opportunity to enhance the development of effective policy, services and mental health interventions.

THE SYNDEMIC APPROACH

The term "syndemic" was first coined by the medical anthropologist Merrill Singer in the 1990s to describe the "SAVA" syndemic of substance abuse, violence and HIV/AIDS in an inner-city population in the USA.[1] A syndemic involves two or more diseases that interact to worsen health outcomes and includes consideration of how the wider environmental context and other socio-economic and political factors contribute over time to mutually exacerbate negative outcomes.[2] Over the past 20 years, the syndemic approach has grown in impact and relevance for both global health and global mental health.[3]

It is well recognized that mental and physical health conditions may co-occur and interact in ways that influence outcomes. For example, co-occurrence of depression and diabetes is known to lead to adverse effects on both morbidity and mortality;[1] depression has been associated with a 1.5-fold increase in mortality in people with diabetes.[4] A key difference between understanding the co-occurrence of conditions and the syndemic perspective is that the syndemic approach moves beyond comorbidity and considers the synergistic effects of the wider social, political and environmental contexts in terms of the factors which influence aetiology and prognosis, at both population and individual levels.[5] Using the example of depression and diabetes, a syndemic approach considers the circumstances under which these conditions interact. This could refer to socio-economic factors that may be associated with depression and diabetes, such as poverty and exposure to trauma or violence, as well as the wider economic context such as trade policies promoting the production of highly processed, high calorie foods and also the health system itself in which these diseases are treated.[1]

Of great significance in 2020 is the global Covid-19 pandemic and it is relevant to ask how using a syndemic approach can enhance our understanding and response to this global pandemic.[6] What are the relationships between cardiovascular and respiratory diseases, gender, ethnicity, socio-economic status, age and Covid-19? How do the health system and wider socio-economic context in which Covid-19 is being managed influence outcomes?[6] Would a syndemic approach enhance our understanding and inform management and policy?

IMPLICATIONS FOR RESEARCH AND CLINICAL PRACTICE

Taking a syndemic approach highlights these wider contexts which may be missed in patient-level clinical practice.[1] Despite the emphasis on personalized, holistic care, generic guidelines may at times lead to a "one size fits all" approach for patients. However, within any patient population there will be diversity in terms of social situation, ethnicity, age, financial circumstances, culture, political views, health beliefs, exposure to adverse events and a range of other factors. In health systems, there will be differences in terms of structure, service style, accessibility and wider policy, economic and environmental influences.[1]

A number of vignettes have been published in which taking a syndemic approach influences clinical practice and increases the effectiveness of interventions.[1] For example, a "syndemic care system" is proposed for managing patients with diabetes and depression in South Africa. For this particular context, a community-based clinic structure is suggested that in addition to testing for single disorders, routinely provides screening for major comorbidities including mental disorders. This would enable formulation of a comorbidity profile and enhance provision of holistic care plans.[1]

It is important to note that a syndemic approach does not necessarily have to lead to more complex multi-level interventions, which might seem unrealistic. Due to the synergistic nature of interacting factors, a syndemic approach suggests a single-component intervention may have scope to influence outcomes at multiple levels.[5] This is of particular relevance in contexts with limited resources, where affordability of multiple component interventions is low.

IMPLICATIONS FOR GLOBAL MENTAL HEALTH

As well as in clinical practice, using a syndemic framework when considering wider public health initiatives can improve outcomes of whole population level interventions. Using a syndemic approach means rather than single disorders being considered one at a time, multiple disorders are considered together and the specific and shared wider context is explicitly taken into account.[2] For example, Brazil's Bolsa Familia Programme in 2003 distributed financial support to a quarter of the population in 2011, with the condition that children would go to school (where they would also receive food, vaccinations and growth monitoring) and women would attend postnatal services.[2] This intervention decreased poverty related malnutrition, diarrhoeal disease and overall mortality among children under five.[2] By addressing social inequality, this intervention benefited wider health outcomes due to the interactive nature of contributing factors.

Using the syndemic approach to develop mental health policy globally is crucial. The mental health "treatment gap" remains high in countries throughout the world and new initiatives are needed to address the increasing burden of mental disorders, especially in low- and middle-income countries, where resources are limited.[7]

CONCLUSION

The syndemic approach is of great relevance to enhancing the development of mental healthcare globally in terms of clinical practice, research and policy. In Russia, the syndemic framework has already begun to shape research priorities. Potential syndemics identified in Russia to date are directly related to mental healthcare, including the syndemic of "incarceration, injection drug use, poverty and alcohol abuse"[8] and "opioid addiction, HIV, hepatitis, tuberculosis, imprisonment and overdose".[9] Further research into how a syndemic framework can enhance development of mental healthcare in Russia will build upon the strong background of integrated mental healthcare currently provided within polyclinics and dispensaries.[10]

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Community Mental Health Practice in the United States: Past, Present and Future

Амбулаторная психиатрическая служба в США: прошлое, настоящее, будущее

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ABSTRACT

Similar to trends in Europe, approaches to mental illness in colonial America and recorded in early United States history were commonly characterized by incarceration and the removal of individuals from communities. In the mid-20th century, a major shift began in which treatment was offered in the community with the aim of encouraging individuals to re-join their communities. In this paper, we will provide a brief history of community mental health services in the United States, and the forces which have influenced its development. We will explore the early antecedents of community-based approaches to care, and then detail certain factors that led to legislative, peer and clinical efforts to create 'Community Mental Health Centers.' We will then provide an overview of current community mental health practices and evolving challenges through to the present day, including the development of services which remain focused on recovery as the ultimate goal.

АННОТАЦИЯ

В колониальной Америке и на ранних этапах становления Соединенных Штатов (США) пациентов с психическими расстройствами так же, как и в Европе, стремились изолировать от общества, вплоть до тюремного заключения. В середине XX века подход начал кардинально меняться: лечение стало проводиться амбулаторно по месту жительства пациентов с целью их последующей ресоциализации. В этой статье содержится краткая история амбулаторной психиатрической службы США, описаны факторы, которые повлияли на ее развитие. Также мы исследовали подходы, предшествовавшие современной амбулаторной психиатрической помощи, а затем подробно рассмотрели основные факторы, которые привели к законодательным, экспертным и клиническим инициативам по созданию амбулаторных психиатрических центров. Мы представили обзор современной амбулаторной психиатрической службы

и ее актуальных задач, к которым в первую очередь относится развитие служб, сфокусированных на социально-личностном восстановлении пациентов.

Keywords: *community psychiatry, community mental health, schizophrenia, recovery, de-institutionalization, psychosis*

Ключевые слова: *амбулаторная психиатрия, амбулаторная психиатрическая помощь, шизофрения, восстановление, деинституционализация, психоз*

INTRODUCTION

The treatment of individuals with significant mental health needs within the United States has a long and complex history. Generally, one of the most significant aspects of that history was the development of community-based mental health services. Importantly, this included a transition from institution-based care to community-based care which took place in the mid-20th century.[1] During this period, the United States experienced a dramatic decrease in the availability of institutional beds, alongside concomitant increases in the number of people seeking mental health services in outpatient, community settings. At a more in-depth level, these changes represented a shift more profound than the relocation of services; they were driven by changing ideas relating to the treatment provided by mental health services and the composition and character of those services. Any understanding of the development of community-based mental health services and more importantly, of its current state and future, thus requires consideration of the more complicated and underlying theoretical issues.

Accordingly, in this paper we will offer a brief history of community mental health in the United States, and the forces which have influenced its development to the present day. We will, firstly, explore the early antecedents of community-based approaches to care, before detailing certain major factors that led to legislative, peer and clinical efforts to create Community Mental Health Centers (CMHC) in the mid-20th century. We will then provide an overview of current community mental health practices and their evolving challenges. Next, we will examine those challenges in light of deeper and more complex issues related to the meaning of care, and recovery as its ultimate goal, which are still being explored, as the field moves forward. We will, in particular, be emphasizing aspects of history and current practice, as they relate to the treatment of individuals with serious mental illness (SMI). As currently structured, community mental health includes a broad array of services for individuals with less severe difficulties, as well as child developmental issues and addiction services. Although these aspects are also essential elements of treatment within the United States, we suggest that many of the issues underlying shifts in treatment with regard to SMI, may largely be generalized in line with other aspects within the larger system.

THE EMERGENCE OF COMMUNITY MENTAL HEALTH CARE

While the history of community care is generally considered to have begun in the mid-20th century, much of its original focus, as well as initial efforts to implement it, have a circuitous history. Similar to trends in Europe, approaches to mental illness in colonial America and recorded in early United States history, were commonly characterized by incarceration and removal from communities. As madness came to be regarded as within the medical purview over time, the early pioneers of American medicine, such as Benjamin Rush, began implementing somatic interventions; early medical interventions included harmful practices such as bloodletting and blistering. Within this framework, treatment was aimed at attacking a 'disease', facilitating a cure and an eventual return home. In response, however, to increasingly inhumane conditions and harsh treatments, new approaches, including the Quakers' Moral Treatment approach, began to highlight the need for milder interventions, including a prescription of activities mirroring those that patients would experience in their own community.[2] Central to the Quakers' philosophy of care was openness to restorative treatments and a return to full participation in the community.

The view that temporary respite in an asylum could lead to full reintegration in the community, gradually eroded over the course of the 19th century, as asylums and an ever-expanding array of experimental somatic interventions were developed. Trends towards long-

term institutionalization with medical models directing conceptualizations and interventions, became increasingly prominent throughout the 19th century, arguably reaching maximum influence at the turn of the 20th century, as Kraepelin's formulation of dementia praecox spread across the United States.[3] Within the paradigm of that era, there were no temporary or episodic aliments. Following Kraepelin's model, individuals were instead commonly viewed as experiencing a progressive medical illness, that required long-term institutionalization and custodial care, which were incapable of halting the deterioration of the illness.[4] This view, in combination with increasingly overpopulated institutions and eugenics laws advocating sterilization and dangerous interventions, such as early forms of shock therapy and psychosurgery, set the stage for rampant iatrogenic harm and abuse in mental institutions across the United States in the first half of the 20th century. However, throughout this period of history, voices of reform raised concerns about the pessimistic prognosis levelled at severe mental illness and highlighted the harmful practices occurring in American mental institutions.[5]

In the mid-20th century, calls for the reform of institutional-based care were heeded, with several key pieces of legislation influencing national trends. In 1946, the National Mental Health Act was passed, creating funding for psychiatric education and research, and ultimately bringing about the creation of the National Institute of Mental Health in 1949. In 1963, the Community Mental Health Center Act and the Mental Retardation and Community Mental Health Centers Construction Act were both passed, prompting an increase in funding for the creation of centres in the community that provided a wide range of psychiatric services. Associated with the increased funding for community-based services was a decrease in funding for public mental hospitals and a dramatic decrease in the number of long-term hospital beds during the same time period. The creation of Medicaid and Medicare in 1965 further facilitated the transition from large, public, psychiatric hospitals to the creation of community-based clinics, as well as nursing homes and intermediate care facilities, with a focus on treatment for individuals in the least restrictive environment. As emphasized by these initiatives, health was not only an attainable outcome, but could be achieved as a result of a connection with the community, and not as a precondition for that connection. Within eight years, a total of 398 community centres were in operation, approximately 0.18 per 100,000 people.[6] Over the next 40 years, tracked by the Substance Abuse and Mental Health Services Administration (SAMHSA), the number of community centres registered in the National Directory of Mental Health Treatment Facilities in 2016 would reach 2,636 with a density of 0.73 per 100,000 people.[7] The staffing of these centres varied across time and region, but generally, community mental health centres could be expected to employ a mix of mental health professionals and paraprofessionals, including psychiatrists, psychologists, counsellors, occupational therapists, social workers, case managers, addictions counsellors and nursing staff, all of whom might be expected to have direct contact with patients.

POST DE-INSTITUTIONALIZATION

Broadly, the legislative, clinical and advocacy efforts of the mid-20th century within the United States were effective in achieving large-scale de-institutionalization of the overpopulated state facilities of the previous era. However, as more outpatient treatment centres were built across the country, their efforts to help individuals with SMI regain their health and remain integrated in their communities were soon thwarted by several barriers. Of significance was the fact that the decades following the passage of the Community Mental Health Act were characterized by declining funding for outpatient centres, which, in light of the increased demand for mental health services, resulted in increasing levels of unmet mental health needs. The growth of mental health services has also not kept pace with the growth in population. From 2000-2017 the population of the United States grew by approximately 42 million. During that time period, the rate of psychologists and psychiatrists per 100,000 people, remained largely the same; between 36.55 and 33.18, and 7.54 and 7.75, respectively.[8]

Efforts were made to reform the American healthcare system by increasing third-party reimbursement and streamlining service utilization. In the 1980s, this was reflected in the emergence of behavioural health-managed care. Managed care involved private companies that dictated service authorization, utilization, claims processing and interagency coordination, with the intention of promoting improved efficiency and effectiveness of mental health services. With limited public funding to support CMHC, agencies became

increasingly reliant on these third-party reimbursements, necessitating interface with managed care entities, as well as demonstrating parallel trends within Medicare and Medicaid. This led to organizations structuring service delivery programmes in order to receive reimbursement from a patient's insurance plan.

While the emergence of managed care in the United States allowed for the survival and expansion of mental health services, in some ways, it probably resulted in a shift away from addressing the needs of individuals with SMI, many of whom were unlikely to have access to insurance or third party reimbursement. The most obvious negative impact of this was that individuals treated within their community were often unable to sustain satisfactory community participation, ultimately resulting in them being incarcerated. In other words, without adequate support, the attempt to help individuals move from asylums into the community led to larger numbers of these individuals challenging societal norms, resulting in legal convictions and boosting the number of state and federal prisoners with histories of significant mental health disorders.[9,10] These observations suggest that the path to de-institutionalization was reversed for some.[11,12] This, along with the more significant issues of underfunding, may also have contributed to a growing pessimism as to whether individuals with SMI could actually become well and fully re-join their communities; views that can be linked with long traditions of paternalism, coercion and control.[13]

The changing financial and political landscapes, in combination with increased treatment of SMI in prisons rather than the community, led to a cultural shift as to the meaning of wellness, in relation to SMI. Notably, in 2003, the New Freedom Commission on Mental Health was commissioned to study the status of the mental health delivery system and provide recommendations for the vision of mental health in the 21st century. The report issued by this commission in 2004 embraced the contributions of the recovery movement within the United States and established at least three expectations.[14] Firstly, it stated unequivocally that recovery was the expected outcome for mental health and substance abuse treatment. Secondly, it defined recovery as patient centred and as a journey that involved hope, autonomy and self-determination. Finally, the commission called for the development of recovery-oriented mental health services. While this report did not solve the problem of prisons emerging as long-term treatment facilities for SMI, it did spur on the development of new forms of recovery-oriented services, including peer counselling[15] and other interventions focused on psychosocial outcomes.[16-18]

CURRENT STATUS

Currently, in the United States, federal governmental regulations determine the monetary value distributed to individual states, as well as determining how monies can be spent. The majority of federal dollars for mental health services are distributed by means of Mental Health Block Grants via SAMHSA. Since its inception in 1992, SAMHSA has contributed varying amounts of money in the form of state-specific block grants to support and grow community mental health and substance abuse treatment centres. From an initial distribution of 1.69 billion dollars in 1992, SAMHSA has seen a gross increase in yearly distributions, ranging from a low of 3.12 billion in 2007, to a high of 4.2 billion in 2017.[19] Additional federal funding sources come in the form of Veterans Administration Benefits and Medicare/Medicaid expenditures. Currently, there is considerable regional variability in the availability of community-based mental care, due to differing levels of local funding, the specifics of state Medicaid and the availability of providers.

As previously noted, by 2017 the United States had a total of 2,381 CMHC, with a density of 0.73 per 100,000 people. The services offered are provided by a broad range of professionals, including psychiatrists, psychologists, counsellors, occupational therapists, social workers, case managers, addictions counsellors and nurses. Services are provided in group, family and individual formats and are expected to be individually tailored to meet the unique needs of any given patient. General services, commonly available, include medication management, case management, and group, family and individual therapies. These types of services should be capable of responding to the full range of psychosocial needs and therefore, vary significantly from site to site, with common services including supportive, psychoeducational, vocational, social, addiction, educational and activity-based interventions. These interventions can be delivered within the physical space of the CHMC or in the home or community of the patient. Additionally, there are state-wide disparities in CMHC densities; California, the most populous state, has 0.22

per 100,000 people, while Wyoming, the least populous state, has 4.15 per 100,000 people. These numbers are dwarfed by the 7,482 for-profit mental health agencies in the United States.[7] The majority of mental health services are provided by agencies that charge insurance premiums or require self-payment at the time of service. Of those seeking mental health treatment, 42% see cost and lack of insurance coverage as the greatest obstacle to accessing services, with 25% stating that they are faced with the dilemma of obtaining mental health services or paying for daily necessities.[20]

Licensed professionals practicing across these settings include psychiatrists and psychologists, commonly functioning as the providers of records, while much of the direct service is conducted by social workers, mental health therapists or addictions counsellors, with either a master's or a bachelor's degree. Healthcare workers from a range of other disciplines, such as nurses, occupational therapists, pharmacists, dietitians and primary care physicians are also found in certain community mental health settings. The expectation for community mental health care involves a continuum of services, not limited to psychiatric medicine, nursing intervention, supported housing and supported employment. Additionally, a host of psychosocial services, consisting of individual and group psychotherapies, skills-based psychosocial rehabilitation, case management and a range of peer services, including individual support, self-help approaches and peer-led clubhouse services are also provided. These services are delivered across a range of settings, including standard outpatient health clinics, in patient's homes or in the community (e.g., grocery stores, coffee shops, government offices, homeless outreach premises, job settings, etc.). Certain community mental health settings are directly integrated with primary care medicine, while others must link their services with other sources of primary care in their communities. Following the national economic recession in the United States, healthcare-related jobs increased between 2008 and 2009, while all other industries saw reduced growth; the total number of healthcare jobs created between 2007-2013 had a value of approximately 1.85 million. Most new jobs in healthcare were positions that required less formal education, particularly jobs with high rates of turnover. The dramatic increase in the number of positions was due, to a great extent, to the Affordable Care Act.[21]

THE EVOLUTION AND FUTURE OF COMMUNITY MENTAL HEALTH SERVICES IN THE UNITED STATES

As discussed at the outset of this report, the community mental health movement in the United States, particularly with regard to the needs of adults with SMI, has, for nearly 70 years, been driven by a vision of treatment that promotes recovery and integration within one's community. As this has unfolded, many social and economic issues have occurred, leading to a rocky progression; prisons have become the new asylums for some, while the professional work force has not grown to meet emergent needs. Looking to the future, we certainly do not see simple solutions to these problems. We do, however, see potential developments which may help offset some of these challenges, as well as counter movements which could resurrect even more intransigent barriers to recovery.

The most significant developments which we see affecting the future of community mental health in the United States are the emerging, nuanced views as to what recovery represents, linked to the way in which services need to be developed and implemented to support recovery. In our view, studies of the experience and perspective of the individual with SMI, including qualitative and quantitative studies, as well as user-led participatory research,[22] have revealed that recovery means attaining a satisfying and meaningful life, with healthy and sustaining, interdependent connections with one's community. Recovery does not constitute the absence of a disease, the development of a skill or anything else that could be considered as happening within one person in isolation.[23,24] Instead, recovery is a return to full participation in the larger, human community.[25] Interventions are thus needed that support individuals with SMI in making meaningful sense of their own perception of mental health and its related life challenges, prior to facilitating their decision making with regard to responding to these challenges.[26]

Importantly, this view of recovery precludes the fact that just one treatment could promote recovery for all. Instead, integrative approaches are needed that go beyond generic support and can be customized to address individual needs and processes of self-direction. Such integrative treatment frameworks would need to be flexible so that service providers could consider and respond to the individual, using a holistic approach. Similarly, these frameworks would have

to move from a didactic or paternalistic model to a fully consultative one. These new models would also need to move beyond the implementation curriculum, which focus on singular problems or skills; instead they would have to be able to flexibly help individuals respond to the myriad of psychiatric, social and psychological problems, which may emerge fluidly during the course of recovery. Examples of recent work, inspired by these newly defined needs, include Metacognitive Reflection and Insight Therapy (MERIT),[24,27,28] Open dialogue,[29] as well as clubhouse-based approaches.[25]

It is important to note that the development of treatments that are able to address meaning in this way face stiff challenges in our current environment. There are competing ideas relating to recovery, which is still considered as a state defined by professionals, rather than an evolving condition experienced by those suffering from mental illness. Additionally, patient-centred treatments face resistance from conventional treatment approaches, as well as social hysteria, linked to the need to compartmentalize and marginalize those deemed dangerous or unwell in the eyes of the community. These counter trends, while understandable in some cases, threaten a regression to past methods of treatment which, although taking place in the community, do not facilitate community membership. Polarization within the psychiatric community may also be fuelling these negative trends. Traditional approaches to mental health, including models of schizophrenia as presented in the DSM 5,[30] neglect the concept of recovery, while other approaches, concerned with the issue of autonomy, call for the dismantling of structures within community mental health, which although flawed, have enabled meaningful recovery work to take place and seem necessary for the growth of future interventions.

SUMMARY

The current community mental health system in the United States was initially developed in the mid-20th century through resurrected values of restorative care from early efforts, including Moral Treatment. The guiding vision of recovery is that people experiencing mental illness should be offered services that help them live as full members of the community, seeking lives of meaning and value, with or without persistent symptoms and/or disability. In the decades following the creation of the original community mental health centres, reduced funding and increased demand has led to difficulties relating to access to care and a large number of people with mental illness finding themselves in the criminal justice system. Increased awareness of this difficulty, as well as the influence of the recovery movement, managed care practices and the more recent changes to the national healthcare system, are likely to continue to influence the evolving nature of available services in the community.

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Community-Based Mental Health Care in Britain

Амбулаторная психиатрическая служба в Великобритании

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ABSTRACT

Community mental health care in the UK was established by two influential mental health acts (MHAs). The 1930 MHA legislated for voluntary admissions and outpatient clinics. The 1959 MHA required hospitals to provide local follow-up after discharge, required them to work closely with local social services and obliged social services to help with accommodation and support. An effect of this was to establish highly sectorized services for populations of about 50,000. These were served by multidisciplinary teams (generic CMHTs), which accepted all local referrals from family doctors. Sector CMHTs evolved a pragmatic approach with an emphasis on skill-sharing and outreach, depending heavily on community psychiatric nurses. The NHS is funded by central taxation, with no distortion of clinical practice by per-item service fees. It is highly centrally regulated, with a strong emphasis on evidence-based treatments.

Since 2000, generic sector teams have gradually been replaced or enhanced by Crisis Resolution Home Treatment teams, Assertive Outreach Teams and Early Intervention Teams. Assertive Outreach Teams were resorbed into CMHTs, based on outcome evidence. The last decade has seen a major expansion in outpatient psychotherapy (Improving Access to Psychological Treatments (IAPT) services) and in specialist teams for personality disorders and perinatal psychiatry. The traditional continuity of care across the inpatient-outpatient divide has recently been broken. During the last decade of austerity, day care services have been decimated, and (along with the reduction in availability of beds) compulsory admission rates have risen sharply. Mental health care is still disadvantaged, receiving 11% of the NHS spend while accounting for 23% of the burden of disease.

