First-Episode Psychosis in a Managed Care Setting: Clinical Management and Research

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The rapid growth of managed care organizations (MCOs) in mental health care has had a profound influence on treatment of and research on most psychiatric disorders, including schizophrenia, one of the most debilitating and costly diseases worldwide (1). An important role of MCOs is to determine whether medical services are clinically necessary and covered under the insurance contract. However, practitioners increasingly find that MCOs use their authority to influence patient care decisions in favor of reducing costs over ensuring best clinical practice (2). This raises the concern that cost-containment efforts now imposed by MCOs leave patients who have schizophrenia vulnerable to suboptimal care. In light of this concern, providing care for patients with first-episode psychosis can be particularly challenging. While patients and their families often struggle to understand and accept that these patients have developed a severe and potentially chronic mental illness, the patients require high levels of psychotherapeutic, pharmacological, and social interventions. Furthermore, effective intervention at this juncture could be critical in determining long-term patient outcome (3).

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The advent of atypical antipsychotic medications has increased pharmacological options in the treatment of psychosis. Most newer agents have fewer adverse side effects and appear to have certain treatment advantages, including the prospect of superior therapeutic efficacy and tolerability, that would potentially enhance compliance. This has generated tremendous research interest, and studies are now evaluating the merits of atypical antipsychotics as first-line agents. Given the ever-increasing penetration of MCOs in the U.S. health care system, these companies are now encountering patients in their plans who opt to enroll in such treatment studies. In our experience, the attitude of MCOs toward member participation in antipsychotic treatment studies exists on a spectrum. Some companies support such enrollment and facilitate a patient's transition into a study. Other companies are hesitant and may impede study enrollment.

Thus, the complex triadic relationship of the patient, physician, and MCO can increasingly be shaped by research enrollment as well. We present the case of an adolescent patient with first-episode psychosis who was admitted to an academic medical center under a managed care plan and was found to be eligible for an antipsychotic treatment study. The case highlights the challenges encountered in this treatment experience.

Case Presentation

Lisa (pseudonym) was a 17-year-old single African American girl brought to the emergency department by her father, who reported 3 days of strange behavior. Lisa was experiencing auditory hallucinations, was responding to internal stimuli, and had disorganized thoughts and behavior (e.g., pouring drinks on herself and throwing food on the floor). Further history revealed that Lisa had been acting oddly since withdrawing from 10th grade 1 year before admission. She had become increasingly fearful, often refusing to go outdoors, and was sometimes observed to be talking to herself. Her hygiene and sleep pattern had deteriorated steadily, and she had lost about 50 lb during the year, weighing 130 lb on admission. She used cannabis several times per month and lived with a physically abusive boyfriend. She had no previous significant psychiatric or medical history. Her family history was notable for a great aunt with psychotic depression. Lisa's parents had divorced when she was 7 years old. She was the product of an uncomplicated pregnancy, and she had reached all early developmental milestones. As a child, she had normal peer relationships and average scholastic performance. Thus, her premorbid status appeared to have been unremarkable.

Lisa was admitted (day 1) to the adolescent psychiatric service under a managed care plan provided through her mother's employer. A full medical workup was performed and included a computerized tomography scan of the head, EEG, chest X-ray, and ECG; all results were negative. The results of initial laboratory studies, including complete blood count (CBC), liver function tests, urinalysis, and measurement of serum electrolytes, glucose, thyroid-stimulating hormone, vitamin B_{12}, and folate, were all within normal limits. The results of rapid plasma reagin and Lyme serologies, a urine toxicology screen, and a test for beta human chorionic gonadotropin (β-HCG) were negative.

On day 2 Lisa hit a staff member. She was placed in seclusion to avoid harm to herself or others. However, her agitation escalated, and she received several intramuscular doses of haloperidol (7 mg total) for safety. She refused to eat and drink or to perform basic self-grooming behaviors. She had a paucity of speech except to ask repeatedly, "Is it okay?" and "Why am I here?" On day 3, after parental consent had been obtained, treatment with risperidone, 1 mg b.i.d., was initiated. She took medication only after much prompting and reassurance. She reported some neck stiffness that day, thought to be mild dystonia. The stiffness responded to 50 mg of diphenhydramine.

On day 5 Lisa was evaluated by the schizophrenia research team as a potential candidate for a double-blind, randomized study of first-episode psychosis using either haloperidol or olanzapine. Comprehensive psychiatric inpatient and outpatient care would be provided at no cost (to the patient or her insurance company) for 2 years from the day of enrollment. Because Lisa was a minor, her parents would have to provide written informed consent, while she would need to give assent to participate. The study staff met with Lisa's parents to provide information about the study and additional psychoeducation about new-onset psychosis. Her parents stated that they would need several days to decide and wanted to explore all available options for their daughter.

As with most first-episode patients, the initial treatment period was difficult for both the patient and the family. They were struggling to understand the nature of the psychotic symptoms and the long-term implications. Lisa had demonstrated virtually no insight into her illness. For patients with psychotic disorders, lack of insight is common. On the other hand, family members are often aware of a change in the patient's behavior and thinking, and the family can feel confused, frustrated, and frightened. These feelings may not be allayed as they begin to learn about schizophrenia, including the uncertainty about etiology, pathogenesis, course, and the limitations of treatment, including the potential lack of medication efficacy and/or undesirable side effects. Because of the difficulty of understanding schizophrenia, the decision of whether to enroll in a research study can be challenging. Also, recent negative media reports have generated some public distrust of psychiatric research in general. The importance of research clinicians' demonstration of sensitivity to all these issues cannot be overemphasized.