АННОТАЦИЯ

Амбулаторная психиатрическая служба в Великобритании регламентируется двумя законами о психиатрической помощи. В 1930 году законодательно были закреплены добровольная госпитализация и амбулаторные клиники. Закон 1959 года требовал, чтобы больницы после выписки предоставляли пациентам амбулаторное наблюдение по месту жительства, обязал больницы работать совместно с местными социальными службами, а социальные службы – обеспечивать пациентов жильем и оказывать им поддержку. Результатом этого стало формирование секторального принципа работы психиатрической службы с прикрепленным населением 50 000 человек на каждый сектор. Психиатрическая служба в каждом секторе представляла собой мультидисциплинарную команду специалистов (в последующем они стали называться «амбулаторные психиатрические бригады» – Community Mental Health Teams (CMHTs)), которая принимала всех пациентов, направленных семейными врачами. Секторальные бригады развили прагматичный подход к оказанию помощи пациентам с акцентом на выработку навыков и на широкий охват помощью, которая предоставлялась преимущественно участковыми медсестрами. Здравоохранение Великобритании финансируется за счет централизованного налогообложения, клиническая практика не искажается налоговыми ставками за отдельные виды медицинских услуг. Медицинская помощь регулируется централизованно, в ее основе лежат принципы доказательной медицины.

Начиная с 2000 года секторальные психиатрические бригады постепенно были заменены или усилены несколькими видами специализированных бригад: кризисными бригадами оказания помощи на дому (Crisis Resolution Home Treatment teams), бригадами настойчивого лечения (Assertive Outreach Teams) и бригадами раннего вмешательства (Early Intervention Teams). Бригады настойчивого лечения после анализа данных об их эффективности стали частью амбулаторных психиатрических бригад. В последнее десятилетие наблюдается значительное расширение амбулаторной психотерапии благодаря работе службы улучшения доступа к психологической помощи (Improving Access to Psychological Treatments, IAPT), а также созданию команд, специализирующихся на оказании помощи людям с расстройствами личности и на перинатальной психиатрии. Традиционная непрерывность стационарной и амбулаторной медицинской помощи недавно была нарушена. В течение последнего десятилетия жесткой экономии дневные стационары были упразднены и, наряду с сокращением числа стационарных коек, резко возрос уровень недобровольной госпитализации. Психиатрическая помощь по-прежнему находится в неблагоприятном положении, получая финансирование в размере 11% от общего фонда здравоохранения, в то время как на психические заболевания приходятся 23% бремени болезней.

Keywords: *Community Mental Health Teams, sectorization, functional teams, general practice*

Ключевые слова: *амбулаторные психиатрические бригады, секторальный принцип, медицинская помощь, функциональные бригады, общая врачебная практика*

WHEN WAS COMMUNITY-BASED CARE ESTABLISHED?

The United Kingdom of Great Britain and Northern Ireland (hereafter referred to as the UK) was in the vanguard of the asylum movement in the early 19th century. Following the example set by the Quaker Tuke family in the York Retreat in 1796, asylums based on 'moral therapy' were established throughout the nation from the early 1800s. These remained the dominant model of psychiatric care for psychotic illnesses until 1930. Strict legislation in the late 19th century, to protect the rights of detained patients, had an unintended consequence of hindering early intervention and flexible care.

The predominantly degenerative view of mental illness was finally shaken by experiences in the First World War and the succeeding decades. Shell-shocked soldiers confirmed the involvement of psychological processes in the causation and treatment of mental illnesses. The dramatic success of malaria treatment for general paralysis of the insane (GPI) and promising early sleep therapies brought psychiatry closer to medicine and began to erode the isolation of the asylums. There had been many individual initiatives prior to this. The first psychiatric outpatient clinics were established at St Thomas's in London and in the Wakefield asylum in 1890, along with hostels for discharged patients (such as that in Dingleton Hospital in 1880) and general hospital outpatient clinics in Portsmouth in 1926. However, these early experiments failed to catch on. The modern era was ushered in with the establishment of the Maudsley Hospital in 1923, devoted to short-term care, and the 1930 Mental Treatment Act.

THE 1930 MENTAL TREATMENT ACT AND THE 1959 MENTAL HEALTH ACT

Community mental health in the UK was effectively established by these two acts. The 1930 act permitted voluntary admissions, outpatient care in mental hospitals and for local authorities (who, at that time, were responsible for all mental health care) to spend money on supporting discharged patients. It also changed terminology from 'asylum' and 'lunatic' to 'mental hospital' and 'mental patient'. This more outward-looking attitude witnessed slow, but informal, growth in outpatient care. The first day hospitals and day centres were opened after WWII, beginning with the Marlborough Day Hospital in London, opened by Joshua Beirer in 1946. In 1948, the National Health Service was established, and mental health care was transferred to it from local authorities. This amalgamation cast into stark relief the contrast between the flexibility of general healthcare and that for mental health, and it prompted much soul-searching.

The development of UK community mental health care as it is now known can be traced to the 1959 MHA. The 1959 MHA reflected the optimistic spirit of its age and the impact of the post-war welfare state, which guaranteed basic financial security for disabled citizens. As well as introducing strict regulations for the use and monitoring of compulsory care, the 1959 MHA contained two specific provisions which profoundly shaped developments. Firstly, the act placed local authority social services at the centre of care for the severely mentally ill. Social workers had authority over compulsory admissions (albeit on the recommendation of psychiatrists). The act also legislated both the resources and the obligation to provide aftercare. Secondly, the act required any hospital that took in detained patients to, itself, provide them with outpatient follow-up and aftercare. To achieve these ends (both cooperation over compulsory admissions and outpatient follow-up), mental hospitals had to develop close working relationships with local authority social workers.

The only practical way to achieve such close working relationships was by establishing catchment areas and, eventually, sectorization. Unlike the French, whose 'secteur' was centrally dictated, UK sectorization (manifest in the growth of local Community Mental Health Services - CMHTs) grew organically as a pragmatic response to these requirements. CMHTs spread in reach and sophistication throughout the 1960s and 1970s and became the default structure for community care until the radical changes introduced in 1999.

THE GENERIC CMHT

By the late 1970s, most of the UK population accessed its specialist mental health care via a generic CMHT.[1] Teams served a defined population and were expected to assess anyone referred to them irrespective of diagnosis or severity of disorder. The populations served initially numbered about 50,000, but this number has shrunk as resources and specialization have increased. The team was responsible for all outpatient and inpatient care, usually having access to a number of beds in the local psychiatric unit. Psychiatry in the UK is explicitly a secondary service. Virtually all patients, other than the homeless and those in chaotic inner-city situations, are referred after assessment by their family doctor.

The traditional CMHT is multidisciplinary, comprising, at a minimum, psychiatrists, community psychiatric nurses and social workers. It may also include occupational therapists, psychologists, healthcare assistants and sometimes other specialists. It is headed by a specialist psychiatrist, and Community Psychiatric Nurses (CPNs) are usually its most numerous members (2–5). CPNs were developed in 1953 as a fledgling service to monitor discharged psychosis patients[2] but have long outnumbered all other community MH staff.[3] They are the case managers for most patients, usually carrying a caseload of 20–30 patients, with contact monthly or more often, as needed. CMHTs accept all referrals from family doctors so must deal with the whole range of disorders, from long-term psychoses to short-term crises, anxiety and depression. Managing referrals to match expectations and capacity has always been a challenge for CMHTs, and this has become increasingly so, often with an explicit focus on patients with a severe mental illness (SMI). CMHTs are usually based in some form of shared community centre, and outreach has been a central feature of practice. In the case of CPNs in particular, most of their contact with patients is home-based, and this practice is common in other disciplines.

The population served by each CMHT was initially geographically defined but has increasingly been based on general practice lists. This strengthens working relationships and continuity between primary and secondary care. Such comprehensive responsibility for a clearly defined population powerfully focuses CMHTs on the most seriously ill patients. Because difficult patients cannot be declined or sent elsewhere, UK mental health care is pragmatic, with little scope for rigid theories. The care provided is, of necessity, eclectic, and there is a long tradition of role blurring and skill sharing.

CPNs are the backbone of the service and the group primarily responsible for monitoring and supporting psychosis patients, often administering long-acting antipsychotic medications. Social workers have specific responsibilities for ensuring accommodation and financial support. Psychologists, where they are present, often take the lead in psychotherapy and talking treatments.

UK CMHTs have strikingly informal working practices. Titles are rarely used; first name terms are the rule, and professional boundaries are not defended. All members spend much of their time on supportive social care. For example, a nurse or psychologist would not hesitate to ring up a housing department. Initial assessments are not always conducted by medical staff where nurses

and psychologists have taken prominent roles. This non-hierarchical style was inherited from the therapeutic community movement that was so influential when CMHTs were beginning.[4]

The extent of role-blurring may also be a consequence of the NHS funding system, with the absence of any 'fee for service' or targeted payments. NHS MH services are funded by a relatively simple block grant. This is based on a capitation formula, plus sophisticated adjustments for levels of deprivations. In recent years, commissioning of services has become more localized, with specific targets for individual services.

SPECIALIST AND FUNCTIONAL TEAMS

CMHTs have always been stratified by age group. Alongside the adult service (for 18–65-year-olds), parallel services were established very early for children and adolescents (up to the age of 18) and old-age services for those over 65. The structure and functioning are essentially similar for all three sets of teams, although the populations served vary. In addition, most regions had specialized teams that the CMHTs could refer to. There were liaison teams in hospitals, forensic services for mentally disordered offenders, and rehabilitation teams for severely and chronically disabled patients. Depending on local resources, there might also be specialized teams for eating disorders and personality disorders, although these were not universal.

These UK community MH services evolved organically through the 1960s to the 1990s. In the 1990s, however, evidence-based practice (ushered in with Stein and Test's study of ACT)[5] began to impact on planning, which became more centralized and specific. In 1999, the National Service Framework for Mental Health[6] proposed replacement of generic CMHTs by four specific services ('functional teams'). These were a Home Treatment Crisis Resolution (HTCR) team to deflect admissions, an Assertive Outreach Team (AOT – essentially an ACT team) to support 'revolving door' psychosis patients, an Early Intervention Service (EIS) for first-episode psychosis and, lastly, a Primary Care Liaison Team (PCLT) for everything else. PCLTs did not survive, and the other functional teams have gradually been rolled out nationally alongside generic CMHTs.

AOT teams were the first functional teams to be introduced. They were subjected to rigorous research and found not to be an improvement on CMHTs,[7,8] so their functions have been resorbed back into CMHTs. The other two specialist teams have not been subjected to anything like the same rigorous research and remain central features of current practice. The provision of standalone personality disorder services[9] is now nationwide, and liaison services in general hospitals have been significantly enhanced. A striking (and unevidenced) recent development has been the splitting of community teams from inpatient responsibilities (the so-called 'functional split'). This arose from concerns about the quality of inpatient care. However, loss of continuity and unanticipated complexities have led to doubts over its wisdom.[10]

PSYCHOTHERAPY SERVICES (IAPT)

UK mental health has had very little private care provision. Apart from some very limited access to psychoanalysis, there has been no tradition of private psychotherapy as in other European countries. Simple psychotherapy has long been available within the NHS, and in the 1970s, psychotherapy was already recognized as a subspecialization within psychiatry, with its own training requirements. While this was intended to protect psychotherapy and its training, it also served to isolate it somewhat. Clinical psychologists in the NHS have increasingly expanded their expertise in, and responsibility for, cognitive behaviour therapy. This is now the primary evidence-based psychotherapy recommended by NICE (the National Institute for Clinical Excellence). In 2007, a separately funded provision (based on a stepped-care model) was introduced, called Increased Access to Psychological Treatments (IAPT).[11] This programme provided advice and self-care but also trained CBT therapists to provide more intensive treatment, initially from primary care. Once established, the service was absorbed into secondary MH care and is now routine. It has ensured much greater access to psychotherapy, with an estimated additional 3000 staff nationally. However, it has been criticized by some for its restriction to CBT, its rather rigid format and the quality of therapist training.

FINANCING AND LEGAL STRUCTURE

UK mental health care is funded by general taxation via the NHS and is totally free at the point of service. There are no patient-level payments (no itemized payments), although some service-level targets may affect funding.

Currently, it accounts for 11% of the total NHS spend (9.8% of GDP, in line with the EU average of 9.7% in 2014). In 2012, the Health and Social Care Act committed to 'parity of esteem' between physical and mental health care by 2020. As mental disorders account for 23% of the burden of disease, there is clearly quite some way to go. Local structures for setting priorities can have significant effects at the margins, but NHS MH services are generally fairly consistent nationally and remain subject to no complex financial distortions of clinical practice.

The 1959 MHA was revised in 1983 and again in 2007, and it is currently undergoing another revision. The UK is out of step with most of Europe in that compulsory admissions and treatment are initiated clinically rather than by a legal decision. They are subject to routine legal ratification of their justification by tribunals at set intervals, but this arrangement is subject to strong criticism and may change. Compulsory admissions are for set maximum periods (one month or six months and, in rare emergencies, three days), with legal representation available for patients at tribunals. The 2007 revision made two major changes. Firstly, it removed the four categories of disorder (mental illness, learning disability, severe learning disability and personality disorder) and replaced them with a single category of mental disorder. The rationale for this was to remove a 'treatability' clause that had been introduced into the 1959 MHA for personality disorder. Now, all patients are detained on the grounds of risk to health and the availability of 'appropriate treatment' (which is very broadly interpreted and can include care and supervision). The second major change was to introduce community treatment orders (CTOs). These are targeted on revolving door psychosis patients to ensure continued follow-up and maintenance medication. They are for six months in the first instance, after discharge from an involuntary admission, and are renewable for one year at a time without limit. Despite the evidence that they provide no benefit for patients,[12,13] about 4000 per year are imposed.

The rate of compulsory admissions in the UK is 114 per 100,000. This is in the mid-range for Europe, with Austria highest at 282 and Italy lowest at 14.5.[14] However, there are two significant issues of concern. The first is that the rate is rising faster than that of most comparable countries, and the second is the persistently high rate of detention among black patients. The number of compulsory admissions has risen from 43,364 in 2007 to 63,048 in 2015, an increase of 45%. This rise has settled at about 4.0% per annum and is in line with France (4.7%) and Australia (3.4%). However, in most other comparable countries, the rate of compulsory admissions has been steady or has declined slightly. This recent rapid rise in the UK has been associated with a substantial reduction in available beds.[15] Currently, one third of all admissions are compulsory, and a further third are converted to compulsory while the patients are in hospital. In many inner-city areas, virtually all inpatients are compulsory. It has been suggested that the current rapid rise reflects not only the risk-averse nature of UK society but also that it may be the only way to secure a bed.

The second area of concern has long been expressed and relates to the very high rates of admission (including compulsory admission) for black patients (Afro-Caribbean men in particular). This was initially attributed to stigmatizing discrimination and over diagnosis.[16] Despite careful epidemiological work to contradict this and demonstrate a genuinely high rate of psychosis in these groups,[17,18] the failure of services to engage with this vulnerable group generates constant criticism.

RESOURCES

The UK lies in the mid-range in terms of the numbers of both psychiatrists and psychiatric beds in Europe.[19] The UK has 19 psychiatrists per 100,000 population, compared with 17 for Ireland, 18 for Italy, 23 for France and Norway, and 22 for Germany and Sweden. There are 46 beds per 100,000 in the UK, compared to a European mean of 21 per 100,000 (ranging from 10 in Italy, up to 128 in Germany and 139 in the Netherlands). Average inpatient stays are about 35 days, but this mean hides a skewed curve, with many crisis admissions of two to three days and a small number of patients with very long stays. Long-stay rehabilitation beds have been in sharp decline for the last couple of decades, but there has been a noticeable rise in secure provision (often in the private sector) for NHS forensic patients. The only three high secure forensic hospitals have been reduced by over 75% during the last two decades, while medium secure forensic units have now become a routine component of local service provision.

Figures for day hospital places (provided by the NHS) and day centre places (provided by local authorities) are difficult to obtain with any accuracy. The strong clinical

impression, however, is that these are also being closed, even more so during the last decade of austerity.

STRENGTHS AND WEAKNESSES

UK community mental health services have been the backbone of psychiatric care since WWII. They have several strengths. They have benefited from a pragmatic approach, avoiding ideological schisms. A relatively simple funding formula avoids perverse incentives and distortions of clinical care. Central monitoring and target setting have resulted in a healthy respect for, and focus on, evidence-based practice. Services have benefitted from a well-established primary care system which filters their referrals and which has taken on most of the milder cases of anxiety and depression. Another strength has been the early development of sectorized multidisciplinary teams, with an emphasis on outreach and highly trained and confident non-medical staff.

Among their weaknesses has been an absence of strong clinical leadership, with an increasingly managerial and risk-averse culture. While there have been significant improvements in the quality and consistency of care, this has been accompanied by an enormous growth in bureaucracy and a fragmentation and over-complication of services. Simple lines of responsibility between patient, family doctor and psychiatric team have been obscured or abandoned, and continuity of care has diminished. UK community mental health services have also struggled to establish a confident and convincing public image and consequently endure problems of low morale and recruitment.

There are, however, encouraging signs that mental health issues have recently moved up the political agenda. The increasing public willingness to be open about mental health problems has focused the government's attention on patchy service provision and the gap between rhetoric and reality as regards funding. Substantially increased funding has been promised, and a review of the mental health act is underway. It would be foolish, however, to make predictions about anything in the UK currently.

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Promotion of Mental Health Rehabilitation in China: Community-Based Mental-Health Services

Амбулаторная психиатрическая служба Китая как средство реабилитации психических расстройств

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ABSTRACT

Community-based mental health services are important for the treatment and recovery of patients with mental health disorders. The Chinese government has made the establishment of a highly efficient community-based health service an enduring priority. Since the 1960s, community-based mental health services have been developed in many Chinese cities and provinces. National policies, including mental health regulations and five-year national mental health working plans, have been issued to support the development of quality of mental health services. The accessibility and efficiency of community-based mental health services are now highly promoted to community residents.

According to the National Standards for Primary Public Health Services, community-based mental health services are one of the most important components of primary public health services. They are mainly provided via Community Health Service Centres (CHCs), by a combination of general practitioners, public health physicians, nurses and social workers. Patients receive individualized and continuous health services according to their rehabilitation status. These services include regular physical examination, health education, rehabilitation guidance, social function rehabilitation training, vocational training and referral services; family members also receive care and psychological support. Future work will focus on expanding mental health service coverage and usage, increasing awareness of mental health and decreasing stigma, and strengthening service capability to establish an integrated model to enhance the overall efficiency of mental health services.

АННОТАЦИЯ

Амбулаторная психиатрическая служба играет важную роль в процессе лечения и восстановления пациентов с психическими расстройствами. Создание высокоэффективной системы амбулаторной психиатрической помощи всегда являлось одним из главных приоритетов правительства Китая. Начиная с 1960-х годов во многих городах и провинциях были созданы локальные амбулаторные психиатрические службы. Государственная политика в области здравоохранения и 5-летние национальные рабочие планы в области психического здоровья способствовали повышению качества услуг. В настоящее время ведется активная информационная работа с населением о доступности и эффективности амбулаторной психиатрической службы.

Согласно «Национальным стандартам первичной медико-санитарной помощи» одним из важных компонентов первичной медико-санитарной помощи является психиатрическая помощь. Она предоставляется преимущественно на базе амбулаторных центров здоровья командой специалистов, которая состоит из врачей общей практики, санитарных врачей, медсестер и социальных работников. Помощь предоставляется

индивидуализированно и непрерывно, а ее наполнение зависит от реабилитационного статуса пациентов. Медицинские услуги включают в себя регулярный физикальный осмотр, просвещение в области здоровья, рекомендации по реабилитации, тренинг социального функционирования, тренинг по трудоустройству и предоставление справочной информации. Членам семьи пациента также предоставляются медицинская помощь и психологическая поддержка.

В дальнейшем необходимо повышать охват населения психиатрической помощью и способствовать обращаемости за помощью, повышать уровень осведомленности населения о психическом здоровье и снижать стигму. Кроме того, необходимо расширять возможности психиатрической службы и создавать интегрированную модель психиатрической помощи, что должно способствовать повышению ее общей эффективности.

Keywords: *China, community-based mental health service, recommendations*

Ключевые слова: *Китай, амбулаторная психиатрическая служба, рекомендации*

THE MENTAL HEALTH SERVICE SYSTEM IN CHINA

Mental disorders are one of the most serious public health challenges, affecting individuals, their families and society. A recent national mental health survey in China showed that the lifetime prevalence of mental disorders was 16.6%, with anxiety disorders, mood disorders, substance use disorders, impulse control disorders and schizophrenia among the most common.[1] Nearly 20% of the burden of diseases in China is caused by mental disorders and suicide.[2] This growing burden highlights the urgent need for an effective mental health service system. Nowadays, nearly 90% patients are living and receiving medical treatments in their communities, which has implications for the development of high-quality mental health services, particularly those based in the community.

The Chinese government has long been committed to providing better quality and more integrated mental health services, aiming at improving the efficiency and continuity of both hospital-based and community-based mental health services. Mental health laws, related regulations and national mental health working plans have also been enacted in recent decades in order to facilitate the development of mental health services. Since the 1960, there has been an integrated three-tier system that includes inpatient, outpatient and community services.[3] In this article, we will mainly focus on community-based mental health services.

Mental health-related policy in China

The first National Mental Health Plan (2002-2010) was signed by the Ministries of Health, Public Security and Civil Affairs, and the China Disabled Persons' Federation (CDPF) in 2002. It aimed to establish an effective system of mental health care, led by the government, with the participation and cooperation of other sectors.[4] The service model was led by psychiatric hospitals, supported by departments of psychiatry in general hospitals, community-based health facilities and rehabilitation centres.

On 26th October 2012, The Mental Health Law of the People's Republic of China was enacted to develop the field of mental health, standardize mental health services and guarantee the legal rights and interests of people with mental disorders.[5] This Law mandated that urban community health centres, rural township health centres and rural village health clinics should establish a registry of people with severe mental disorders, periodically follow up such people who live at home, instruct patients about the use of medication and rehabilitation, and educate guardians about mental health and care of the mentally ill.

Following this Law, the National Mental Health Plan (2015-2020) was proposed by the State Council. It contained more specific aims and requirements to improve the mental health system and to develop mental health services.[6]

1.2 A three-tier mental health system

An integrated, three-tier hospital-community service model has been established and has become a crucial component in the reform of China's mental health services.[7] Mental health services are mainly provided by psychiatrists, psychiatric nurses, social workers and

clinical psychologists in mental health centres, by general practitioners and community nurses in community health centres and by social workers, clinical psychologists, rehabilitation therapists and occupational therapists in other government or social organizations. These services cover inpatient and outpatient treatment, hospital and community rehabilitation, health education, psychotherapy and vocational rehabilitation. Patients with mental illnesses can seek mental health services both in mental health centres and community health centres. The government has clearly defined the responsibilities of different medical institutions at all levels in the model. Psychiatric hospitals are mainly in charge of medical treatment for severe mental disorders, through inpatient and outpatient treatment, hospital-based rehabilitation and health education. When a patient's condition has stabilized, they are referred to CHCs, which are responsible for rehabilitation and health education. If the patient is willing to accept follow-up services, mental health service providers will provide patients and their guardians advice on how to maintain stability. If the patient is relatively stable, they may attend community-based rehabilitation facilities. These facilities provide services including antipsychotic maintenance therapy, behaviour therapy, social skills training, vocational rehabilitation and family education. If the patient relapses, they are referred to hospital.

The mental health workforce and resources

The mental health workforce is a key component of the quality and efficiency of mental health services. In the past, mental health services were mainly hospital-based, delivered by psychiatrists or psychiatric nurses in psychiatric hospitals. The capacity of community-based services was limited, as there were far fewer mental health professionals working in community health centres, which also severely affected the continuity of mental health services. To meet this challenge, governments at all levels were committed to improving community-based mental health services and strengthening professional capacity and human resources.

In 2002, there were only 13,397 registered psychiatrists,[8] but by the end of 2016, this number had risen to 31,910[9] (2.31/100,000 population; above the average of 2.11/100,000 in upper-middle income countries).[10] By the end of 2015, there were about 1.2 million certified psychological counsellors, however, only 0.03-0.04 million were involved in psychological counselling work, part-time or full-time and there were only about 5000 psychotherapists.[11] The number of mental health social workers is not clear. By the end of 2016, there were 1,650 psychiatric hospitals, containing 297,637 beds (21.5/100,000 population; below the average of 24.3/100,000 population in upper-middle income countries). The average length of inpatient stay is 51.7 days.[9] The quality and coverage of mental health services have been greatly improved.

COMMUNITY-BASED MENTAL HEALTH SERVICES: FOUNDATIONS AND DEVELOPMENT

Following the first National Mental Health Meeting in 1958, community-based mental health rehabilitation work started in Beijing, Shanghai, Hunan, Sichuan, Jiangsu and Shandong provinces, before gradually expanding to other places in China. As the vast majority of patients receive treatments and therapies in the communities where they live, the provision of comprehensive, continuous and coordinated mental health care services is very important for patient recovery. The Chinese government has promised to make continuous efforts to develop a better community-based hospital-community integration service model in order to meet individual need for qualified mental health services in communities.

Service development 2002-2018

In 2002, the State Council issued the National Mental Health Working Plan (2002-2010), which emphasized the building of a better mental health service delivery system for the prevention, treatment and rehabilitation of mental disorders, based on medical institutions, communities and families. In 2012, the Mental Health Law mandated that CHCs must provide technical support to help residents' committees to provide mental health education to all residents living in the community. They are also responsible for keeping records of patients with severe mental disorders, follow-up services, medication guidance, rehabilitation training and mental health and nursing knowledge education for guardians.[12] In 2014, the updated National Mental Health Working Plan (2015-2020) was implemented. This proposed a clear aim: continuing to improve the mental health services for prevention, treatment and rehabilitation of mental disorders to meet individual need for mental health services.

In 2018, 10 related departments jointly announced the Pilot Working Plan for the Construction of a National Psychosocial Service System. This policy highlighted the importance of improving the continuity of community-based mental health services. It encouraged treatment and rehabilitation information-sharing and the use of information technology.[13] Also in 2018, the Ministry of Civil Affairs, the Ministry of Finance, Health and Family Planning Commission and the CDPF jointly issued Guidance on Accelerating the Development of Community Rehabilitation Services for Mental Disorders. These two documents mean that patients can receive health services covering disease prevention, treatment, recovery and relapse prevention in their communities.[14] Patients can begin their rehabilitation treatment as soon as possible with continuity between hospital and community rehabilitation.

The structure and function of community-based mental health services

In 2004, the Central Government Support for the Local Management and Treatment of Severe Mental Illnesses Project ('686 Programme')[15] was implemented to expedite the process of exploring and establishing a better hospital-community integration service model. In order to further standardize service quality and scope, in 2009 the National Standards for Primary Public Health Services (First Edition) were issued. As mental health is one of important public health issues, mental health services, especially for severe mental illnesses, were included.[16]

These two policies aimed to promote and standardize community-based mental health services via CHCs in urban and rural areas. Governments at all levels have led the construction and development of the community-based mental health service system, with CHCs, psychiatric hospitals and Centres for Disease Control and Prevention (CDCs) for mental health. CHCs are obliged to deliver basic public health services, i.e., community-based health services are mainly provided by general practitioners, public health physicians and nurses working in these centres. To alleviate the shortage of human resources, psychiatrists and nurses from mental health centres are responsible for providing technical support to this workforce. CDCs are largely responsible for community mental health service quality control and supervision, the introduction of new interventions and rehabilitation techniques for mental health services, information management and disease surveillance for patients with severe mental disorders.

Community Health Service Centres

In accordance with the requirements of the 686 Programme and the National Standards for Primary Public Health Services, community-based mental health services have many responsibilities, including: establishing individual health records, health assessment, annual physical examination, follow-up after hospitalization or outpatient treatment at least four times a year, appropriate intervention and prevention measures according to severity of illness, referral services, health education for patients and their guardians, rehabilitation guidance and psychological support for family members. Importantly, these services are voluntary, and all expenditure is covered by government.[17]

After outpatient or inpatient treatment in psychiatric hospitals, patients are referred to their CHC, where they (or their guardian) are asked to consent to follow-up services. Health assessment, diagnosis and treatment information are added to their health record. Patients can receive a follow-up service at least four times a year according to their rehabilitation progress. These include assessments of relapse risk, mental state, physical illnesses, social function, medication and laboratory tests, which inform individualized health services tailored to patients' needs. Regular physical examination, health education, rehabilitation guidance, social function rehabilitation training, vocational training and referral services; plus care and psychological support for family members are also included. To facilitate convenience and efficiency, some of the services can be delivered at home or at the CHCs by experienced general practitioners and community psychiatric nurses. If a patient's condition is found to be unstable, referral to mental health centres for hospitalization or outpatient treatment, or hospital-based home care, are provided.

Rehabilitation is one of crucial goals for community-based mental health services. Patients with stable conditions can choose to receive a variety of services to promote rehabilitation. Many provinces and cities have established community rehabilitation institutes, supported by many organizations including CDPF, the Civil Affairs Department, CHCs and social work organizations. Rehabilitation treatments gradually shift focus from disease to people; from symptom elimination

to recovery of social functions. Individualized services are provided for patients at different stages, to support rehabilitation in cognitive ability, life skills, hobbies, social ability, vocational skills and to improve overall quality of life.

OUTCOMES AND IMPACTS OF COMMUNITY MENTAL HEALTH SERVICES

Historically, mental health services were mainly hospital-based, but reform and development of community-based health services has seen the establishment of an integrated hospital-community model.

Decades of development have led to substantial improvements in the quality of medical treatment and rehabilitation therapies, the continuity of mental health services, the coverage of patients with severe mental health disorders, the immediate treatment rate of patients, medicine-taking rate, treatment adherence and support for family members. There are now more than 35,000 CHCs and more than 1,600 institutions that provide high-quality mental health rehabilitation services. By the end of the 2016, there were more than 5 million patients with severe mental health disorders registered with community-based mental health services. More than 90% of these patients had opted to receive support and 75% received regular follow-up services.[18] Other important indicators, such as (regular) medication-taking rate and number of patients in a stable condition, are also rising every year.[19] The construction of an electronic health records system facilitates the transfer of information about patients' medication, treatment and rehabilitation therapies to general practitioners after hospital discharge, meaning that patients receive a more individualized treatment and rehabilitation service. Community residents, especially those with severe mental health disorders, benefit from much-improved access to mental health services. The median radius of the mental health service network of each service site exceeds 184 km, which covers more than 90% of patients with severe mental disorders.[18]

CHALLENGES AND FUTURE DIRECTIONS

The Chinese government has made the establishment of a highly efficient community-based health service an enduring priority. However, there are still many challenges that need to be addressed.

Mental health service coverage and usage

China is a huge country; unequal distribution of mental health service resources hinders the capacity of community-based mental health services. Despite the rapid development of mental health services in recent years, resources are still concentrated in rich coastal or eastern areas and most are allocated to patients with severe mental health disorders. Studies have indicated that utilization rates of community-based mental health services are not high enough,[20] as individuals still prefer mental health centres or general hospitals when seeking medical treatment. Efforts to expand coverage and accessibility of mental health services in communities is encouraged by health reform.

Mental health awareness and stigma

As in other countries, lack of knowledge and stigma surrounding mental health disorders mean that people are reluctant to seek mental health service resources.[21] Health education to improve knowledge of mental disorders seems insufficient to address this problem.[22] Rather, there is a need for more anti-stigma interventions and systematic health education focusing on changing attitudes, including those of mentally ill patients, to help reduce stigma and improve mental health literacy.[23]

Mental health service capability

The number of medical practitioners in CHCs is a key element in determining the quantity, quality and effectiveness of mental health service delivery and capability. Currently, there are not enough psychiatrists and other mental health professionals in CHCs to meet the needs of all residents in communities. Training of psychiatrists and nurses has already accelerated in many places. Psychiatrists in tertiary hospitals should be encouraged to obtain a multi-site licence to practise in CHCs, so that they can enhance service capability and provide technical guidance. Teamwork among practitioners from psychiatric hospitals, CHCs and social work organizations is also recommended to maximize existing service capabilities.

In summary, establishing an integrated service model is crucial for the development of community-based mental health services. The hospital-community integration service model has become the most common and recommended model. It has been developed significantly and plays an important role in the mental health service

system. However, closer coordination among mental health centres, CHCs and related government sectors is still needed. The coordination mechanisms between related services providers also need to be further strengthened to provide better community mental health services to meet the mental health needs of all individuals in China.

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Abbreviations:

CDPF: China Disabled Persons' Federation
CHCs: Community Health Service Centres
CDCs: Centres for Disease Control and Prevention

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Diagnosis and Treatment of Depression in Patients with Schizophrenia

Диагностика и лечение депрессии у больных шизофренией

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ABSTRACT

Depression is the third most common illness among patients with schizophrenia which negatively affects the course of the disease and significantly contributes to the mortality rate, due to increased suicide. Depression, along with negative symptoms and cognitive deficits, is one of the main factors that significantly decreases the quality of life and the disease prognosis in patients with schizophrenia. In addition, depression increases the frequency of exacerbations and readmissions, decreases the quality and duration of remissions and is associated with more frequent substance abuse and an increased economic burden. Data on the prevalence of depression among patients with schizophrenia are contradictory and are associated with a low detection rate of depression in such patients, a lack of clear diagnostic criteria and difficulties in differentiation between extrapyramidal and negative symptoms. The average prevalence of depression that meets the diagnostic criteria of major depressive episodes in patients with schizophrenia is 25% at a specific point, and 60% over the course of a lifetime; the frequency of subsyndromal depression is much higher. It is essential to distinguish between primary (axial syndrome) and secondary depressive symptoms (extrapyramidal symptoms, psychogenic or nosogenic reactions, social factors, etc.) to determine treatment strategies.

The published data relating to randomized clinical trials for the development of evidence-based guidelines are limited. Current recommendations are based mainly on the results of small-scale trials and reviews. Certain atypical antipsychotics (quetiapine, lurasidone, amisulpride, aripiprazole, olanzapine, clozapine) are superior to typical antipsychotics in the reduction of depressive symptoms. Clozapine is effective in the management of patients at risk from suicide. The additional prescription of antidepressants, transcranial magnetic stimulation and electroconvulsive therapy are not always effective and are only possible following the management of acute psychosis in cases when antipsychotic monotherapy proved to be ineffective.

АННОТАЦИЯ

Депрессия является третьим по частоте синдромом шизофрении и существенно осложняет прогноз и течение заболевания, а также вносит главный вклад в показатель смертности вследствие суицида. Депрессия, наряду с негативными симптомами и когнитивными нарушениями, является одним из важнейших дезадаптирующих факторов у больных шизофренией, что в значительной степени снижает качество жизни и прогноз заболевания в целом. Помимо этого, депрессия увеличивает частоту обострений и повторных госпитализаций, снижает качество и продолжительность ремиссий, связана с более частым злоупотреблением психоактивными веществами, повышенным экономическим бременем заболевания. Данные о распространенности депрессии в популяции больных шизофренией достаточно противоречивы, что связано с низкой выявляемостью депрессии

у данной категории пациентов, отсутствием четких диагностических критериев, сложностями клинической дифференциации с экстрапирамидной и негативной симптоматикой. В среднем распространенность депрессий, отвечающих диагностическим критериям развернутого депрессивного эпизода, при шизофрении в моменте составляет 25%, а на протяжении жизни – до 60%; частота субсиндромальных депрессий значительно выше. Необходимо различать первичную (осевой синдром) и вторичную депрессивную симптоматику (экстрапирамидные симптомы, личностная реакция, нозогения, социальные факторы и др.), что определяет терапевтическую тактику.

В литературе крайне мало данных рандомизированных клинических исследований для формирования рекомендаций с высокой степенью доказательности. Клинические рекомендации основываются в основном на обзорах литературы и результатах небольших исследований. Некоторые атипичные антипсихотики (кветиапин, луразидон, амисульприд, арипипразол, оланзапин, клозапин) лучше, чем традиционные нейролептики, редуцируют депрессивную симптоматику. При наличии суицидального риска предпочтительно назначение клозапина. Присоединение антидепрессантов, транскраниальной магнитной стимуляции и электросудорожной терапии не всегда оказывается эффективным и возможно только после купирования острой психотической симптоматики и неэффективности антипсихотической монотерапии.

Keywords: *depression, schizophrenia, therapy, antipsychotics, antidepressants, evidence-based therapeutic algorithm*

Ключевые слова: *депрессия, шизофрения, терапия, антипсихотики, антидепрессанты, терапевтический алгоритм на основе доказательных данных*

Alongside negative symptoms and cognitive impairment, depression is one of the most significant deconditioning factors among patients with schizophrenia, which significantly reduces the quality of life and the disease prognosis as a whole.[1-3] In addition, depression increases the frequency of exacerbations and rehospitalizations, and decreases the quality and duration of remissions; it is associated with more frequent substance abuse, an increased economic burden with regard to the disease and is also the main cause of suicide.[4-8] The risk of suicide among people suffering from schizophrenia is 20 times higher than among the general population; around 50% of patients with schizophrenia attempt suicide and around 10% die from suicide.[9] Data relating to the prevalence of depression among the population of patients with schizophrenia are rather contradictory, due to the low detectability of depression in this category of patients, the lack of clear diagnostic criteria and the difficulties in clinical differentiation between extrapyramidal and negative symptoms. In various studies, the reported data on the prevalence of depression among patients with schizophrenia vary considerably from 25 to 70%, depending on the methodological approaches used.[10-12] On average, the prevalence of depression in schizophrenia at one particular moment is 25% and at lifetime is 54%.[13] Up to 60% of patients with a verified diagnosis of schizophrenia have at least one episode of major depression;[14] 40–50% of both inpatients and outpatients have mild or moderate depressive episodes. Depression can develop at any stage of schizophrenia: depression was observed in the premorbid period before the onset of psychotic symptoms in 50% of patients, in 33% of patients during the first episode, in 38% of patients during psychotic episodes and in 27% of patients in remission.[15]

From a historical aspect, it should be noted that the founder of the concept of schizophrenia, E. Bleuler, identified a whole layer of affective states within this disease, including “schizophrenic melancholy”, considering it a manifestation of an endogenous process.[16] Moreover, it could be both an independent syndrome and an optional syndrome, developing within a psychotic episode. In addition, Bleuler did not exclude a psychological mechanism of depression as a reaction to psychotic experience, which is often encountered during the first episodes of the disease. Almost all clinicians who have studied depression among patients with schizophrenia indicate that the schizophrenic process makes an impact on the phenomenological manifestations of depression. Bleuler also described the so-called schizophrenic “tension”, incompleteness, rigidity, superficiality and pretentiousness of the hypothymic

manifestations, associated, in particular, with a limited emotional resonance and an inability of such patients to give vivid, affective responses. A.V. Snezhnevsky also noted the absence of a differentiated feeling of anguish, effacement and incompleteness of affective and vital manifestations among these patients.[17] Indeed, vivid, vital and autonomic symptoms with typical daily fluctuations of mood, are observed less often in such patients; on the contrary, apathy, anergy, mental anaesthesia, dysphoria, gloominess, irritability, grumbling and other atypical manifestations of depression are more common.[18,19]

In DSM-III the possibility of independent (comorbid) diagnosis of overt depressive syndrome was determined for the first time within the framework of schizophrenia, in accordance with the criteria of a major depressive episode, with the development of post-schizophrenic depression being diagnosed in remission. This was caused by a number of epidemiological studies in the United States, which showed that syndromal depression among patients with schizophrenia occurs 29 times more often than among the general population,[20] and in 59% of patients with schizophrenia, depression meets the criteria for a major depressive episode.[21] Subsyndromal or minor depression that does not meet the criteria of the diagnostic threshold, occurs much more often among 80% of patients with schizophrenia.[21] Meanwhile, subsyndromal depressive symptoms, like major depression, are associated with social and financial problems, a poor quality of life, an increased volume of medical care, a general worsening of symptoms, demoralization, frequent recurrence and an increased suicide risk.[13,22,23] Thus, M. Birchwood et al.[24] prospectively monitored the condition of 105 patients, diagnosed with schizophrenia according to ICD-10, after psychotic episode and on at least five subsequent occasions within 12 months: depression was identified among 70% of patients in an acute psychotic state and reduced simultaneously with a reduction in psychotic symptoms; 36% of patients developed post-schizophrenic depression without the exacerbation of psychotic symptoms and more than half of patients had suicidal thoughts. In accordance with the ICD-10 diagnostic criteria for post-schizophrenic depression,[25] in relation to the reduction of psychotic symptoms and the meeting of formal criteria for a depressive episode, such patients may exhibit certain residual symptoms of schizophrenia, primarily negative symptoms.

In accordance with the new dimensional classification paradigm of schizophrenia, depression within the five-factor model is one of the independent domains (dimension) of schizophrenia symptoms, which is less prevalent only than psychotic (positive) and negative symptoms.[26] The modern conceptualization of depression among patients with schizophrenia describes it as one of the key components of schizophrenia,[13,27] with some input of secondary psychological reaction to psychosis and/or psychosocial stress, [22,28] as well as, to a lesser extent, of neuroleptic side effects (in up to 15% of cases).[29]

Clinically, depression in schizophrenia can be divided into two main categories: related and not related to the psychotic episode. In the first case, depressive symptoms are immediately present in the structure of the psychotic episode and are usually reduced along with psychosis. This example is the most typical and occurs among around 50% of all patients with schizophrenia with depression. Phenomenologically, such depression is usually characterized by apathy, anergy, anhedonia, phenomena of depressive depersonalization and feelings of guilt, although patients often blame others rather than themselves. According to G.E. Mazo, the presence of anergic depression results in a continuous course of the disease and a less favourable prognosis.[6] In certain patients, depression, at the beginning of the psychotic episode, which is usually masked by significant hallucinatory-delusional symptoms, is apparent after the reduction of psychosis as a result of effective, antipsychotic therapy, therefore, a kind of "stratification of the syndrome" and "filtering out" of depression occurs[30] (the so-called "revealed depression").[31]

Depression can also be caused by pharmacogenic factors and resulting from a antipsychotic therapy complications (the so-called 'neuroleptic depression'). Long-term dopamine receptor blockade can lead to the development of anhedonia and, possibly, depression.[32] The data concerning the relationship between neuroleptic medication and the onset of depression are very contradictory, and these observations primarily involved the use of the first generation of antipsychotic drugs – conventional neuroleptics.[33,34] A typical manifestation of neuroleptic depression, along with psychomotor retardation and anhedonia, is the presence of akinetic-rigid symptom complex and other phenomena of neuroleptic pseudoparkinsonism. The addition of akathisia in such patients can cause a temporary change in the modality

of the hypothymic affect, with the development of dysphoria and suicidal behavior.[35-37] However, in the literature there are descriptions of pharmacogenic depression without clinically pronounced extrapyramidal symptoms. These include, e.g., "akinetic depression".[38] In this case, the authors consider akinesia as a new extrapyramidal symptom that is not part of the structure of parkinsonism and is mainly associated with the blockade of dopaminergic neurotransmission at the cortical level. Therefore, previously, we classified these peculiar states, which respond poorly to any thymoanaleptic therapy and are associated with impaired dopamine metabolism by neuroleptic agents, as dopamine-dependent depression.[39,40] Another clinical example of pharmacogenic depression, occurring without clear extrapyramidal symptoms, are conditions that are phenomenologically similar to negative symptoms: apathy, anhedonia, poverty of speech, decreased emotional expressiveness, which, however, respond to antidepressant therapy and are reduced along with a termination of the psychotic episode.[41]

Finally, reactive moments play an important role in the development of depression associated with a psychotic episode. Schizophrenic psychosis is a severe psychological burden for patients; therefore, it is not surprising that they often develop reactive states that can be characterized as nosogeny and adjustment disorders. The reasons for this are stigma, the emotional experience of one's own failure, as well as social maladjustment. Certain patients may show symptoms resembling the so-called demoralization or frustration syndrome.[42] It is not always easy to differentiate this syndrome from depression in schizophrenia. It is characterized by feelings of hopelessness and helplessness, combined with self-doubt and feelings of failure. Of course, the most cases of depression in schizophrenia cannot be explained by reactive mechanisms. If we assume the opposite, there would be a direct relationship between the severity of depression and the degree of restoration of a critical attitude to the disease, i.e., depressive symptoms should have occurred more frequently as the psychotic symptoms were reduced by treatment. However, in practice, the opposite has been observed – the symptoms of depression often disappear after the elimination of positive symptoms.[43] Therefore, in the first example, it is important to trace the dynamics of depressive symptoms during psychotic episode and to find out its genesis, its provoking factors, as well as the connection with other psychopathological symptoms.

The second example concerns the development of depression not directly associated with an acute psychotic episode and separated from it by a certain period of time. In these cases, depression should be initially differentiated from primary negative symptoms since depression can be overlaid on these symptoms.[44]

A series of studies have shown that negative symptoms and depression have a number of common clinical manifestations that can complicate differential diagnosis.[45-47] Decreased interest, motivation and emotional expression, anhedonia, anergy and psychomotor retardation, as well as cognitive impairment, are all overlapping features of these conditions.[48] Nevertheless, there are certain symptoms that make it possible to differentiate between depression and negative syndrome.[49-51] In contrast to affective flattening and abulic negative symptoms, depression is characterized primarily by a distinctly depressed or melancholic mood and specific cognitive impairments, such as depressive ruminations, feelings of helplessness, ideas of guilt and low value of life, which sooner or later lead the patient to suicidal ideas and intentions. In addition, for a more accurate diagnosis, it is necessary to pay attention to the onset of depressive symptoms, their progression and their prevalence in relation to the use of certain drugs.[44] According to a recent study with a multivariate analysis of symptoms,[52] hypothymic affect, as well as pessimistic and suicidal thoughts are significantly more common in depression, and in negative symptoms, such as poverty of speech (alogia), flattening of affect and social isolation; other symptoms intersect and cannot be reliable indicators for differential diagnosis. The Calgary Depression Scale for Schizophrenia (CDSS), developed specifically for this purpose, helps significantly to distinguish between depressive and negative symptoms.[53] CDSS surpassed the Hamilton Depression Scale (HAM-D), the PANSS Depression Factor (PANSS-D) and the Beck Depression Inventory (BDI) in terms of its sensitivity and specificity.[54]

In recent years, close attention has been paid to depression in schizophrenia as an axial independent syndrome, in particular, outside the stage of psychotic exacerbation. The terms post-psychotic depression, post-schizophrenic depression and secondary depression have been used most frequently to describe

these manifestations. Of course, the variety of terms and their interpretations does not add clarity to the understanding of this issue. The diagnostic criteria for post-schizophrenic (ICD-10) or post-psychotic depression (DSM-IV, DSM-V) in modern classifications do not directly link the development of depression with the termination of the psychotic episode and the presence of a stressful psychological reaction to schizophrenic psychosis. Post-psychotic depression is a complex psychopathological formation, and as it develops, residual positive, negative and affective symptoms, as well as reactive personality and pharmacogenic factors, become apparent.

Another fact confirming that depression is an axial syndrome in schizophrenia, is the frequent onset of depression before appearing of psychotic symptoms in the form of a prodrome.[13,55] A.V. Snezhnevsky attributed affective fluctuations to the so-called outpost or 'forpost' symptoms and noted their occurrence even at the pre-manifest stage of schizophrenia.[17] According to various studies, depending on the severity, depressive symptoms before the first psychotic episode are observed in 20–60% of patients and are an important sign of an impending psychosis manifestation.[43,56]

Finally, depressive episodes that meet the criteria for major depression in schizophrenia can develop as an independent syndrome, regardless of psychotic symptoms, then it becomes more common to speak of comorbid depression.[57,58] In fact, comorbid depression in schizophrenia alone, is the purest primary depressive syndrome; when other symptoms occur, secondary mechanisms may play a significant role (according to certain data, up to 80%), including positive (hallucinatory-delusional) and negative symptoms, as well as reactive-personality and pharmacogenic (pseudoparkinsonism and depressogenic effect) factors. For example, depression often develops within the framework of chronic extrapyramidal neuroleptic syndrome, in particular, with tardive dyskinesia and the phenomenon of dopamine hypersensitivity.[59]

Another approach that explains the formation of depressive symptoms in schizophrenia is the concept discussed by S.G. Zhislin and G.Ya. Avrutsky relating to pharmacogenic pathomorphosis.[30,60] Long-term exposure to antipsychotics is accompanied by the transition of the course of schizophrenia to the level of affective disorders, with an increase in the phase and circularity factors during the course of the disease. Specific epidemiological studies carried out in our clinic in the 1960s and 1970s showed an increase in depression among patients with schizophrenia just after spreading of neuroleptic treatment widely. Therefore, in episodic forms of schizophrenia, there was a tendency for prolongation of psychotic episodes, as a result of which, instead of the completion of psychosis, inapparent residual, usually sub-depressive syndromes or so-called neuroleptic depression appeared. Therefore, the development of a number of different types of post-psychotic depressions can be explained in terms of drug pathomorphosis of schizophrenia course and clinical picture.[10]

The development of psychopharmacotherapy and other methods of treatment increases the importance of correctly diagnosing depression at an early stages of the disease. The therapeutic goal is to significantly reduce the excess morbidity and mortality associated with depression. An additional objective is to prevent suicide, from which 5 – 15% of patients with schizophrenia die.[9,61,62] The following clinical manifestations correlate with suicide in schizophrenia: depressive symptoms, dependence on psychoactive substances, the severity of psychotic symptoms and cognitive impairment, early stages of the disease, insomnia, agitation and restlessness, as well as a history of depressive episodes and/or suicidal activity.[23,63] According to the recent data, clozapine is the first choice treatment for patients at a high risk of suicide.[64,65] It is believed that the unique anti-suicidal effect of clozapine (many other atypical antipsychotics were ineffective in this respect) is associated less with its antidepressant effect and more with one's own ability to suppress suicidal ideas, which correlates with its specific neurochemical profile, in particular, with antagonism to 5-HT_2 and D_4 receptors.[66]

Pragmatic approaches to the treatment of depression in schizophrenia include the use of various antipsychotic agents or their combination with antidepressant drugs. Although there are several studies and observations in the literature relating to the ability of certain first-generation antipsychotics (FGAs) to reduce depressive symptoms (e.g., with the use of small doses of sulpiride, thioridazine and flupentixol),[67-70] most conventional antipsychotics in therapeutic doses increase the manifestations of depression, primarily due to extrapyramidal side effects and hypersedation.[71] Often, dysphoria also occurs with the development of akathisia or more delineated

neuroleptic depression. Therefore, lowering the dose of the antipsychotic agent as a first step can decrease the severity of depressive symptoms.[12,72] Prescribing anticholinergic drugs to correct extrapyramidal symptoms also reduces the severity of depression.[46,73]

Pharmacoepidemiological studies show that clinicians usually solve the problem by adding antidepressants, which are prescribed in around 40% of patients both in hospital or outpatient clinics.[15,74] In most cases, selective serotonin reuptake inhibitors (SSRIs) are prescribed, although there are more research data available in relation to tricyclic antidepressants.[75,76] Approximately 30% of physicians prefer combination therapy with atypical antipsychotics and SSRIs. A pharmacoepidemiological study evaluating the frequency of use of antidepressants to treat schizophrenia in Moscow, found that 30-40% of physicians in the dispensary and 70-80% of physicians in the hospital prescribe antidepressants; in 80% of cases these were tricyclic antidepressants, primarily amitriptyline, and SSRIs were used in 14% of patients.[77] However, only 30% of inpatients received adequate therapeutic doses of amitriptyline (> 150 mg/day) and 15–20% of outpatients.

Depressive symptoms during an exacerbation of schizophrenia should not necessarily lead to the prescription of antidepressants, as they are traditionally believed to cause an increase in psychotic symptoms. However, new studies show that the risk of psychosis induction, resulting from antidepressant use is low.[78] There have been very few randomized, double-blind, placebo-controlled clinical trials (RCTs) evaluating the effectiveness and tolerability of combination therapy in the treatment of depression among patients with schizophrenia. One meta-analysis which involved evaluating the effectiveness of tricyclic antidepressants, showed an improvement in only five out of 11 RCTs.[76] In general, according to this meta-analysis, the prescription of a tricyclic antidepressant in combination with an antipsychotic after the relief of acute psychotic symptoms, is associated with a minimal risk of exacerbating positive symptoms, but increases the risk of anticholinergic side effects, due to the pharmacokinetic drug interactions. Several studies have shown that imipramine is the most effective tricyclic antidepressant in the treatment of depression among patients with schizophrenia, possibly due to its distinct psychostimulatory properties.[75,79]

Clinical studies of SSRIs have generally confirmed their effect on depressive symptoms in schizophrenia. Sertraline is the only SSRI that has been shown to be effective for the management of depression in 26 stable patients with schizophrenia: the reduction in the mean Hamilton score in the sertraline group was 31% versus 8.6% in the placebo group.[80] However, another RCT, conducted in 48 patients meeting the DSM-IV criteria for schizophrenia in remission and for major depressive episode found a significant placebo effect, which did not prove the effectiveness of sertraline.[81] An earlier limited RCT (40 patients) comparing sertraline and imipramine for post-psychotic depression found that they were comparable in efficacy, but sertraline had a faster onset of effect and better tolerance.[82] In general, SSRIs are considered to be effective in treating depression in schizophrenia.[72,74] Considering their relative safety compared to tricyclic antidepressants, they seem to be the drugs of choice. However, it is necessary to bear in mind possible drug interactions with antipsychotics, due to the inhibitory effect of certain SSRIs on the activity of cytochrome P450.[83-85]

There are small positive open-label add-on studies of the selective serotonin-norepinephrine reuptake inhibitors, venlafaxine and duloxetine, to the antipsychotics in resistant post-psychotic depression,[86,87] trazodone[88] and dopamine-stimulating drugs,[39,40] the use of which, however, is associated with the risk of exacerbation of psychosis, as well as several RCTs of bupropion[89] and a limited RCT of mirtazapine.[90]

In the latest meta-analysis evaluating the effectiveness of antidepressants among patients with schizophrenia undertaking antipsychotic therapy, the entire group of SSRIs did not find significant advantages over placebo in the degree of reduction of depressive symptoms in 42 RCTs (1849 patients), however, trazodone, duloxetine, sertraline and amitriptyline were the most effective.[91] At the same time, in more severe depressive episodes (7 RCTs, 422 patients), the entire SSRI group was significantly more effective than the placebo group.[91]

In general, most current clinical guidelines do not consider antidepressant drugs as the treatment of choice when treating depression among patients with schizophrenia. Depressive symptoms during acute psychosis are often reduced in parallel with psychotic symptoms, so it makes sense to wait for the antipsychotic effect and not to prescribe an antidepressant too quickly.

The use of antidepressants is only recommended for the treatment of depression in patients with stable chronic schizophrenia, i.e., with persistent depressive symptoms that arise outside of psychosis, while the prescription of antidepressants in an acute psychosis is considered inappropriate.[92-96] The most of the recommendations for prescribing antidepressants as an adjuvant therapy for schizophrenia, have limited evidence of efficacy. The use of antidepressants is recommended in the following cases: 1) when symptoms correspond to a major depressive disorder (symptoms are severe and clinically significant); 2) when symptoms cause stress or affect functioning. Certain methodologically more accurate guidelines highlight the lack of data on the use of novel antidepressants alone or in combination with second generation antipsychotics (SGAs) for the treatment of depression in schizophrenia.[72,96] However, in post-psychotic depression, according to ICD-10 criteria, antidepressant prescription should be discussed on the basis of its clinical appropriateness for the individual patient.

The most interesting and promising approach in the therapy of depression in schizophrenia is associated with the emergence of SGAs, which, due to their multimodal neurochemical action, were found to have an antidepressant effect.[58,74] Unfortunately, in most antipsychotic studies the assessment of depressive symptoms was not the main task, the degree of their severity was not indicated in the inclusion criteria and the reduction of depression was not considered as an efficacy criterion.

A new meta-analysis of the comparative efficacy and tolerability of 32 antipsychotic agents, covering nearly 90 RCTs with 20,000 patients[97] showed that most antipsychotics were significantly superior to placebo in terms of the reduction of depressive symptoms, according the PANSS scale. Obviously, we are referring to depressive symptoms within the structure of an acute psychotic episode, which are reduced along with positive symptoms and are closely related to it. Sulpiride, clozapine, amisulpride, olanzapine, aripiprazole, cariprazine and paliperidone had the most significant effect (in descending order). The question of the superiority of SGAs over FGAs in terms of the reduction of depressive symptoms in schizophrenia remains controversial. There are surprisingly few quality RCTs investigating the effectiveness of SGAs in the treatment of depressive episodes among patients with schizophrenia.[98] In one of them, e.g., quetiapine showed no significant differences compared with haloperidol.[99] A number of studies have also failed to establish differences between haloperidol and SGAs (in particular, risperidone) in the reduction of depressive symptoms.[100,101] At the same time, a meta-analysis, based on 50 RCTs, demonstrated the significant superiority of a number of SGAs (amisulpride, aripiprazole, clozapine, olanzapine, quetiapine) over FGAs in terms of the reduction of depressive symptoms on the PANSS scale in acute episodes of schizophrenia.[102] In this meta-analysis, there were no new SGAs that appeared recently on the market. Lurasidone and cariprazine also have thymoanaleptic properties; in a pooled analysis of four RCTs, lurasidone was superior to placebo in terms of its effect on depressive symptoms in the treatment of exacerbations of schizophrenia within six weeks.[103] At the same time, the reduction in depression only slightly correlated with the decrease in the PANSS scores, which indicates the independent antidepressant effect of lurasidone, which is not associated with its antipsychotic effect. We performed a specific analysis of the effect of lurasidone on symptoms according to the PANSS scale within a five-factor model of schizophrenia who participated in short-term RCTs of the drug in Russia and Ukraine, similar to previous trials with other SGAs.[104] It transpired that the symptoms of depression and anxiety in the local sample were reduced beginning from Week 1 of the therapy, with an even greater effect[105] than in the global world sampling.[106]

There have been practically no direct comparative RCTs of FGAs and SGAs in schizophrenia, evaluating their efficacy against depressive symptoms. In a large-scale independent 18-month CATIE study among patients with schizophrenia with severe symptoms of depression, quetiapine was significantly more effective than risperidone in terms of the reduction of depressive symptoms.[107] There is evidence of the superiority of quetiapine over risperidone in terms of the effect on depressive symptoms in schizophrenia.[108] In a comparative RCT of cariprazine and risperidone, evaluating the reduction of primary negative symptoms, no differences were found in relation to the effect of the drugs on depressive symptoms.[109] In one open RCT, it was found that replacing risperidone therapy with amisulpride therapy leads to a decrease in the severity of depression among patients with

schizophrenia, compared with patients who continued administering risperidone.[110] When clozapine was compared with other antipsychotics in combination with an antidepressant or placebo, patients treated with clozapine were less depressed.[98]

Certain of the aforementioned FGAs and SGAs (in particular, in the case of quetiapine, aripiprazole, amisulpride and sulpiride) have been shown to be effective in the treatment of a depressive episode in recurrent depressive disorder,[111] and in the case of quetiapine and lurasidone, in bipolar depression.[112,113] Although it is difficult to extrapolate these findings to patients with schizophrenia, drugs with a high affinity to D_2 receptors appear to be less effective in the treatment of comorbid depression (or may even increase symptoms when taken in high doses), while a blockade of 5-HT_2 receptors and a partial agonism to $D_{2/3}$ receptors are associated with a more pronounced thymoanaleptic effect.[114]

In addition, in clinical practice involving patients with schizophrenia, it can be difficult to differentiate secondary negative symptoms associated with depression, therefore, in the absence of a response to the adequate antipsychotic and antidepressant therapy in such patients, the strategy recommended for the treatment of persistent negative symptoms can be considered.[115]

Among the non-pharmacological therapeutic methods for pharmaco-resistant depression in schizophrenia, the most studied are electroconvulsive therapy (ECT) and high-frequency cyclic transcranial magnetic stimulation (rTMS). The American Psychiatric Association (APA) usually recommends ECT for the treatment of patients with schizophrenia with comorbid depression and/or suicidal ideation in situations where emergency therapeutic intervention is required. At the same time, data from systematic reviews that analysed 31 studies of ECT use in schizophrenia were contradictory and generally confirmed its rapid effect on depressive symptoms, but not on suicidal behavior.[116,117] TMS has been recommended for the treatment of depressive episodes in recurrent depression,[118] but there are insufficient data on its efficacy in the treatment of depressive symptoms in schizophrenia. A systematic Cochrane review of five studies with limited samples, identified a small-scale beneficial effect of rTMS.[119] In our clinic, in an open-label study of 15 Hz rTMS of the left dorsolateral prefrontal cortex, the method has also shown to be effective in the treatment of outlined depression in schizophrenia.[120-122] However, a large multicentre RCT with pseudo-TMS control, which included 157 patients with schizophrenia with a predominance of negative symptoms, did not identify the beneficial effect of 10 Hz rTMS of the left dorsolateral prefrontal cortex on depressive symptoms.[123] Among other non-pharmacological methods of biological therapy in our clinic, the effectiveness of intravenous laser blood irradiation[124,125] and adaptation to periodic normobaric hypoxia[126] in post-psychotic depression resistant to psychopharmacotherapy, was also identified.

In addition to biological therapies, attention should be drawn to the proven effectiveness of exercise, including fitness, in reducing depression among patients with schizophrenia,[127] as well as cognitive behavioural therapy[128,129] and psychosocial rehabilitation measures.[129]

Thus, a rational approach to the treatment of depression in schizophrenia follows the differential diagnosis and the determination of the contribution of reactive-personality and pharmacogenic factors to its development. If a patient receiving FGA has an episode of depression, the question arises as to how much antipsychotic therapy is responsible for the symptoms similar to depression, both extrapyramidal (akinesia or akathisia) and dysphoria directly induced by neuroleptic agents. This problem can be solved in three ways: 1) reduction of the antipsychotic dose, subject to the time available to do it safely; 2) adding and dose titration of antiparkinsonian (anticholinergic) drug, benzodiazepine or beta-blocker (the latter are effective for akathisia); 3) replacement of FGA with SGA. If a patient already receiving SGA develops an episode of depression, the same approaches apply. Dose reduction and the addition of anticholinergic agents are most advisable when using SGA, which have dose-dependent extrapyramidal side effects (risperidone, amisulpride, ziprasidone, cariprazine). An alternative option is to replace one SGA with another. In patients with schizophrenia having no positive effect of antiparkinsonian drugs, antidepressants can be prescribed to achieve the desired result. Based on the aforementioned analysis of the literature data and in accordance with the principles of evidence-based medicine, we proposed an algorithm for the treatment of depression in schizophrenia,[130,131] the latest version of which is shown in the Figure 1. The algorithm indicates the levels of evidence and strength of recommendations for proposed interventions, as recommended by the World Federation of Societies for Biological Psychiatry (WFSBP).[132]

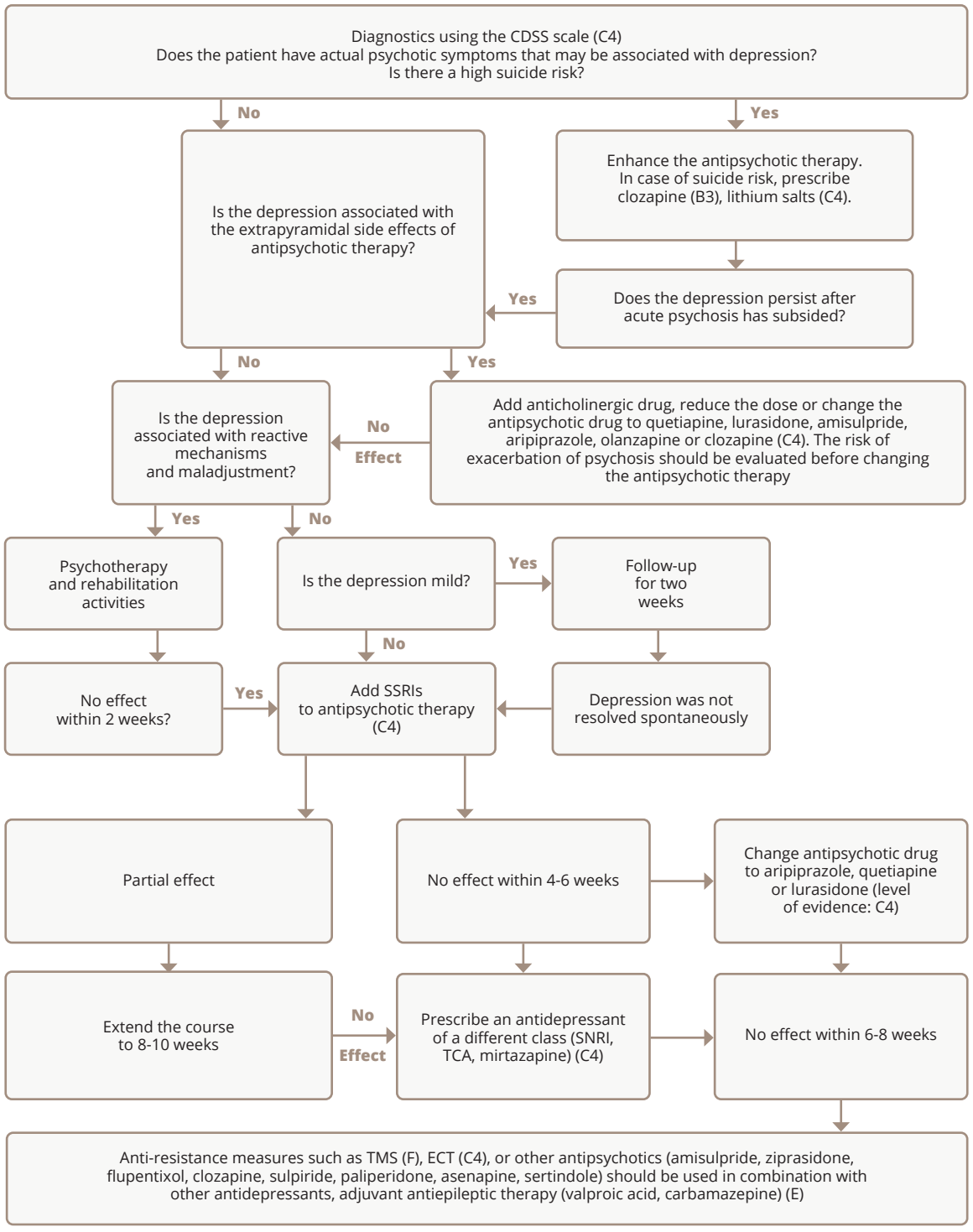

Figure 1. Algorithm for the treatment of depression in schizophrenia with a degree of evidence and recommendation

In conclusion of this review, the following moments, that are important for clinical practice, should be noted. Depression is the third most frequent syndrome of schizophrenia, significantly complicating the prognosis and course of the disease, which considerably contributes to the mortality rate in such patients. It is necessary to distinguish between primary (axial syndrome) and secondary depression (extrapyramidal symptoms, personality reaction, nosogeny, social factors, somatogeny, etc.), which determine the choice of therapeutic strategies. Since comorbid depression has a decisive influence on the increase in mortality among patients with schizophrenia, the clinician is required to ensure a correct diagnosis in a timely manner, prompt intervention in accordance with existing guidelines and close monitoring of the patient's state. There are very few RCT data available in the literature to formulate robust evidence-based recommendations; clinical guidelines are mainly based on literature reviews and are limited by the amount of studies. Certain SGAs (quetiapine, lurasidone, amisulpride, aripiprazole, olanzapine and clozapine) reduce depressive symptoms better than FGAs. If there is a suicide risk, clozapine is preferred. Treatment with the antidepressants, TMS and ECT, is not always effective and is only possible after the relief of acute psychotic symptoms and the ineffectiveness of SGA monotherapy.

Additionally, further well-designed RCTs are needed to develop more evidence-based clinical guidelines.

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Negative Symptoms of Schizophrenia: New Prospects of Cariprazine Treatment

Негативные симптомы шизофрении: новые перспективы лечения карипразином

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ABSTRACT

Background. Cariprazine is a new piperazine derivative atypical antipsychotic, like aripiprazole and brexpiprazole. It has been approved for treating schizophrenia in many countries and has recently been included on the List of Essential Medicines in Russia. Unlike most other atypical antipsychotics, it shows high *in vivo* occupancy of dopamine D2 and D3 receptors at clinically relevant doses. In animal models, cariprazine has demonstrated dopamine D3 receptor-dependent pro-cognitive and anti-anhedonic effects, suggesting its potential for treating negative symptoms. This review summarizes the efficacy of cariprazine in the treatment of negative symptoms of schizophrenia.

Methods. A literature search of databases covering international and Russian journals, for articles published between 1st January 2010 and 1st June 2020.

Results. Cariprazine demonstrated at least comparable efficacy in the treatment of schizophrenia symptoms to active comparators including risperidone, olanzapine or aripiprazole. The drug has a good safety profile. It appeared to be associated with a lower risk of metabolic syndromes and most extrapyramidal symptoms. The positive effect of cariprazine on the negative symptoms of schizophrenia may be associated with the elimination of secondary negative symptoms. However, of all the atypical antipsychotics to date, only cariprazine has a convincingly, methodologically robust proven advantage over risperidone in eliminating the predominant negative symptoms of schizophrenia. Yet only four studies have investigated the effect of cariprazine on the negative symptoms of schizophrenia. There is a lack of research into its direct impact on emotional-volitional disorders, anhedonia, cognitive symptoms and personality changes. However, there is evidence to suggest cariprazine is effective in treatment-resistant cases, but this requires further confirmation.

Conclusion. Cariprazine is an effective and well-tolerated agent for the treatment of schizophrenia and may be effective in cases where other antipsychotics have failed. Cariprazine has been shown to have a positive effect on negative symptoms. Further studies are needed to collect more data on long-term treatment of schizophrenia and especially negative symptoms.

АННОТАЦИЯ

Введение. Карипразин, новый атипичный антипсихотик, подобно арипипразолу и брекспипразолу представляющий собой производное пиперазина, был одобрен для лечения шизофрении во многих странах и недавно включен в России в список жизненно необходимых лекарственных препаратов. В отличие от большинства других атипичных антипсихотиков, карипразин *in vivo* в клинически значимых дозах проявляет высокую активность в отношении как дофаминовых D2-рецепторов, так и D3-рецепторов. В моделях на животных карипразин продемонстрировал зависимые от D3-рецептора дофамина прокогнитивные и антиангедонические эффекты, предполагая возможность лечения негативных симптомов. Данный обзор нацелен на выяснение данных об эффективности карипразина при лечении негативных симптомов шизофрении.

Методы. Был проведен поиск литературы по базам данных международных и российских журналов, опубликованных в период с 1 января 2010 года по 1 июня 2020 года.

Результаты. Эффективность карипразина в отношении симптомов шизофрении была сопоставима с эффективностью препаратов сравнения, в частности, рисперидона и арипипразола. Установлен хороший профиль безопасности. В частности, при использовании карипразина отмечен низкий риск развития метаболического синдрома и появления большинства экстрапирамидных симптомов. Положительное влияние карипразина на негативные симптомы шизофрении может быть связано с устранением вторичных негативных симптомов. Однако из всех атипичных нейролептиков на сегодняшний день только карипразин имеет убедительно, методологически обоснованное преимущество перед рисперидоном в устранении преобладающих негативных симптомов шизофрении. В то же время изучению влияния карипразина на негативные симптомы шизофрении было посвящено всего 4 исследования. Остается неизученным непосредственное действие на эмоциональные, волевые расстройства, проявления ангедонии, когнитивные симптомы и изменения личности, происходящие у пациентов. Имеются данные, позволяющие предложить наличие лечебного эффекта у карипразина в резистентных случаях. Однако это требует дальнейшей проверки.

Выводы. Карипразин – эффективное и безопасное средство лечения шизофрении, которое может быть эффективным в тех случаях, когда применение других антипсихотиков оказались недостаточно результативным. Карипразин доказал свое лечебное действие в отношении негативной симптоматики. Однако для сбора дополнительных данных о долгосрочном лечении шизофрении и особенно негативных симптомов необходимы дальнейшие исследования.

Keywords: *cariprazine, negative symptoms, schizophrenia, mental disorders, treatment*

Ключевые слова: *карипразин, негативные симптомы, шизофрения, психические расстройства, лечение*

Emotional-volitional disorders were first identified as manifestations of a primary mental defect and early dementia (dementia praecox) by Emil Kraepelin at the end of the 19th century.[1] Other seminal research of the time, from the highly influential neurologists Sir John Russell Reynolds (1861)[2] and John Hughlings Jackson (1884),[3] advanced the notion of positive and negative symptoms of neurological disease. Since then, over a hundred years of study have shown that negative symptoms of schizophrenia differ from other symptoms (psychotic, cognitive, affective), both in patients with early psychosis and in the chronic stages of the disease. These negative symptoms affect quality of life, recovery and general functioning.[4,5] In recent years, an international consensus has been reached on negative symptoms, proposing two large clusters: apathy / abulia, which includes direct abulia, anhedonia and decreased social activity, and decreased expressiveness, which includes poverty of speech and affective flattening.[6-8] The experiences of positive symptoms at different stages of schizophrenia are very diverse and have generated much debate regarding diagnostic signs, the definitions of the disease and its

variations.[6,9-12] According to Smulevich et al. (2020), interactions between negative and positive symptoms act as 'transformers' that modify the characteristics of originally nosologically neutral disorders.[13] In addition, negative disorders create a significant burden of disease and persist during periods of remission when positive symptoms have been greatly reduced. Ultimately, negative symptoms are the greatest determinants of poor social integration and decreased functioning, which deeply affect all aspects of patients' daily lives. They can also delay entry into specialized care.[11,14-20]

Negative symptoms rarely appear in isolation. Negative changes arising during the prodromal stage are usually transformed by constitutional chromosome anomalies or previously latent personality issues. This can result in different variants of personal distortion, the extreme forms of which are the syndromes of expansive or defensive schizoidia. During disease stabilization, negative symptoms combine with residual positive symptom complexes, creating psychopathological formations characteristic of schizophrenia and distinct from other mental disorders. Moreover, positive symptoms lose their intensity and other qualitative characteristics over time and, thereby, expand the negative component of the general psychopathological syndrome.[13]

Negative symptoms of schizophrenia have an enduring nature with a broad range of consequences. They present with irregular severity, exacerbate other psychopathological symptoms, can affect all aspects of patient functioning throughout the course of the disease and have a particular low sensitivity to treatment. Negative symptoms therefore began to be considered as a distinct area for investigation with special pathophysiological and therapeutic consequences.[6,12] Early treatment can reduce disease progression and improve outcomes.[20] However, knowing when to begin treatment can be challenging, because the disease often develops gradually and the symptoms form various clinical combinations. They are often difficult to identify or distinguish from symptoms of other clinical conditions, especially the depressive and cognitive symptoms.[21-23] If negative symptoms appear much earlier than the presentation of psychosis, there is a high probability that the disease will take a continuous course with poor prognosis.[24-28] The predominance of negative symptoms without noticeable psychotic signs significantly complicates diagnosis, leading to an increased duration of untreated psychosis,[29] closely associated with a worse functional outcome.[30] However, even with accurate diagnosis via modern psychometric instruments and timely initiation of treatment, there is not an equal chance of reducing the severity positive and negative symptoms, since the latter are much less sensitive to any modern therapy.[6, 31,32]

Both first- and second-generation antipsychotics demonstrate good efficacy in eliminating or ameliorating the positive symptoms of schizophrenia.[33,34] Direct or indirect anti-negative effects are seen by a decrease in the score on negative scale of the Positive and Negative Syndrome Scale (PANSS).[35] There is also a significant increase in the frequency of the most severe disease outcomes in patients who have not received treatment for a long time.[20] However, for a long time, the lack of progress against florid symptoms of schizophrenia outweighed other effects of antipsychotics. There has been an urgent need to develop means of prevention and treatment of negative symptoms, restoring psychosocial, family and professional functioning, improving quality of life while simultaneously minimizing the side effects of psychopharmacotherapy.[33,34]

The use of second-generation antipsychotics has led to a significant decrease in neurological side effects, enhancing the efficiency of correction of affective disorders, improving medication compliance and increasing patients' social integration. It was originally assumed that first-generation atypical antipsychotics would be effective in treating primary negative symptoms and second-generation antipsychotics have shown themselves to be more effective.[34] However, in recent years, it has increasingly been suggested that these drugs did not change path of development of the disease or general prognosis.[36-38] A meta-analysis comparing first- and second-generation antipsychotics found that only four second-generation drugs (amisulpride, clozapine, olanzapine and risperidone) were more effective than first-generation drugs in treating negative symptoms (effect sizes from –0.13 to –0.32). The other five second-generation antipsychotics (aripiprazole, quetiapine, sertindole, ziprasidone and zotepine) did not show any significant effects.[39] It has been questioned whether the efficacy in treating negative symptoms can be considered the main component of antipsychotic atypicality.[38] In a second meta-analysis, antipsychotics showed better efficacy in treating negative symptoms than

placebos. However, the effect size for negative symptoms (–0.39) was smaller than for general symptoms (–0.51) or productive symptoms (–0.48).[39] It should be noted that most studies included in these meta-analyses examined patients with predominantly positive symptoms, so some improvement may have been associated with changes in other areas, e.g., reduced acuity of psychosis, decreased depression or neurological complications of pharmacotherapy.[38] The treatment of negative symptoms remained the main unmet need.[38]

To some extent, raised expectations of second-generation antipsychotics were associated with their more complex and multimodal neuroreceptor effects. In addition to the usual D2-blocking action of classical antipsychotics, second-generation antipsychotics include affinity for D3 receptors, selective effects on various dopamine pathways, antagonism of several serotonin receptors and blocking of serotonin reuptake.[35] Over the past 15 years, the D3 receptor has been a potential neurochemical target for the treatment of negative, cognitive and emotional symptoms associated with schizophrenia, due to its predominant expression in the mesolimbic pathway.[40-45] Moreover, D3 activity appeared to be associated with the regulation of dopamine synthesis and release.[46-48] Antagonism of the D3 receptor has been suggested to enhance dopaminergic and cholinergic neurotransmission in certain brain areas, such as the prefrontal area.[49,50] In addition, targeting the D3 receptor is driven by the need to develop a new drug that will not cause psychopathological, neurological and autonomic side effects characteristic of D2 antipsychotics.

Further search for molecules with affinity for the D3 receptor led to the synthesis of a new active and strong partial antagonist of D3 and D2 receptors and a partial 5-HT1A agonist.[44,51] A new drug with the chemical formula trans-N- (4- (2- (4- (2,3-dichlorophenyl) piperazin-1-yl) ethyl) cyclohexyl) -N ', N'-dimethylamide was registered with the international non-proprietary name 'cariprazine'. Chemically, it belongs to piperazine derivatives, similar in structure to aripiprazole and brexpiprazole.[33] Its brand names are Vraylar® (USA) and Reagila® (Europe).[52] In contrast to other antipsychotics, cariprazine in clinically relevant doses demonstrates high in vivo occupancy of both D2 and D3 receptors.[51,53] In animal models, it demonstrated a D3-dependent positive effect on cognitive functions and an antidepressant-like effect on manifestations of anhedonia, which indicate its potential for treatment of negative symptoms.[54,55] Cariprazine and aripiprazole both act as partial agonists of D2 and D3 receptors, but cariprazine is much more selective with respect to D3 than to D2.[43] It is inferior only to clozapine in terms of its affinity for D3 receptors. Various studies on cloned human receptors in vitro have shown that the affinity of cariprazine for D3 receptors is six to 10 times that for D2 receptors.[43,56-58] In a recent trial using positron emission tomography in healthy adults, cariprazine showed significant occupancy of the D3 dopamine receptor (N60%) even at a dose of 1 mg/day.[53] In patients with schizophrenia at a dose of 1.5 mg/day, the occupancy rate of D2 and D3 receptors exceeded 69–75%.[59] The fact that cariprazine is a weak partial agonist rather than a full antagonist of D2 and D3 receptors makes it possible to achieve a very high occupancy rate (approaching 90-100%) during treatment with therapeutic doses without the development of pronounced extrapyramidal symptoms. This is an advantage over use of full D2 antagonists, either classical or atypical antipsychotics, as they lead to the development of severe extrapyramidal symptoms and even absolute akinesia.[50,60] It is hoped that cariprazine will be effective in cases where other antipsychotics have only achieved 60–80% of the occupancy rate of D2 receptors, which is insufficient to obtain a therapeutic effect.[50,60] Moreover, long-term administration of cariprazine can increase the density of D3 receptors in a number of brain regions. In untreated schizophrenic patients, the expression of D3 receptors (formation on the cytoplasmic membrane) is usually initially reduced in contrast to the increased expression of D2 receptors. Therefore, upregulation of D3 receptors (regulation aimed at increasing receptor density) is likely to be a beneficial effect of cariprazine.[61] The indirect administration of cariprazine leads to upregulation and functional activity of NMDA receptors which is not observed in other non-clozapine antipsychotics.[61] NMDA receptors can be considered the most important therapeutic target in schizophrenia, since hypofunction indirectly causes disorders in the dopaminergic and serotonergic systems of the brain. Drugs affecting this, including cariprazine, are therefore highly sought.[50]

As a partial agonist with receptor selectivity, cariprazine increases the activity of systems that are not stimulated enough by internal agonists and prevents excessive and harmful stimulation by an increased level of endogenous

agonist in another system. It predominantly suppresses the excessive spontaneous activity of mesolimbic dopaminergic neurons, which determines its general and selective antipsychotic activity, and increases the activity of neurons in the mesocortical tract, which provides its possible anti-negative and pro-cognitive effects.[58] It also has a slight impact on the dopaminergic neurons of the nigrostriatal pathway and therefore has a low risk of provoking extrapyramidal symptoms, akathisia and tardive dyskinesia. It only weakly affects the receptors of the tuberoinfundibular pathway, which explains the low risk of hyperprolactinemia and sexual dysfunction.[50,62]

In relation to serotonin receptors, Cariprazine is an agonist of 5-HT1A, a strong antagonist of 5-HT2B, a moderate antagonist of 5-HT2A and a weak antagonist of 5-HT2C.[43,57,63] These receptor properties increase the levels of dopamine and noradrenaline in the prefrontal cortex and the level of dopamine in the nigrostriatal and tuberoinfundibular pathways. This further reduces the probability of extrapyramidal symptoms, hyperprolactinemia, neuroleptic depressions, antipsychotic-induced negative disorders and cognitive deficiency.[50,57]

Another advantage of cariprazine is the absence of antagonism for M3 cholinergic (muscarinic) receptors, as well as a low affinity for H1 histamine and 5-HT2C serotonin receptors. This predetermines an almost complete absence of effects such as excessive sleepiness, increased appetite and weight gain, and a low risk for metabolic disorders and diabetes mellitus.[50,57,64,65]

In summary, the predominant effect of cariprazine on D3 receptors in combination with partial agonism gives reason to expect a beneficial effect on the negative, cognitive and depressive symptoms of schizophrenia,[33,42,43,55] a therapeutic effect in recalcitrant cases[33,60] and low risk of adverse effects.[33]

Several randomized clinical trials have demonstrated its superiority over placebos in various doses (from 1.5 to 9 mg/day) on the PANSS and the Clinical Global Impressions Scale.[57,62,66-68] However, it is no more effective on acute psychotic symptoms than other antipsychotics, for example, risperidone.[62]

In randomized clinical trials of cariprazine in long-term maintenance therapy (with recommended doses of 1.5 to 6 mg/day), it performed twice as well as a placebo for anti-relapse activity,[65] safety and high tolerability.[69,70] It has also been shown to be superior to risperidone in addressing negative and affective symptoms and cognitive impairments, and positive effects on quality of life.[71,72] Good effects were also obtained via lower doses of cariprazine. However, pronounced differences in the effect on negative symptoms were only observed with long-term therapy, i.e., longer treatment than usual may be necessary to assess the effect on positive symptoms.[71]

A meta-analysis of 21 randomized clinical trials found that of all non-clozapine antipsychotics, only cariprazine compared favourably with risperidone and was statistically superior in schizophrenic patients with a predominance of negative symptoms.[38] However, these findings were based on one large trial sponsored by the pharmaceutical company that produces cariprazine.[73] In relation to all other atypical antipsychotics, only an advantage over the classical antipsychotic (haloperidol) has been demonstrated. Pairwise comparisons of other second-generation non-clozapine antipsychotics have yielded conflicting results; sometimes the sample sizes were not large enough to draw firm conclusions.[38]

Decrease in severity of negative symptoms over time via cariprazine is observed both in clinically stable patients with predominantly negative symptoms, and in patients with a worsening of the course of disease.[73] For example, at a dose of 4.5–6.0 mg once a day for six weeks was effective in treating moderate to severe negative symptoms without pronounced positive symptoms.[73] This trial included patients with predominantly negative symptoms for at least six months, scoring at least 15/24 on the negative symptom scale of the PANSS, or four or more on two of the three main negative disorders (flattening of affect, passive-apathetic social withdrawal, lack of spontaneity and fluidity of conversation). For both doses of cariprazine (3 and 4.5-6.0 mg, respectively) compared with placebos, the proportion of patients who met the response criteria for the PANSS factor score for negative symptoms (PANSS-FSNS) was significantly higher, including on the following items: flattening of affect (N1), emotional disengagement (N2), insufficient rapport (N3), passive-apathetic social withdrawal (N4), lack of spontaneity and fluidity of conversation (N6), motor retardation (G7) and active social avoidance (G16).[74] In particular, cariprazine resulted in a significantly more pronounced decrease in the PANSS-FSNS score by the 26th week of treatment than in the risperidone group (-8.9 vs. -7.44; p = 0022; effect size -0.31).

In contrast to cariprazine, there were no statistically

significant differences in PANSS-FSNS scores for risperidone and aripiprazole compared with placebos.[38] It was shown indirectly that improvement in patients with a predominance of negative symptoms did not depend on the improvement of other (positive, depressive, extrapyramidal) symptoms.[73] This latter finding is very important, since the improvement of negative symptoms is often secondary to effects in other psychopathological domains, which makes it difficult to identify the specific effects of treatment on primary negative symptoms.

Finally, there is interest in the efficacy of cariprazine in relieving symptoms and restoring social functioning in patients who received no treatment for many years and had both persistent positive and severe negative manifestations of schizophrenia.[38] Cariprazine is much less likely than aripiprazole to cause exacerbation of productive psychopathological symptoms (delirium, hallucinations), agitation, anxiety or insomnia at the beginning of therapy, because it has lower internal agonistic activity on the D2 receptor.[33]

Due to rather high neuroreceptor selectivity compared with aripiprazole and brexpiprazole, cariprazine has lower potential for causing metabolic side effects and has improved tolerability and safety. In particular, it is less likely to cause weight gain, hyperlipidaemia, hypertriglyceridemia, hypercholesterolemia or hyperglycaemia and less likely to lead to the development of type two diabetes or metabolic syndrome. Levels of metabolic side effects are the same as those from a placebo.[57,65,68] The low frequency of metabolic side effects and the probability of sedation means that it compares favourably with other second-generation antipsychotics. Among extrapyramidal symptoms arising from cariprazine, akathisia is most often noted, which is explained by the mechanism of effect of the drug.[33] However, the increased probability is only small compared with placebos, and less than in aripiprazole. Cariprazine-induced akathisia is usually not severe.[65]

In conclusion, cariprazine has the potential to be good addition to existing treatments for schizophrenia and other primary psychotic disorders. It has proven remitative and anti-relapse antipsychotic activity, can eliminate prevailing negative symptoms, shows efficacy independently from other antipsychotics and has a good safety profile. However, its effects on certain domains of negative disorders (abulia, anhedonia, decreased social activity) remain insufficiently studied. Further research is needed to examine the effects of a new antipsychotic on complex psychopathological syndromes, including positive, negative, cognitive and affective symptoms at different stages of schizophrenia.

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Long-Acting Injectable Drugs in the Maintenance Therapy of Patients with Schizophrenia

Инъекционные препараты пролонгированного действия в поддерживающей терапии больных шизофренией

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ABSTRACT

This article discusses case reports of treatment with paliperidone palmitate in comparison with data from recent publications. Second-generation long-acting injectable antipsychotics have been shown to provide better control of psychiatric manifestations, reduce the severity of negative symptoms, improve social functioning and quality of life of patients and relatives, and reduce the burden of disease for both the healthcare system and the caregivers. The case reports presented in this article demonstrate better quality of remission in schizophrenia patients treated with one-monthly and three-monthly paliperidone palmitate formulations, due to higher efficacy in preventing relapses, better safety and good tolerability regardless of patient age.

АННОТАЦИЯ

В статье обсуждаются клинические случаи применения палиперидона пальмитата в сопоставлении с данными современной литературы. Показано, что выбор инъекционных антипсихотиков II поколения пролонгированного действия позволяет обеспечить контроль психопатологической симптоматики, уменьшить выраженность негативных расстройств, улучшить социальное функционирование и качество жизни пациентов и их близких, уменьшить бремя болезни как для системы здравоохранения, так и для ухаживающих лиц. Клинические случаи демонстрируют улучшение качества ремиссии шизофрении благодаря высокой противорецидивной эффективности, безопасности и хорошей переносимости палиперидона пальмитата с применением 1 раз в месяц и в 3 месяца независимо от возраста пациентов.

Keywords: *paliperidone palmitate, schizophrenia, long-acting injectable, personal recovery*

Ключевые слова: *палиперидона пальмитат, шизофрения, инъекционные пролонги, личностное восстановление*

INTRODUCTION

Recovery and satisfactory quality of life are the criteria for the effectiveness of modern therapy for schizophrenia. The ultimate treatment goals are to improve functional capacity, minimize residual symptoms and reduce the frequency and duration of relapses, since each relapse potentially worsens prognosis. Continuity of maintenance treatment is essential for a long-term positive outcome in patients with schizophrenia. Antipsychotics are the basis of schizophrenia treatment and long-acting injectable antipsychotics are designed to increase the effectiveness of therapy for schizophrenia spectrum disorders.

One representative of the atypical long-acting antipsychotics group is paliperidone palmitate, available

in injectable suspension dosage form with a dosing schedule of once per month (PP1M). In the Russian Federation, this form of the medication is produced under the brand name Xeplion. The paliperidone molecule is the active metabolite of risperidone. By avoiding hepatic metabolism, paliperidone has acquired distinctive properties that provide a better tolerability and safety profile while retaining higher efficacy. A modern delivery system of paliperidone palmitate enables maintenance of the plasma concentration of paliperidone within the therapeutic range for up to five weeks and eliminates fluctuations in the drug levels. If the dose is missed, the level of the drug decreases slowly, creating a safety net in the case of patient non-compliance which thus gives time for medical intervention and minimizes potential adverse events.

Data from a multicentre study of PP1M (n = 645) indicated significant reductions in the frequency and duration of hospitalizations of patients with schizophrenia and schizophrenia spectrum disorders.[1] These data showed that Xeplion therapy is associated with better treatment adherence of outpatients,[2] which is essential for long-term continuous therapy of schizophrenia.

A new second-generation long-acting injectable antipsychotic agent emerged in 2016. Trevicta, a three-monthly injectable formulation of paliperidone palmitate (PP3M), is the only product that offers an extended three-month 'window' of stable plasma levels. It is an ester of paliperidone and palmitic acid for intramuscular administration once every three months. It contains the same active substance as PP1M and is made by the same technology, but has a different strength and particle size, enabling the three-monthly administration schedule. PP3M is indicated for patients who are clinically stable and who have been adequately treated with PP1M for at least four months before switching to PP3M.[3] It is suggested that PP3M offers a substantially longer dosing interval compared with other long-acting formulations.[4]

The efficacy of PP3M (175–525 mg) was similar both in Europeans and non-Europeans when it was compared with PP1M (50–150 mg) in 487 European adult (18–70 years) patients (PP3M, n = 242; PP1M, n = 245) and 508 non-European adult patients (PP3M, n = 241; PP1M, n = 267) with schizophrenia. However, the rate of adverse events was lower in Europeans (56% with PP3M, 59% with PP1M) than in non-Europeans (80% with PP3M, 73% with PP1M). The most common increase in body weight was in non-Europeans, especially in the Asian population.[5]

The safety and efficacy of PP3M have been demonstrated in double-blind randomized clinical trials.[6,7] However, there is a need to better understand treatment regimens with PP3M in real world settings. From May 2014 until September 2016, a retrospective cohort study was conducted examining the treatment of adult patients with schizophrenia via documentation in the Symphony Health Solutions (SHS) database. The study included two cohorts: all patients with PP3M prescriptions (first cohort) and patients transferred from PP1M to PP3M according to a strict clinical transfer protocol (second cohort). Every four months and over a 12-month period, PP1M treatment regimens, the proportion of days covered by psychotropic drugs and health resource use patterns were evaluated. It was found that out of 1545 patients with PP3M (first cohort), 68.8% transferred from PP1M to PP3M (forming the second cohort). In both cohorts, the proportion of patients with the number of days covered by psychotropic medications (≥80% for antipsychotics, antidepressants, anxiolytics and mood stabilizing agents) increased. The proportion of patients making one or more visits to the emergency department, inpatient or outpatient departments decreased with the start of PP3M therapy. Among the patients followed up for four months or more after the first dose, 85-88% received the second dose; among the patients followed up for four months or more after the second dose, 87-90% received the third dose. PP3M was usually prescribed to patients with schizophrenia in accordance with the instructions. The most common first PP3M dose was 819 mg (the highest available) and most patients received a constant dose with the first three injections. The average number of days between subsequent PP3M statements was also consistent with the recommendations. The main reason for not transitioning as recommended to PP3M was the presence of gaps greater than 45 days in PP1M four months prior to PP3M initiation. A high proportion of the patients were in stable condition and were adherent to the treatment with PP3M.[8]

PP3M has been approved for use in the long-term maintenance treatment of patients with schizophrenia who are clinically stable on PP1M therapy for at least four months. Since the available data confirm the efficacy and tolerability of PP3M compared to PP1M and placebo, PP3M should be considered as an appropriate treatment option

for the patients who received maintenance therapy with PP1M.[9] It should be noted that these recommendations are followed in real clinical practice. Moreover, most patients who are prescribed paliperidone palmitate have already had exposure to risperidone, including its long-acting form. Consecutive transfer to PP1M and PP3M is accompanied by improvement of the clinical and functional characteristics of remission.

The practice of transfer from two-week long-acting injectables to PP1M and PP3M is in line with the current clinical guidelines. García-Carmona et al. (2020) compared PP1M and PP3M with two-week long-acting injectables for the following outcomes: the number of rehospitalizations, the number of the verified suicidal actions/attempts and the use of concomitant treatment, including benzodiazepines, oral antipsychotics and biperiden. A total of 431 patients diagnosed with schizophrenia spectrum disorder who had received the appropriate treatment over at least 12 months were evaluated. The results showed a significant decrease in the number of rehospitalizations during PP3M therapy compared to two-week injectables and aripiprazole once a month, while no significant differences in suicidal behaviour were found. There was a significantly lower level of benzodiazepine consumption in the PP1M and PP3M groups compared to the two-week injectables group. In addition, patients who received PP1M and PP3M medications used a significantly lower dose of haloperidol equivalent compared to the patients who received two-week long-acting injectables. Finally, significantly higher doses of biperiden were used by the two-week long-acting injectables group. These data indicate the advantages of PP1M and PP3M over two-week long-acting injectables.[10]

A comparative analysis was conducted of the treatment results of PP1M and PP3M in patients with schizophrenia (n = >1100) who were taking and not taking oral risperidone/paliperidone (RIS/PALI). Results indicated that there was an improvement in mental state as assessed by the Positive and Negative Syndrome Scale (PANSS), both during and after relapse. The tolerability of the therapy was comparable regardless of the prior treatment of RIS/PALI.[11]

It should be emphasized that PP3M has a number of advantages in addition to better adherence.[12] Symptomatic remission and a decrease in the severity of both positive and negative symptoms reflect the stability of treatment with PP3M. Moreover, significant functional remission, reduced frequency of drug administration and freedom from daily monitoring of the patient have a positive effect on the patient and reduce the burdensome aspects of their care. PP3M is a valuable antipsychotic treatment option that deserves consideration in terms of its broader role in the long-term treatment of schizophrenia; its utility should not be limited to prescribing in patients with poor adherence or when oral antipsychotics have failed.

Compared to two-week long-acting injectable antipsychotics, patients treated with PP1M and PP3M had a reduction in the number of rehospitalizations and concomitant medications.[10] This is consistent with information from domestic clinical practice showing improvements in extrapyramidal symptoms following transition to paliperidone palmitate therapy and the absence of the need for correctors.

Pharmacokinetic and pharmacodynamic models were designed to investigate the relationship between plasma concentrations of paliperidone and the risk of schizophrenia relapse in patients treated with PP1M and PP3M. In study A, patients (n = 305) were randomized to PP3M or placebo in the double-blind phase; in study B, patients (n = 1002) were randomized to PP3M or PP1M in the double-blind phase. Risk of relapse decreased with higher paliperidone concentrations for both PP1M and PP3M. Risk of relapse increased in patients with a higher number of previous hospitalizations and/or with a higher pre-randomization paliperidone concentration (study A) and in patients using concomitant benzodiazepine medication. The analysis confirmed that both PP1M and PP3M are comparable in preventing relapse.[13]

Negative symptoms in schizophrenia are associated with impairments in social and cognitive functioning, leading to substantial long-term disability. A study investigating the impact of PP1M and PP3M on negative symptoms randomized patients (n = 1,016) to receive PP3M (n = 504) or PP1M (n = 512). Treatment with PP3M or PP1M demonstrated comparable improvement regarding negative symptoms in patients with moderate to severe negative symptoms and patients with prominent negative symptoms. Long-term treatment with PP3M demonstrated benefit, suggesting that continuous antipsychotic medication treatment for over one year is needed to achieve greater benefits for negative symptoms.[14]

We now present several cases of the use of second-generation long-acting injectable antipsychotics to illustrate our own experience of PP1M and PP3M use.

CLINICAL CASE 1*

Patient R., born in 1981 (age 39) in Leningrad. She has no known family history of mental disorders, however, according to the patient's mother, the father has pronounced characterological features, he is aggressive and displays violent behaviour. The patient also has an elder brother who is healthy. The patient's parents have been divorced since she was 16 years old. The patient did not have any disturbances of early development or adolescence. Menstruation started from the age of 14, with a regular cycle. The patient did not have any difficulties in social adjustment when she was a child. She attended preschool institutions, then school from the age of seven, she graduated from nine classes with an average academic performance and her favourite subject was French. After school, she worked as a checkout operator, but since 2008 she has been unemployed, with a lifetime disability group classification. She is single and does not have children.

The patient first noted changes in her mental state at the age of 16, when she became withdrawn and unsociable after her parents divorced. She refused food, hid it under her pillow, lost too much weight and did not explain her behaviour in any way. At the insistence of her mother, she was examined by a private psychiatrist and was treated for two months on an outpatient basis, taking medications. Her mental state improved and she started to eat. According to the patient, at that time a psychotic state was diagnosed. However, she decided not to take maintenance therapy. At that time, her attitude towards her mother changed dramatically, she reported that 'I began to hate her', 'I used obscenities towards her' and 'I wanted her to die'. She blamed mother for her father leaving the family, because 'I loved him very much, despite his violent behaviour'. The condition worsened again at the age of 17, with presentation of similar symptoms. The patient again refused to eat, became withdrawn—'blah'—and called her mother 'every name in the book'. She was examined by a private psychiatrist and took thioridazine for two months with further recommendation that she be monitored by a district psychiatrist. However, she did not go to a psychoneurological dispensary (outpatient community mental health clinic), as according to the patient, 'her condition has improved'. During this period, her father returned to the family and she communicated only with him, ignoring her mother. At the age of 18, she got a job as a store assistant. During this period, she became gentler in her relationship with her mother. After working for four years, she quit, explaining that 'there are a lot of non-Russians, they can cheat and not give money'. She started to think that she was being watched and followed everywhere. She got a job in another store, but only worked for a few months. Subsequently, she changed places of work frequently. Since the age of 25 (since 2006), she has not worked regularly anywhere, explaining that it is too heavy a load. According to the patient, she 'began to hate everyone', was suspicious, and refused to fill in CV forms when looking for a new job, because she believed that 'these data could be used against her'. She lost interest in previous activities, lost acquaintances and withdrew into herself. A year later, her aggressive behaviour towards her mother returned in verbal form, as she obscenely scolded her mother. From the beginning of spring 2008, she claimed that 'the air in the house is bad' because her mother's 'deodorant is especially poisonous' and believed that her mother put 'something' in her food. Since May 2008, she stopped leaving the house, it seemed to her that she was being 'watched from a vacant lot', that there was video surveillance in the apartment; she turned off the phone and drew the curtains. She was involuntarily admitted to a psychiatric hospital for two and a half months (May to the end of July). Upon admission, she expressed delusional ideas of exposure and poisoning. She strained her ears as if she were hearing something and looked like she suffered from hallucinations, asking doctors 'do you feel this smell, as if they want to poison us?' and 'are you in cahoots with them?'. She shouted, was agitated, tense, angry and generally negatively predisposed. She stated that 'there are cameras everywhere at home'. She did not express any recognition of her condition. She was taking zuclopentixol at 20 mg per day. Her condition improved and quickly stabilized, with a reduction in the hallucinatory-delusional symptoms. In the ward she kept to herself, did not communicate with other patients and did not make plans for the future. Diagnosis according to ICD-10: F20.0 Paranoid schizophrenia.

Immediately following discharge from hospital, the patient's condition remained stable, but she felt sleepy and apathetic. She failed to find a job. Over time, she began to suffer from muscle stiffness. When trying to reduce the dosage of zuclopentixol to 10 mg per day, she again became irritable, aggressive towards her mother and expressed delusional ideas of poisoning. She was referred to a psychoneurological dispensary, where she was treated from October 2008 to February 2009. Diagnosis: F20.0 Paranoid schizophrenia. Disease course type: shift-like protracted delusional syndrome. Moderate apathia and abulia syndrome.

In the psychoneurological dispensary the patient received therapy via atypical antipsychotics (amisulpride, clozapine and risperidone). Her condition improved, her behaviour became more organized, the delusional symptoms resolved and the extrapyramidal symptoms reduced. She was then referred to rehabilitation department, where she attended occupation therapy groups and performed uncomplicated work, but coped very slowly. She was referred for medical and social expert evaluation and assigned to disability group II for one year.** She was discharged from the rehabilitation department with a recommendation to continue taking medication (risperidone 4 mg per day, trihexyphenidyl 4 mg per day). After a few months, she began to take the recommended medications on an irregular basis. In March 2009, she was transferred to therapy with long-acting haloperidol (intramuscular solution) with injections of 50 mg once every 14 days. On this therapy she noted an increase in apathy, indifference and lack of initiative. During this period, she got a low-skilled job but could not keep it. In May 2010, she missed a planned injection of the drug and her condition worsened, the behavioural disorders increased and she began to run away from home. She was examined by a district psychiatrist during a home visit. The doctor noted anxiety, delusions and hallucinations ('smells were suspicious', 'voices', 'asked not to send her signals', she would speak to someone who was not there), the patient was aggressive towards her mother and expressed no awareness of her condition. She was admitted to a psychiatric hospital for one month (May to June 2010) and received risperidone therapy. After stabilization of her condition, she was discharged with a recommendation to continue taking risperidone at 2 mg per day. Subsequently, she was observed by a district psychiatrist and received risperidone at a dose of 6 mg per day and trihexyphenidyl at a dose of 4 mg per day. Due to the fact that the patient developed

* *In the description of clinical cases, the personal data of the patient and the places of his treatment are not given.*

** *In Russia, there are three disability groups that are assigned depending on performance incapability. A disability group can be assigned for a certain period of time or for the whole lifetime.*

extrapyramidal symptoms, the dose of risperidone was reduced to 3 mg per day. The patient was also prescribed a course of diazepam injections of 10 mg intramuscularly for five days, with further transfer to the tableted form of low doses of benzodiazepines at night for a month. This treatment had a positive effect. The patient's condition remained stable for eight years and could be regarded as medically induced remission without admissions to a psychiatric hospital or a psychoneurological dispensary. However, social maladjustment persisted, and the patient could not find a job. Over time, social and domestic incompetence and emotional-volitional decline increased. In 2012, the Disability Determination Services classified the patient into disability group II for lifetime. In November 2018, she again cancelled maintenance therapy and was admitted to a psychiatric hospital with hallucinatory-delusional symptoms, where she was treated for three weeks. She was discharged with a recommendation to continue treatment with risperidone at a dose of 2 mg before bed, followed by transfer to intramuscular administration of the long-acting suspension of risperidone at a dose of 37.5 mg once every two weeks. In May 2019, she was transferred to injectable paliperidone palmitate at a dose of 75 mg once a month.

State at the moment of examination: During the year of taking injections of paliperidone palmitate at a dose of 75 mg once a month, no exacerbations were observed. The patient lives with her mother, family relations are good, she helps with the housework, is looking for a job, attends interviews and is registered with the employment centre. She regularly visits a psychoneurological dispensary, where no adverse effects of antipsychotic therapy have been registered. Her mental state can be described as a sustained medically induced remission for more than a year.

Discussion

Noncompliance is a common problem in patients with schizophrenia, which is the most common cause of relapse. The above clinical case demonstrates problems of compliance with the treatment regimen and associated relapses and repeated hospitalizations during disease progression. The long-acting antipsychotics reduce the frequency of drug admission and, therefore, can effectively improve compliance. Research conducted by Global Data shows that physicians often prefer long-acting injectable antipsychotics to pills, especially in patients with a history of non-compliance. In the described case, switching to a first-generation long-acting antipsychotic could not solve this problem, because of side effects that were difficult for the patient to tolerate. The transfer to a second-generation long-acting injectable antipsychotic neutralized the adverse effects and facilitated adherence to therapy. The intended effect of PP1M treatment is to ensure the social functioning of patients, especially work and study, interpersonal contacts, self-care and the elimination of disorganized behaviour and aggression. This clinical case demonstrates not only the possibility of ensuring compliance in a patient who is prone to violation of the therapy regimen, but also the improvement of social adjustment, improvement of functioning and quality of remission, and an effective impact on negative symptoms in a patient when transferring to paliperidone palmitate in injectable form at a dose of 75 mg once a month.

CLINICAL CASE 2

Patient N., born in 1966 (age 54) in the Leningrad region, the second child in the family. She has no known family history of mental disorders. Her mother is a paramedic, and her father was an engineer (he died at an advanced age of cardiovascular morbidity). The patient did not have any disturbances of early development or adolescence. Menstruation started from the age of 14, with a regular cycle. She went to school at the age of seven and studied satisfactorily, with a preference for humanities. Following graduation from school, she entered a medical institute, after which she worked as a paediatric neurologist in a hospital for many years. In 2000, she got married and her son was born. In 2002 she got divorced from her husband, as they 'turned out to be incompatible'. Overall, she had four pregnancies and three abortions. She experiences the onset of menopause at the age of 54.

The patient noted a change in her mental state after childbirth, when she became depressed and indifferent, but she did not seek medical help. According to her statement, 'everything cured itself'. In 2003, she began to notice sleep disorders, woke up 'as if pushed' and became irritable. She sought a psychotherapist, who prescribed amitriptyline at a dose of 25 mg before bed for two weeks. Her state improved and subsequently, she took this medication occasionally when sleep was disturbed. A year later, she began to experience the effects of 'electrical stimuli from the ambient environment', in the form of an unpleasant physical feeling, 'contraction' of the scalp 'as if the brain is moving'. The patient self-medicated using the fabomotizol, tofisopam and pyracetam. During this period, she moved to Saint Petersburg (2004). She got a job as a doctor, but worked for less than six months before quitting and subsequently changed jobs frequently for delusional reasons, as she 'felt an influence everywhere'. She had disturbed sleep, constantly experienced anxiety and depression, and 'sat at the table, looking at nothing for several hours'. She has been unemployed since 2007. She became withdrawn, uncommunicative, abandoned the household, stopped cooking and expressed delusional ideas that her mother and her son were not her own relatives. She suspected that she was under 'surveillance **[**and**]** wiretapping'. She refused the help of medical specialists and started attending church. In March 2008, she was admitted to a psychiatric hospital for three months (March to June 2008). On the day of her hospitalization, she opened a balcony window, shouting 'darling, I love you, I'm coming to you'. She could not explain her behaviour. She had incoherent monologic speech, said that she was hearing 'voices', was agitated, anxious and suspicious. She looked around, paused and strained her ears to hear something. She expressed delusional ideas, saying 'I'm a doctor of the highest category, I was put here especially, I'm in the way of someone'. Diagnosis: F20.0 Paranoid schizophrenia.

In the inpatient department, she received haloperidol at a dose of 20 mg per day with further transfer to the long-acting injectable form of haloperidol at a dose of 50 mg once every 10 days and trihexyphenidyl at a dose of 6 mg per day (due to extrapyramidal symptoms). She made no complaints, kept to herself in the ward and communicated with other patients in a formal manner. Clinical assessment revealed

auditory hallucinations, delusions of persecution, influence, relationships and love charm. The patient was assigned to disability group II for life. She was discharged and referred for further observation in a local psychoneurological dispensary, where she received maintenance therapy with the long-acting injectable form of haloperidol at a dose of 100 mg intramuscularly once every 14 days. The course of the disease was shift-like. The patient's mental state remained stable for a long time, but in 2010 she began to notice apathy, depressed mood and 'inhibition of thoughts'. She was transferred to risperidone therapy at a dose of 6 mg per day. She noted an increase in activity during the day, her mood improved and she expressed explicit awareness of her condition. She regularly visited the psychoneurological dispensary, had partial insight and socialized to an extent; she got a job as a medical statistician and coped with her work well. She was again admitted to a psychiatric hospital in July 2012 because of hallucinatory-delusional symptoms and psychomotor agitation. When examined in the ward, she was suspicious, strained her ears to hear something and confirmed that she was experiencing auditory hallucinations. She received haloperidol at a dose of 20 mg per day and was subsequently transferred to the long-acting injectable form of haloperidol at a dose of 100 mg intramuscularly once every 14 days and trihexyphenidyl at a dose of 4 mg per day. At the time of discharge, the patient's state was satisfactory, but when visiting the psychoneurological dispensary, she stated that she could not work after haloperidol injections, she experienced loginess and indifference. In December 2012, she was successively transferred to the injectable form of risperidone suspension at a dose of 37.5 mg intramuscularly once per month, then to an injectable form of paliperidone suspension at a dose of 75 mg intramuscularly once per month. The patient's mental state improved and she coped with her job well. In June 2015, after the workload at work increased, she became anxious, had difficulties with concentration and developed sleep disorders, asthenia and depressive symptoms. After 30 days of treatment in a day hospital, her condition improved, she did not experience delusions and hallucinations, and no suicidal thoughts were present. She received the injectable form of risperidone suspension at a dose of 100 mg intramuscularly once a month and amitriptyline in tablet form at a dose of up to 150 mg per day. On this therapy, the negative symptoms became more visible. The patient was transferred to PP3M at a dose of 350 mg intramuscularly.

State at the moment of examination: the patient's mental state is stable, determined as a medically induced remission. She continues to work and has learned how to use a new computer program. She does not miss doctor's visits or injections and is satisfied with her general state. Hallucinatory-delusional symptoms are not detected.

Discussion

The above clinical case demonstrates that the transfer from a first-generation long-acting injectable to a second-generation long-acting injectable drug contributed to improving the quality of remission and its stability. There were no relapses that required hospitalization. The progressive improvement in social functioning was noted, especially when transferring to the injectable form of paliperidone suspension at a dose of 350 mg intramuscularly once every three months.

CLINICAL CASE 3

Patient A., born in 1958 (age 62) in Leningrad. Her mother suffered from mental health problems, was often treated in a psychiatric hospital and died at the age of 57. Her father was addicted to alcohol. The patient did not have any disturbances of early development and adolescence. Menstruation started from the age of 11, with a regular cycle. She started school at the age of seven and studied well. She finished 10 classes and tried to enter a higher education institute, but did not pass the entrance test and 'cried a lot, worried'. Later, she graduated from a technical university and worked as an engineer at a factory for a year. She got married at the age of 23 and her husband worked in a tram and trolleybus fleet. She had five pregnancies, with one childbirth and four abortions. She experienced menopause from the age of 50.

The patient noticed changes in her condition at the age of 21 (1979), when she went on a solo vacation to the seaside. According to the patient, during the vacation period she dated a man, a local resident, who went on to blackmail and harass her. After returning home, she told her relatives that she was constantly being called at the door and on the phone, saying 'it is still the same lover trying to find me'. At the same time, the patient herself could not contact this man, as 'he always called from different cities, constantly moved'. She was waiting for her fiancé to return from the army. She constantly felt a sense of guilt, a 'guilty conscience that I cheated on him'. Her sleep was disturbed, she became suspicious and 'constantly looked around'. During this period, a psychosis developed acutely: she experienced visual hallucinations in the form of 'a blurry picture, like slow-motion video, I saw children playing volleyball in this video', it began to seem that 'all the people around are getting old, and my fiancé is young, beckoning me to follow him'. She was afraid that she would turn 'into another being'. It seemed to her that she 'jumped through many years and lives in a different political system', and she was agitated. She was admitted to a psychiatric hospital. Upon admission, she developed hallucinatory-delusional symptoms and mental automatism, shouting 'my fiancé is calling me, I must be with him', spoke to herself and showed verbal aggression. She received therapy with a solution of insulin for subcutaneous injection and thioridazine in tablet form (no information is available on dosages of these medications). Her mental state was unstable, her behaviour was childish and she continued to experience hallucinatory-delusional symptoms from time to time. She experienced tension, anxiety and olfactory hallucinations appeared, which she described as 'it seemed that everything around me is rotting'. She began to tell that she 'split up, physically she was in the ward but her brain was in the dining room'. Trifluoperazine in the form of a 0.2% solution for intramuscular injection and small doses of haloperidol (per os) were added to treatment, after which her mental state improved. Diagnosis: F20.0 Paranoid schizophrenia.

After discharge from hospital, she received maintenance therapy with haloperidol at a dose of 1.5 mg per day, trihexyphenidyl at a dose of 4 mg per day and trifluoperazine at a dose of 10 mg per day. She worked as a cleaner, raised her son and ran a household. Until 1988, the mental state was determined as medically induced remission. Several years later, the emotional-volitional decline increased, the patient was repeatedly treated in a day hospital because of the development of paranoid symptoms and was transferred to olanzapine therapy. Negative symptoms were highlighted by clinical assessment. She stopped working and at the age of 42 (2000), she was assigned to disability group II for life. In May 2004, she was admitted to a psychiatric hospital because of a relapse, in which she stopped sleeping, began to attend church and expressed delusional ideas of sinfulness, of 'possession by the Devil'. On the day of admission to the hospital, she jumped from a third floor balcony and was hospitalized involuntarily. She was discharged after two months with a recommendation of clozapine in tablet form at a dose of 150 mg

per day. She received this maintenance therapy for a year, during which time she felt well. Her mental state worsened in December 2007, with the appearance of sleep disorder and abnormal preoccupations. She was treated in a day hospital from December 2007 to June 2008, with risperidone at a dose of 6 mg per day, followed by transfer to risperidone for intramuscular injection at a dose of 37.5 mg once every two weeks. The patient was discharged in a satisfactory mental state and got a job as a cleaner. In 2012, her mental state deteriorated again with the appearance of neurosis-like symptoms and she was prescribed clozapine therapy at a dose of 150 mg per day in a day hospital. After discharge, while taking this drug she complained of apathy, a lack of initiative and indifference. In December 2013, she was transferred to a suspension of paliperidone palmitate at a dose of 50 mg once a month, with a further increase in dose to 75 mg per month. In the following years, she was not hospitalized, her state was determined as stable medically induced remission and she has been in employment. In July 2017, she was transferred to PP3M at a dose of 263 mg intramuscularly.

State at the moment of examination: on the maintenance antipsychotic therapy, the patient notes an increase in activity, runs a household in the summer cottage, continues to work, her family relations have improved and she lives with her husband and son. Currently, the patient's state is determined as a stable medically induced remission.

Discussion

It can be noted that the administration of risperidone in injectable form to the patient contributed to the formation of a fairly stable medically induced remission for four years. The change of therapy (clozapine prescription) was apparently due to an increase in anxiety, which was regarded as signs of relapse, but psychosis did not develop and hospitalization was not required. Poor tolerability of clozapine, which significantly reduced the patient's quality of life, led to the decision to transfer to PP1M, leading to a decrease in antipsychotic therapy side effects which improved the quality of remission along with effective control of schizophrenia symptoms. The transfer to PP3M led to further improvement in the patient's mental state and quality of remission. This clinical case illustrates the possibility of a noticeable improvement in the social functioning of a patient with chronic schizophrenia, combined with good tolerability of second-generation long-acting injectable antipsychotics.

CLINICAL CASE 4

Patient T., born in 1982 (age 38) in Leningrad, the only child in the family. Her maternal grandparents abused alcohol. Her mother is hyperactive, in the past she worked as a librarian, a guide and later ran her own real estate agency. Her father, according to the patient, was 'ideal': calm and good-natured. At the same time, her father has another family and the patient was born out of wedlock. She maintains a relationship with her father. She was raised by her mother was overprotective. The patient did not have any disturbances of early development or adolescence. Menstruation started from the age of 14, with a regular cycle.

In early childhood, the patient did not have problems with social adjustment. From the age of 10 months, she attended a nursery, then a kindergarten. She started school from the age of seven, attended various groups (drawing, dancing and gymnastics), but left the groups 'because of shyness'. The patient stated that 'my mother said that I have always been a sickly child' because she was diagnosed with biliary dyskinesia, which did not bother her in any way, 'but my mother constantly stuffed me with all sorts of medications'. After school, she wanted to go to a medical university, but at the insistence of her mother, she entered a faculty of foreign languages of a pedagogical institute. She graduated from the institute 'with difficulty, because I fell in love'. For a year after graduation, she worked as an English teacher at a medical school, then quit. After that, she taught English privately for several years. In 2009, she gave birth to a daughter out of wedlock and did not maintain relationship with the child's father. The patient noted that since childhood she was 'thoughtful, withdrawn, shy, afraid of everything'.

Around the age of 19 (2001), she noticed a high mood, became hyperactive, attended various entertainment events, 'strongly fell in love' with a university professor, stopped spending time studying, 'mooned over him' and 'thought that she would dance with him in a ballet all over the world'. During that period, the patient's mother began to notice that her daughter's behaviour changed; she became secretive, 'started a diary, kept writing in it'. After the professor left the institute, she 'continued to seek his affection', called him, found out where he lived, 'began to go there, wait for him' and wrote about him in her diary: 'I must give birth to his son, and then our planet will be saved, I will give birth to the Messiah'. This state lasted for more than a year and she barely graduated from the institute. In 2006, she became aggressive and quick-tempered. She tried to find the professor. She believed that her mother wanted to cause her harm 'so she does not allow her to arrange her personal life', 'envies that I am the chosen one', noted that 'everyone is in cahoots, they want to kill me', became suspicious and stopped going outside. At that time, she lived alone, called her mother in tears, saying that 'someone is standing outside my door and wants me dead', had a feeling that 'she was dying', felt her heartbeat and was afraid that 'her breathing would stop'. She stopped eating as it seemed to her that 'the food could have been poisoned'. In May 2006, she was first admitted to the university psychiatric clinic. Upon admission, she developed hallucinatory-delusional symptoms, psychic automatism, spoke to herself and showed verbal aggression. Diagnosis: F20.0 Paranoid schizophrenia. She was on treatment for two months, during which she received trifluoperazine at a dose of 10 mg per day and trihexyphenidyl at a dose of 4 mg per day. Her mental state stabilized, abnormal preoccupations and hallucinatory-delusional symptoms reduced, and her mood stabilized. In the ward, she kept to herself, did not communicate with anyone and did not express any awareness of her state.

After discharge from hospital, the patient took maintenance therapy for a year. She began to engage in private teaching, but after a period of work overload, her sleep was disturbed and she became irritable and anxious. The dose of trifluoperazine was increased to 20 mg per day. She began to notice tremors, 'problems with the tongue **[**and**]** jaw' and felt stiffness of muscles. In November 2007, she was transferred to risperidone therapy at a dose of 4 mg per day in the psychoneurological dispensary. She continued to experience extrapyramidal symptoms, so she stopped taking the drug on her own. She did not receive the maintenance therapy for two years. During this period, she met a man and got pregnant. According to her mother, during pregnancy, 'she started indulging in illusions again' and was sure that the child's father was actually her professor, but her behaviour was not disturbed and she was calm. She gave birth

to a daughter in 2009, out of wedlock. After the birth, she did not maintain a relationship with the child's father, saying 'he just vanished, who cares'; she did not worry, she 'was up in the clouds' and took care of the child under the supervision of her mother. A few months after birth, she began to express ideas of reference towards her mother, blamed her that 'her husband left her, she was jealous of me, she was in love with him and broke our relationship', became angry, irritable and decided to find her professor, 'because this child had to be his'. She stopped taking care of the child, did not feed her and according to the patient's mother 'the child did not bother my daughter in any way'. When the patient's mother wanted to take the child into her care, the patient showed aggression, saying 'you're a witch, you want to kill my child'. She became suspicious, checked the food again because she thought that 'her mother might have poisoned her', listened to sounds coming from the street at the window, drew the curtains, closed the windows in the room and sat in silence for a long time 'so as not to give herself away'. She reported that 'they show me on the Internet, they know what shampoo I use' and turned off lights in the apartment. She began to think that she was being 'shot on camera'. In September 2009, she was admitted to a psychiatric hospital involuntarily. During the transportation, she resisted, cursed and shouted 'you are all in collusion, I did not give birth to the Messiah, you want to kill me'. Upon admission, she developed hallucinatory-delusional symptoms. In hospital, she received risperidone at a dose of 2 mg per day. During the therapy, her condition stabilized and hallucinatory-delusional symptoms were resolved. Thought disorders, negative symptoms and increasing apathy and abulia symptoms came to the forefront in clinical assessment. In the ward, she kept to herself, did not communicate with other patients and did not make plans for the future. After discharge, she was assigned to disability group II for a year. Her mental state was stable on the maintenance therapy for several years, but negative symptoms and personality changes came to the forefront in clinical assessment, and autism symptom were growing. She was engaged in raising her daughter together with her mother, and the relationship in the family was satisfactory. In 2011, she stopped taking medication, became wary and anxious, relations with her neighbours and her mother worsened, she stopped taking her child to kindergarten, was afraid to go out and expressed delusional ideas of persecution and exposure. She began to leave the house at night, returning in the morning with no explanation and stopped cleaning her room. In her diary, she addressed 'God, the angels' and 'the people who have been following her for many years'. She wrote about 'information leaks, loss of energy and devil worship'. She began to believe that 'her mother is in cahoots with the devil worshippers'. She reported that there was an invasion of her life, that someone 'is constantly filming her on camera, laughing at her', asked to 'turn off the broadcast of me' and that 'these are experiments on me'. The patient was involuntarily admitted to a psychiatric hospital. Upon admission, she developed hallucinatory-delusional symptoms, was agitated and screamed 'Freemasons, stop trying to force powerful thoughts on me'. She tried to escape, saying 'I must jump from a roof and die'. In the ward, she was tense, negatively predisposed, anxious, suspicious, psychomotor agitation persisted and periodically increased, she was impulsive, spiteful and her speech was in monologue. She revealed pronounced disorders of thinking, expressed affective delusional ideas of reference, persecution, significant influence and gave a delusional interpretation of what was happening, considering hospitalization to be the result of 'collusion of doctors with my mother', reporting that her mother 'spoils my energy, wants to replace my aura with hers' and accusing her of 'practising black magic'. At first, she received therapy with haloperidol at a dose of up to 10 mg per day, but noted pronounced extrapyramidal symptoms and was transferred to therapy with quetiapine at a dose of 600 mg per day. Her state showed some improvement, but a week after starting quetiapine, she again began to express delusional ideas. She was transferred to risperidone at a dose of up to 9 mg per day and trihexyphenidyl at a dose of 4 mg per day. On this therapy, her state improved, her behaviour was ordered, delusional symptoms stopped and extrapyramidal symptoms were reduced.

After discharge, the patient was observed by a district psychiatrist and received maintenance therapy. Her condition remained stable for a long time, determined as a stable medically induced remission for three years without hospitalization. She got a low-skilled job (as a cleaner) and helped her mother to raise her daughter. However, she experienced personality changes along with increases in social and domestic incompetence and emotional-volitional decline. In March 2014, she again cancelled the maintenance therapy herself and her mental state worsened. She was admitted to a psychiatric hospital with hallucinatory-delusional symptoms. After treatment, she was discharged with a recommendation for risperidone at a dose of 9 mg per day and trihexyphenidyl at a dose of 4 mg per day, before being transferred in June 2014 to long-acting risperidone at a dose of 37.5 mg once every two weeks. This dose was later increased to 50 mg once every two weeks. In April 2015, the patient was transferred to PP1M at a dose of 100 mg intramuscularly. She regularly visited the psychoneurological dispensary, did not miss injections, was not hospitalized, became more active, helped her mother with the household, began to give private English lessons and occasionally worked as a cleaner. In March 2020, she was transferred to PP3M at a dose of 263 mg intramuscularly.

State at the moment of examination: on the maintenance antipsychotic therapy the patient's condition is stable, she continues to work, has plans for the future, family relations have improved and she has become more caring for her daughter. Her condition is determined as a stable medically induced remission.

Discussion

Clinical case 4 illustrates the stabilization of the patient's state on PP1M with high medication tolerability. The following transfer to PP3M—Trevicta—brings benefits of treatment adherence, which helps to maintain a stable remission, prevent rehospitalization and improve social functioning of the patient.

The above clinical cases confirm previous data in the literature that treatment with PP1M and PP3M enables a more stable mental condition. There is evidence that since patients are in a more stable state, the burden of disease with treatment of PP1M and PP3M is lower than from usual treatment, as it reduces the burden on psychiatric services and the hospital sector. When treated with these medications, the burden associated with a person's disease is outweighed by the benefits to their health.[15,16]

According to the literature, in real clinical practice, patients with schizophrenia who are transferred from PP1M to PP3M show a decrease in the use of health resources and an increase in treatment adherence within months of starting PP3M, as well as adherence to PP3M therapy.[8] All the clinical case studies we

have presented are consistent with previous research findings and illustrate a steady reduction in negative symptoms, reflected by improvement in the functioning and psychosocial adjustment of patients and effective relapse prevention.

CONCLUSION

Second-generation long-acting injectable antipsychotics can provide control of psychopathology to improve social recovery and quality of life of patients and their families, reduce the burden of disease on both the health system and families or caregivers. The experience of using paliperidone palmitate indicates that this drug allows patients to maintain a stable state for a long time and reduce the severity of negative disorders. When using paliperidone palmitate, there are no adverse events in the form of excessive sedation and loginess, or extrapyramidal symptoms. This contributes to adherence to therapy and destigmatization of patients with schizophrenia. The clinical cases presented here demonstrated an improvement in the quality of remission of schizophrenia due to high anti-relapse effectiveness, efficacy against negative symptoms, safety and high tolerability of PP1M and PP3M regardless of patient age. We may conclude that PP3M is no less effective than PP1M.

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The Virus Covid-19 and Dilemmas of Online Technology

Вирус Covid-19 и дилеммы онлайн-технологий

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ABSTRACT

Commentary on the COVID-19 pandemic must necessarily consider the medical issues in social and political context. This paper discusses one important dimension of the context, the long-term history of human activity as intrinsically technological in its nature. The pandemic has accelerated the use of technology to mediate relations between people "at a distance". This involves not only a change in the skills people have (though acquiring these skills has become the central project of work for many people), but changes the sort of person they are. Our notions of "closeness" and "distance", or of "touching" and "being touched", and so on, refer simultaneously to states that are spatial and emotional, factual and evaluative. Inquiry into the differences in human relations where there is physical presence and where there is not raises very significant questions. What are the differences and why are they thought, and felt, to matter? What are the differences when the relationship is supposed to be a therapeutic one? What are the financial and political interests at work in enforcing relations at a distance by new media, i.e., "mediated" relations? How is a person's agency affected by a lack of freedom to move or a lack of face-to-face contact? What happens to all those human relations for which physical presence was previously the norm, relations such as those performed in the rituals of birth, marriage and death, or in activities like sport and the arts? Can it be said that new technologies involve a "loss of soul"? The present paper seeks to provide a reflective and open-ended framework for asking such questions.

АННОТАЦИЯ

Комментируя ситуацию с пандемией COVID-19, медицинские вопросы необходимо рассматривать в социальном и политическом контекстах. В данной статье обсуждается один из аспектов этого контекста – технологический характер человеческой деятельности. Пандемия значительно ускорила использование технологий, которые дали возможность осуществлять взаимодействие между людьми «на расстоянии». Этот феномен повлек за собой не только изменение навыков, приобретение которых стало центральным аспектом работы многих людей, но и изменение личностных аспектов. Наши представления о «близости» и «дистанции», «прикосновении к другому» и «прикосновении другого» и т. д. относятся к состояниям, которые одновременно представлены в пространстве и в эмоциях, несут информацию и оценку. Исследование различий человеческих отношений, когда человек присутствует физически и когда не присутствует, поднимает очень важные вопросы. В чем заключаются эти различия и почему мы думаем и чувствуем, что они важны? Каковы эти различия, если мы говорим о терапевтических отношениях? Какие финансовые и политические интересы стоят за навязыванием при помощи новых медиа отношений на расстоянии – «опосредованных» отношений? Как влияет на человека отсутствие свободы передвижения или отсутствие возможности личного контакта? Что происходит с человеческими отношениями в ситуациях, для которых физическое присутствие всегда считалось необходимым, например, в ритуалах, посвященных рождению,

заключению брака и смерти человека, или в таких видах деятельности, как спорт и искусство? Можно ли сказать, что новые технологии приводят к «потере души»? Задача данной статьи – задать концептуальные рамки для размышлений на эту тему и поиска ответов на эти вопросы.

Keywords: *COVID-19, online communication, technological change, touch, movement*

Ключевые слова: *COVID-19, общение онлайн, технологические изменения, прикосновение, движение*

"NATURAL" HUMAN TECHNOLOGY

There are clouds of commentary, and not a little fog, on the medical dimensions of the impact of the virus Covid-19. Factually grounded surveys of people's reactions and fears, and calls for appropriate online responses, are therefore most welcome. An appreciation of the wider historical and social setting is, however, still needed. The issues are very complex, and in this commentary I focus on the restrictions to people's movement and the rapid shift to online rather than face-to-face encounters. I discuss the shift to technologically-mediated communication. It is true that, for many millions of individuals, digital encounters were a daily, sometimes almost continuous, reality or norm, long before the pandemic. Earlier, however, personal face-to-face meetings accompanied the digital reality, and face-to-face meetings formed a default position or base-line with reference to which people experienced and assessed relations at a distance. Moreover, many areas of everyday activity, including work, childcare, education, rituals of the life cycle, entertainment, conversation, sport and the arts, centred on people physically coming together. During the pandemic, relations at a distance suddenly, literally overnight, became the new norm, enforced by police powers and not freely chosen. In this commentary, I raise existential, as opposed to specifically medical, questions about what happens when people do not physically come together and are not allowed physically to come together, but instead relate via technology.

Humans are by nature instrumental in activity; human beings do not exist and then add technologies to what they do, rather they use technologies to enlarge the capacities they have in their nature: "We are designers by nature".[1] It is wrong to discuss technology merely as a means, available to be used or misused; technology is not "added on" but "given in" the very notion of what it is to be human. Technology is the form of human self-making.

We therefore cannot say that the shift to online relations is unnatural. However, we can ask whether the technological innovation is on such a scale that it marks a break or revolution in history. Observers in other ages reported a sense of overwhelming novelty of the technological change, for example, in response to the speed of movement and the shrinking of distance, with the advent of railway transport. It is commonplace today to refer to the "revolutionary" transformations underway as a result of new biomedical and digital technologies. It is a judgment which follows from the belief that new technologies alter the very nature of being a person by rebuilding or re-engineering the body, whether through genetic manipulation, prostheses, cyborg systems, drugs, surgery, or in some other way. There is similar talk about the "revolutionary" replacement of reality with electronic virtual realities. There is discourse about "the trans-human"; some people judge that the category "human" is so closely associated with beliefs about the fixed character of universal, basic and natural human qualities or capacities, that given the changes that technology now makes possible, it is of no further use. With all this acknowledged, though, it is not clear that contemporary changes are completely novel. We must also question whether we can distinguish what is new from people's experience of what is new.

New technologies appear to challenge the presumption that human nature stays the same, that all people have had and will continue to have large areas of capacity and character in common. Stanisław Lem, half a century ago, accurately foresaw the social event now taking place, the event questioning the very notion of a fixed human nature: "Man remains the last relic of Nature, the last 'authentic product of Nature' inside the world he is creating. This state of events cannot last for an indefinite period of time. The invasion of technology created by man into his body is inevitable".[2] When people use new communications technology, the technology appears to substitute for the body. Yet this could also be

said about the invention of the technology of the wheel, or of the stirrup, technology which enabled people to be carried rather than having to walk.

With these general points in view, it is possible more clearly to formulate the question people are asking: What changes are occurring with the switch, imposed by government controls, from physical encounters to digital encounters between people? We cannot think that people will remain exactly the same when they adapt to physical isolation technologies. I am not making the obvious point that people will have different habits and different skills, though they will, rather I am suggesting that *acquiring these habits and skills changes the sort of person they are mentally, morally, or if you will, spiritually, as well as materially*. At the level of detail, the changes vary enormously from society to society, group to group, situation to situation and individual to individual. It is an empirical matter to study this, as surveys do, while each of us can contribute impressionistic knowledge. I am now suggesting a framework to enable the creation of a general picture.

PHYSICAL PRESENCE AND THE MEDIATION OF RELATIONS

These general points enable us to avoid being trapped by questions about the newness or revolutionary nature of present technologies, or about whether they have entirely new evaluative dimensions. The new technologies and circumstances of isolation pose no absolutely new dilemmas. However, they do give people new experiences and pose social, medical and political choices in *particular* terms.

In all media of communication, including verbal messages, signalling, letters, books, the telegraph, the telephone, radio and TV, a person may have relations with other people who are not physically present, not within touchable range. Individual reactions to working and communicating via contemporary media vary enormously, just as earlier reactions varied. These reactions are laden with values and emotion. *Whenever we talk about closeness and distance and "being in touch" we are at one and the same time talking in spatial, emotional and evaluative terms*. This is how ordinary language works. Technological change cannot but affect emotional and evaluative worlds.

Training and habit are certainly factors in the way people feel the closeness or distance of others when using different media. These factors may be so deeply embedded that they feel natural, though the experience of what is natural is also cultural. We *do*, as matter of fact, in many circumstances, but not all, value the physical presence of others. There are undoubtedly special emotional pleasures and pains associated with this. It has been reported that even teenagers devoted to continuous online relations with friends, in conditions of lockdown began to miss physical presence. Even these people, the most habituated to relations at a distance, find something different in presence. Why is this?

Humans are embodied subjects. Thus, it can be said that if a human is truly present, an embodied subject is present. Online, therefore, "the whole person" is not there. "Presence" is the here and now of embodiment. We may imagine a culture in which the presence of the embodied subject does not matter, but this would not be a human culture as currently understood. Many people will think the physical closeness of mother and new-born child as "natural" because the child is at first embodied in the mother. An influential body of psychoanalytic thought (in the Kleinian tradition) maintains that the qualitative character of literal contact between mother and child, perhaps already in the foetal state, and certainly with contact through lips and breast after birth, determines all subsequent forms of relations. The child does not feed at the breast by Zoom. If a medium, like a bottle, mediates lips and breasts, or if a mother is absent, it follows that the child's psyche develops differently.

It is from being embodied and present that people can "touch" and "move" another person, and themselves "be touched" and "moved". This is language which simultaneously describes the moral, or spiritual, and physical dimensions of life. (It is not a matter of metaphor running from physical to mental worlds, or vice versa, but of commonality of meaning.) The rich content or resonance of such language is lost online. Wholeness in touching and moving, and it may be argued also in healing, requires the embodied person. The importance of touch is widely recognized. It features in a large survey recently carried out in the UK.[3] It is also evident in the large financial investment IT corporations are making in developing tactile media, turning tactile reality into marketable commodities which will not actually require presence. In many circumstances, what we think of as good relations involve physical

contact, are three-dimensional, implicate and respond to the whole embodied person, and involve continuous movement. Think, for example, of the friendship and trust embodied in the handshake, let alone the kiss or placing the ring on the finger.

With physical distance, there certainly can be relationships, but they are different. With modern technology, though relations may still be visually face-to-face, the faces are two-dimensional, more like masks than embodied faces. The people communicating are not in three-dimensional moving spatial relations. There is no touch, and there is no "con-tact". Though in ordinary speech we talk about "getting in touch" and "getting in contact" by email, by phone or by Skype, taken literally this is precisely what all existing communication media do not permit: they do not permit touch or contact. There are many situations in which relations at a distance are much desired, for example, regulating the spread of a virus. However, there are many other situations, such as the relationship between mother and child, or in caring for an ill person, where the opposite is the case. In English, people talk about the importance of "hands-on" experience.

Intimate relations are by no means the only situations in which actual physical presence is thought to be of decisive importance. For example, people have fought wars over claims about the literal physical presence of the blood of Christ in the Christian mass, as opposed to the symbolic presence. Or, consider the wish that people have physically to attend marriages or funerals, though that attendance is symbolic. In the arts there is a wish to attend live performances and not only to watch or listen to a recorded performance or a performance specially created for a digital medium (such as pop music or dance videos). Similarly, people wish to attend football matches, or travel, even though they can see much more, much more clearly, on the screen at home. This kind of argument is not limited to the world of the arts or sport. There is, for instance, a direct parallel in the experience of landscape, in the contrast between moving *in* a landscape while walking, and in gazing as a visitor *at* a landscape.[4]

The concept of *presence* is valuable, as it makes possible an understanding of the difference between a live performance and a recording, of walking in a landscape as opposed to watching a travel film, or of dancing as opposed to watching a dance video. The concept of presence is central to discussions around performance aesthetics; it is also of great importance to healing.

For people in the culture in which I write, concern with existence inescapably involves inquiry into the embodied subject, that is, physical presence. "Being close" or "being distant", "moving" or "being moved", is the source of the very notion of significance, of something mattering. How individual people feel varies, but it is the *mattering* that is the source of the qualities of physical face-to-face encounters. The value that comes with being alive rather than dead, requires the feel of something in relation to something else.[5,6] Things and events have value to people because something in the world "pushes back", something offers resistance. The moving body knows such resistance from the earliest moments of sensory consciousness. This may be expressed in abstract philosophical terms or in concrete psychological terms, recognizing the primary significance of kinaesthetic sensation in the subjective world.

All this confirms "the obvious": in the societies in which we actually live, with the forms of life we have, as a matter of fact people place a great deal of weight on physical presence. The question is whether this is changing as a response to the virus and if it is, what are the consequences of people reducing or diminishing their desire to act with other people who are physically present? In brief, what changes are happening and in what sense can we say they matter? To answer these questions require attention to the social and political implications of closeness and distance, and of the technology that mediates relations at a distance.

AGENCY AND THE TECHNOLOGY OF MEDIA

Particular experiences and practices are infinitely varied, they are highly individual and they are not entirely rule-bound. These are characteristics that machines find difficult to reproduce. This is the subject matter of a film inspired by Herbert Dreyfus, the early proponent of the belief that artificial intelligence machines will not reproduce human actions because human actions involve innovation and risk.[7] The distinctive characteristics of individual practices, or of the practices of the group to which people belong, are felt to be part of what matters about the practices. The imposition of new technologies, whether by commercial pressure or police powers, may threaten or even eliminate such distinctiveness. If the same technologies mediate all relations, the

value that any particular relation has, the *mattering* it has to a person, becomes homogenized, flattened. (There is a logical point at issue here: if there was no differentiation of values there would be no value at all – quality depends on difference.) Value is value to me, and it cannot be dissociated from my embodied difference. If the only permissible route to doing something is the route that all others must take, there is no longer anything of value to defend. This is the dystopian dream of pure instrumentality, everyone doing the same thing through the same technology to achieve the same outcome. It is the power of media technologies to move society in this direction. However, new technologies may at the same time offer new possibilities in practice to those with access to, and mastery of, the technologies.

As the word "media" indicates, contact through a medium, i.e., contact at a distance, creates a space or "medium" where forces or powers are at work other than the will and reason of the communicating people, powers that are embedded in the medium. This is the case for all communication technologies, beginning with gesture and language, and it is emphatically the case for digital technologies. Corporations design and manufacture these technologies, and institutions and governments regulate their use, establishing vast zones in which individuals do not have the power of decision. Media *mediate* political and financial powers. Any judgment about the effects of a switch to online communication must therefore take into account the relations of individual or local agency and the technological agency mediating corporate and political powers. To say this is to say nothing new; there is a considerable amount of discussion of these issues in media and cultural studies. If we think of a person as a locus of individual agency, and if the agency of that person is mediated online, then we have to consider the person as a person in whom a range of social powers is at work. This is how one Greek correspondent, a businesswoman, expressed her new experience of work during lockdown (personal email, June 21, 2020): "**[**it**]** is not a different depiction of reality, not even a different, technologically mediated interaction with reality; it is a different reality altogether, one which is not bound by the rules we, collectively, had negotiated and agreed upon or at least consented to. To exchange one for the other … is to accept a different social contract without even been given the opportunity to understand its implications. From face recognition, to internet trade, to the abolishment of the physical workplace, our immediate understanding of our own life, of our individuality, of our connection to others, is vanishing – to be substituted with what?"

Questions of spatial distance are thus inseparable from questions of agency and power. Everything that exists is in relations – from electrons to people. In stating knowledge of relations, we map an understanding of cause and effect and describe where the power lies to cause something to happen. Being face-to-face with someone, we recognize a person's capacity to influence another person, either directly through physical coercion or caress, or indirectly through speech, emotional display or gesture. This capacity is more difficult to recognize in contact mediated by a technology, since this involves assessing the influence that the technology itself has in the field of relations. Behind the technology is the long and complex history of the workings of powers that have produced the technology and made it available under certain conditions. It is striking and often painful that, for many users of modern digital media, especially for an older generation for whom these skills are harder to acquire, it is the technology that determines the range of options, rather than the will of the person using the technology.

There is deep ambivalence in people's responses. Digital technology *empowers* people by making communication possible where otherwise it would be impossible. Some people, especially children growing up with the technology, feel this creates opportunity. At the same time, these technologies introduce into communicative relationships a large raft of powers to which the people in communication have to conform, and this *disempowers* individual people understood as agents. The emotional distance, and in many cases alienation, that many people feel when "in touch" by digital media, is an expression of this disempowerment. As teachers adapt to teaching online, who is empowered, who disempowered?

Policies to contain the virus require people to go online rather than use transport and public buildings or public spaces in order to work and to meet. Such policies have narrowed the range of choice of communication, requiring people to adopt a restricted range of technologies and, effectively to use those technologies to conform to practices imposed by police powers or by employers. Some people have quickly become comfortable with new conference or teaching technology, others have

not. To become comfortable, people study and train as users of the technology, engage in activities different from the activities which previously defined their occupational identity. Online conferencing illustrates a common phenomenon in the spread of IT culture in general: the technology shapes the time and expertise that people have. The massive advantages this has for management and bureaucracy, bringing diverse activities under a common description, and hence common possibilities for planning and assessment, is all too clear in universities. There is a massive transfer of time, effort and commitment to mastering IT technologies rather than using competencies for activities not so easily planned and assessed. The same process is evident at the level of national governance, in health services, and so on.

CONCLUSION: THE RECREATION OF RELATIONS

All this would seem to confirm the characterization of modernity presented, for example, by the philosopher Heidegger: the contemporary age has an instrumental understanding of Being – all actions and judgments are subsumed by the value of technical efficiency.[8] Observers more sensitive to politics than Heidegger would add that this very much serves the interests of capital and authoritarian government. The capacity to transfer relationships online and recreate relationships in terms of instrumental understanding, is powerful indeed.

The recreating of relationships, this commentary argues, involves narrowing the range of responsiveness. With a person physically present, all the bodily senses are at work. Movement, even if slight, gives the person three dimensions, and there are much greater possibilities for flexibility, subtlety and articulacy in communication because of the involvement of the whole body. Noise introduced by the technology is absent. (By noise, I mean sound or other data which are not part of the communicative act.) It is a large question as to whether there is a lessening of emotional concern online, a tendency towards affectively relating to people as technologically constructed objects rather than subjects. This links with what I am saying regarding the gaze, the constitution of identity and power relations through visual presentation, the look that each person presents to others, and the relationship of each performance artist with their audience. Here again, there is a great deal of literature, much informed by ethnic and gender identity issues. I suggest that perception in two- rather than three-dimensional terms is not only visually different but evaluatively different. In the moral sphere, to recognize three-dimensionality is to recognize complexity, to attribute to the subject of the gaze ("the other"), a richness that a two-dimensional representation does not have. The novel is a paradigm of the three-dimensional form of representation, the advertisement a paradigm of the two-dimensional form. Online relations appear to encourage familiarity with and acceptance of two-dimensional moral relations. This is reduced to parody in recording "like" or "dislike" using the up-turned or down-turned line of the mouth, the two-dimensions that the machine recognizes, emotions reducible to digital relations, on or off, black or white, them or us.

The opposite condition to this technological distancing is the state of literally being "in touch", that is, touching. Touching is the human relationship in which the life-worlds of individuals most materially flow together and each person has the status of a multi-dimensional subject. For this reason, we have large experience and training in learning when to touch and when not to touch. I would add that touching, whether active or passive touching, involves movement, and that the sense or touch is always informed by bodily senses and by the kinaesthetic sense.[5] At an online conference, these senses are narrowed down to mild physical discomfort sitting before a screen on which people in awkward poses speak in a mainly monological manner. Of course, with practice, the online experience may improve. However, if forced to go online, I have to learn to shift my freely chosen way of life and to restrict my mobility.

Physical presence matters not just because it is a habit, but for what we may call existential as well as for moral and political reasons. Lem provided an analogy which helps us to understand this. Discussing the difference between an authentic and a forged painting when only an expert can tell the difference (and indeed when even experts may have different opinions), he wrote: "**[**The forgery**]** is empirically indistinguishable from the original, but is not *the* original, as it has a different history".[3] Analogously, the difference between reality and virtual reality, or between physical presence and contact at a distance, is that these states have different *histories*; they occupy different positions in the stories with which we give meaning to ourselves and the world. Removing the possibility of physical closeness removes the stories,

with all their meaning, that we might want to tell about being significant subjects in meaningful relations. We have to learn to tell new stories – stories imposed on us and, as such, carrying a different meaning. This is a very significant argument. Reality and virtual reality differ for us because they bear a different meaning given by their different histories. An online course of education does not have the same history as a course with teacher and student physically present with each other. Online medical advice is part of a story that differs from "hands-on" contact.

I am tempted to use the language of "loss of soul" in relation to the shift to online practices. This is risky, because the language of soul is open to considerable vagueness and misunderstanding. If I turn to this language, I borrow from what I understand of the world of black slaves in the formation of African-American culture, the culture which spread the reference to soul in modern secular English. Slave culture used the word "soul" to refer to the individual quality of a person, imagined in ideal terms, the quality that is not and cannot be the property of another person. The soul, understood in this way, can be killed or destroyed, or possessed by an alien spirit, but it cannot be bought or sold. If people "sell their soul", the soul is lost. By analogy, if something is said to have soul, it is said to have value that cannot be exchanged for something else (especially money). Thus used, reference to soul does not refer to an "I" but to a condition of being in relationship to value. To be "soul-less" is to be in a place or time where no such value is possible or imaginable. This language, I want to make explicit, does not argue for the soul as a metaphysical or transcendent entity but refers to a culturally embedded conception that certain kinds of human relations, existing in particular social times and places, cannot be exchanged. Such conceptions are individually and collectively central to many people's sense of purpose and identity.

IT technologies narrow down the scope of soul as a viable category of self-understanding. Large social institutions, especially corporations and governments, have an interest in narrowing the scope of soul, because it is by definition outside of ownership and regulation. Thus, the fear is that policies of lockdown hurt the soul. Face-to-face encounter has the potential to restore the scope of the language of the soul.

It is the thrust of this essay that technologies change ways of life and forms of being human. The transformation of media technologies was well underway before the Covid-19 pandemic, but the virus very much speeded it up. The rate of change has been central to the way people have reacted. The sudden spread of the new technologies in conditions of isolation has forced even conservative users of technology to question any conventional separation between natural and technologically mediated activity. Policies imposed in response to the virus have accelerated a pattern of change, rather than imposed anything new, bringing more people, more quickly, under new regimes of management and governance, making everybody, and not just those already fully engaged with online relations, face the relativity of the natural/technological distinction.

The sudden switch to online relations has dislocated many people's everyday ways of sustaining relations and meaning. There has been damage to feelings of self-agency and identity that heretofore depended on direct contact with other people. In these circumstances the resulting change in attribution of agency, or causal power, has varied hugely with individual, social, economic and political context. Nevertheless, it is surely right to say that the pandemic very rapidly led governments to enhance the agency of the technology, and through the technology enhance the agency of those social institutions which can use the technology for their own ends. These institutions are, firstly, governments themselves, secondly, the corporations that design and supply the technologies, and thirdly the institutions like universities or health services that use the technologies to take greater control of the lives of the people they employ and, in principle, serve.

The internet is a technology for creating relations "out there", in space, or hyperspace, though this too is a social space. People who live on the internet live differently from people who do not; literally, their identity is different. If, because of the virus, or because of the attractiveness of new powers of technologically-mediated governance, we are all forced online for everything, then the identity of being a person changes. Life has a different history and a different meaning.

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To Say or Not to Say: Medical and Social Project

Медико-социальный проект «Сказать не могу молчать»

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ABSTRACT

Mental health and psychological education activities are being carried out in Moscow (the Russian Federation), along with measures aimed at prevention of social stigma in mental health care. The medical, social and educational project *To Say or Not to Say* has been developed by a group of experts from the Mental-health clinic No. 1 named after N.A. Alexeev, for Moscow residents. The title chosen for the project urges participants to make a choice: continue living with their problems or take a step towards solving them. A new educational activity format has been created and tested in the course of the project, and this format provides an opportunity to largely overcome the stigmatizing barriers that prevent people from seeking psychological and psychiatric help in Moscow. Sixteen events involving over 7,000 citizens have been held, and the psychiatrists engaged in the project have spent 2,280 man-hours in this volunteering activity. We believe that this educational activity could help to overcome social stigma in psychiatry, further research is needed to measure the effect of our educational project on social stigma associated with mental health.

АННОТАЦИЯ

В Москве (Российская Федерация) ведется работа в области психопрофилактики и психопросвещения, а также проходят мероприятия по дестигматизации в психиатрии. Группа специалистов ГБУЗ «Психиатрическая клиническая больница №1 им. Н.А. Алексеева ДЗМ» для реализации в городе разработала просветительский медико-социальный проект «Сказать не могу молчать». Смысл этого словосочетания-амфиболии состоит в том, где поставить запятую, оно побуждает участников сделать свой выбор – продолжать жить с проблемой или шагнуть навстречу к ее решению. В ходе проекта разработан и опробован новый формат просветительских мероприятий, позволяющий в значительной мере преодолеть стигматизирующие барьеры перед обращением за психолого-психиатрической помощью к специалистам у населения на примере города Москвы. Проведено 16 мероприятий, в которых приняли участие более 7000 горожан, 2280 человеко-часов было затрачено специалистами-психиатрами на волонтерской основе. Мы предполагаем, что описанная психопросветительская работа может помочь дестигаматизации психиатрии. Влияние нашего психопросветительского проекта на преодоление стигмы психических расстройств необходимо оценить в рамках исследовательского проекта.

Keywords: *education, stigma, prevention of social stigma, mental disorder, psychiatry*

Ключевые слова: *просвещение, стигма, дестигматизация, психическое расстройство, психиатрия*

Tolerance, declared to be a civil society standard in the Declaration of Principles on Tolerance at the UNESCO General Conference on 16 November 1955, has since attained even higher status and is now seen as a moral imperative. This is a widely accepted fact. Generally, the term *tolerance* means tolerance of any other view of the world, lifestyle, behaviour and customs. Furthermore, it is important to understand that tolerance is not equal to indifference.

People with mental and behavioural disorders often experience social stigma. According to the World Health Organization, breach of freedoms and limitation of civil, political, economic, social and cultural rights for people with mental disorders are typical of many countries and take place both inside and outside healthcare facilities.

Social stigma is distressing not only for patients but also their families. Mental illness in a family member often causes alienation from other family members, which is why families may attempt to hide this fact, thus creating barriers between the person who is sick and access to modern professional medical assistance. People who need psychiatric care do not seek doctors' assistance promptly due to psychological patterns and social stereotypes. This causes further emotional stress in addition to that caused by the mental illness itself, which makes individuals feel different from other people, and worsens social adaptation by preventing sufferers from living a normal social life. It also makes them feel guilty. Such people often experience a sense of social stigma that is directed towards themselves, with different reactions to the disease being internalized.

A more tolerant attitude towards people with mental disorders may be created, firstly, by means of prevention of social stigma – by various actions aimed at gradually easing off stigmatizing perceptions of a sick person. It is therefore important to inform people about any social prejudice and help society understand the psychological nature of people and the risk factors that may cause mental diseases.

The Department of Health, Department of Labour and Social Protection, and the Ministry of Civil Defence, Emergencies and Disaster Relief of the Russian Federation are now working in Moscow (Russia) on prevention of mental and behavioural disorders, and development of a behavioural health system. The Moscow Psychological Counselling Service has been created with a 24/7 psychological support hotline. The centre for emergency psychological assistance of the Russian EMERCOM renders psychological assistance to people who have suffered in emergency situations and to people who have found themselves in complicated conditions. Moscow's psychiatric service organizes different events, conferences and forums, including those on prevention and public education.

Taking into account the need for real progress in mental health and psychological education, and measures to prevent social stigma in psychiatry, the group of experts of the Mental-health clinic No. 1 named after N.A. Alexeev, led by Chief Psychiatrist of the city of Moscow, Professor George P. Kostyuk, has developed the educational, medical and social project *To Say or Not to Say*, for the city. This phrase urges participants to make a choice: continue living with their problems or take a step towards solving them.

Moscow's Chief Psychiatrist, Prof. George P. Kostyuk (*on the left*), and President of the Interregional Non-Governmental Organization of the Psychiatrists' Club, Arkadij L. Shmilovich (*on the right*), at the event related to the *To Say or Not to Say* project, in Zurab Tsereteli's gallery (22 November 2018). Photo by Aleksandr Iu. Shchapin.

Group psychological training, part of the *To Say or Not to Say* project in Zurab Tsereteli's gallery (22 November 2018). Photo by Aleksandr Iu. Shchapin.

Individual counselling, part of the *To Say or Not to Say* project in Dom na Brestskoy (13 October 2018). Photo by Aleksandr Iu. Shchapin.

Considering aspects of such a complicated subject as stigmatization of patients with mental disorders in society, the team has made the project modern and unique. It is far removed from classical ideas of psychiatry, mental disorders and defects in people's mental health. The event is for the general public: young people and students, middle-aged and elderly people, families with children, family members and close friends of people with mental disabilities.

Individual counselling, part of the *To Say or Not to Say* project in Zurab Tsereteli's gallery (22 November 2018). Photo by Aleksandr Iu. Shchapin.

The idea of "open psychiatry" was used as a foundation for the project's communication strategy, as society generally sees psychiatry as a closed, rather negative medical domain with lots of myths. To disprove these notions, it was decided to go beyond social stereotypes. Creation of a sustainable system of efficient dialogue between healthcare professionals and people outside hospitals became an organizational component of the strategy.

As the *To Say or Not to Say* project is particularly complex, each meeting lasts for five–six hours. The programme includes medical and therapeutic interventions (psychological and psychiatric consultancy support; psychodiagnostics and testing; art therapy workshops), information and education (science education lectures on psychiatry, online educational webinars, etc.), and creative components (musical, poetic and theatrical sketches performed by inclusive teams, and exhibitions of work created by artists who have experience of psychiatric disorders etc.).

A unique feature of the project is its informal and trusting atmosphere, which helps participants understand that they are not alone in their need for such assistance, support, relief and removal of barriers. The core of each campaign (and a key part of the project) is a lecture about mental health, which is, at the same time, the subject of the meeting. The meeting programme was devised to ensure that each participant can take part in most of the activities, depending on his or her interests. Voluntary consultants, workshop speakers

Workshop by renowned caricaturist, artist, essayist and former psychiatrist Andrei Biljo. *To Say or Not to Say* project's event in the *Blagosfera*, community center and creative spase (27 January 2019). Photo by Aleksandr Iu. Shchapin.

Workshop by Russian artist and sculptor Zurab Tsereteli, part of the *To Say or Not to Say* project in Zurab Tsereteli's gallery (22 November 2018). Photo by Aleksandr Iu. Shchapin.

and lecturers include employees of all specialized health clinics providing psychiatric assistance: psychiatrists, psychotherapists, clinical psychologists, social work specialists and administrative staff.

The project has been functioning since 2018; offline educational campaigns (not internet-based) are held for Muscovites on a monthly basis, on a weekend day, in public and cultural zones of Moscow, during which participants can access the full range of expertise offered by Moscow's psychiatric service. In total, there were nine campaigns within the project for Muscovites in 2018 and seven in 2019. The total number of project participants during this two-year period was 7,000.

Most of the participants during all periods of the project were young people aged 19–25, i.e., people whom the team primarily focused on. The event was also popular among participants from other age groups, which, of course, proves its universal nature.

It is interesting that the largest number of attendants of all ages was in October and November 2018–2019. During these months, the project was implemented as a large-scale, city-wide campaign, and it coincided with both World Mental Health Day and Psychology Day. This has also contributed to its popularization and the active involvement of new participants.

Community organizations, mass media and social activists also joined the project.

By providing Muscovites with a positive experience of complex educational psychological work, the project has demonstrated its social significance and efficiency, covering a vulnerable social group – people with mental disorders and borderline states who feel psychologically uncomfortable and require consultations but are not yet ready to seek psychological and psychiatric assistance in healthcare institutions.

The following tasks have been carried out as part of the work performed:

1. The public's attention has been drawn to the need for discussion of people's mental health, considering the continual changes associated with the pace of life in modern societies and the appearance of new stress factors;
2. A trust-based dialogue platform has been created, especially for young people, addressing the matter of mental health, and measures have been put in place to overcome the barrier between users of psychological and psychiatric assistance and the specialists who provide such assistance;
3. A trust-based attitude to psychotherapists, psychiatrists and psychologists has been formed by providing regular, specialized advisory assistance and a mutual search for solutions and ways to solve problems;
4. Understanding of the lives of people who have experienced psychiatric problems has been expanded by demonstrating their creative abilities;
5. Different media have been incorporated into the project (to varying degrees), with a focus on creation and elaboration of a modern language for the media environment in this area and a respectful attitude towards psychiatry.

The project is currently active, and due to the COVID-19 pandemic, the main psychological and educational efforts are being implemented online.

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