By day 6 the risperidone dose was increased to 2 mg b.i.d., and benztropine, 0.5 mg b.i.d., was added for mild parkinsonism. Although Lisa had become more trusting of the staff and slightly less disorganized, she still required much redirection in tasks such as dressing, bathing, and eating and considerable coaxing to take medications. She had perseverative thoughts and attended to internal stimuli. She continued to receive nursing checks every 15 minutes.

From the day of admission, the MCO called for daily updates on Lisa's progress. One day after risperidone treatment was begun, the MCO representative stated that the dose was being increased too slowly. Given Lisa's early signs of extrapyramidal side effects and ongoing difficulty with medication compliance, the treatment team was reluctant to advance the antipsychotic dose too rapidly, but ultimately, because of Lisa's gradual therapeutic response and the encouragement of the MCO, the dose was escalated. By day 7, certification for further inpatient care was denied. In the first peer-to-peer case review that followed, Lisa's attending psychiatrist was told by the MCO psychiatrist that Lisa should be an outpatient by this time and that her antipsychotic dose had been titrated too slowly. During this first review, the MCO psychiatrist was informed of Lisa's disorganization, paranoia, poor food intake, inability to perform activities of daily living (e.g., she would stand still in the shower until helped with water, soap, etc.), medication-induced side effects, and frequent refusal of medications. He replied that the MCO philosophy was to focus on intensive family work and that, with frequent outpatient visits, Lisa's parents could now take care of her. He said he understood the attending psychiatrist's difficult position, given his responsibility for the patient, but that the majority of these patients do no worse if sent home before their psychosis clears. Attempts were made to educate the MCO reviewer regarding the importance of treating first-episode psychosis effectively and to explain how effective treatment at this point may reduce future morbidity and decrease the risk of rehospitalizations. The MCO psychiatrist did not change his decision to decertify, but the attending psychiatrist did not discharge Lisa, because of the severity of her psychosis. An appeal was filed for the decertification.

Lisa's clinical course to date highlights several important aspects of treating new-onset psychosis. First, a common belief is that higher antipsychotic doses generally produce a better antipsychotic effect. However, McEvoy et al. (4) found that the majority of patients with acute psychotic symptoms typically respond to low doses of antipsychotic medication (e.g., 2–4 mg/day of haloperidol). The same study also showed that a substantial dose escalation for initial nonresponders does not improve the response rate (4). Moreover, comparisons of the treatment responses of patients with first-episode schizophrenia and those with chronic, multiepisode schizophrenia have shown that first-episode patients require doses that are as much as 50% lower (4, 5). Lisa had developed some rigidity while taking 2 mg b.i.d. of risperidone, and this situation made continued dose escalations undesirable. Since Lisa had demonstrated a few signs of clinical improvement and the dose fell within a clinically effective range (6), further dose escalations were not felt to be necessary at this time.

Another common belief is that rapid dose escalation will necessarily speed up the antipsychotic effect. While it is well known that dopamine receptors are rapidly blocked

after a few doses of most antipsychotic medications, the onset of antipsychotic effect usually takes days to weeks to occur (7, 8). To our knowledge, no studies have demonstrated that one antipsychotic acts more rapidly than another. Also, while first-episode patients are highly responsive to treatment and are able to achieve a good outcome, they often require an extended period of time to improve (9). Within this population, clinical response appears related to specific patient characteristics. An important predictor of both the response rate and the degree of response in first-episode psychosis is the prior duration of illness. A longer duration of untreated illness correlates with longer time to remission and a smaller degree of remission (10). Other factors that correlate with poorer symptom response include male gender, early age at onset, insidious onset without precipitating factors, negative symptoms, family history of schizophrenia, poor premorbid history, and lack of support systems (11). Lisa's first psychotic symptoms were noted about 1 year before admission, occurred at an early age, and developed insidiously without precipitating factors. Mitigating these negative prognostic factors were Lisa's gender, her good premorbid history, and the lack of family history of schizophrenia.

The MCO's decertification of Lisa after 1 week of inpatient treatment was difficult to understand given her serious clinical condition. The MCO's stated focus on intensive outpatient treatment, although laudable and appropriate when a patient can safely be discharged from the hospital, did not seem justified in this instance since Lisa was too psychotic to perform most activities of daily living and needed constant attention. She was at considerable risk of self-injury owing to her level of disorganization. Realistically, this type of care can rarely be provided by family caregivers under the best of circumstances, especially not by a single parent. Lisa routinely resisted taking her medications, and her risk for noncompliance outside of the hospital would have increased dramatically. The MCO's complaints that the risperidone dose was not being increased rapidly enough and that the dose was not high enough are not substantiated by available research.

Finally, this MCO reviewer was not very receptive to our efforts to educate him about first-episode psychosis and the long-term benefits of effective initial treatment. However, educating MCOs about chronic mental illness and linking short-term treatment approaches with negative outcomes has proved successful in similar clinical scenarios involving attempts to obtain longer inpatient certification, as described by Bailey (12). In seeking certification for costly services, such as longer inpatient treatment, the long-term financial advantages of such treatment must be emphasized. If the case is framed in economic terms, the MCOs are more likely to be receptive. Although this approach may not always be successful, it can increase physician control in relationships with MCOs.

On day 7 Lisa's parents indicated that they did not wish to enroll their daughter in the research study. The research staff informed the parents that if they changed their minds, Lisa could be reconsidered for the study in the future. When their reluctance was explored, the parents revealed that the MCO social worker felt that the research protocol was a poor option for their daughter and that Lisa was considered for the study because the attending psychiatrist did not know how to treat her illness effectively. The parents had also repeatedly been informed by the MCO that Lisa was ready for discharge. The parents were confused by this information since it countered the attending psychiatrist's recommendation, and they knew their daughter was still very ill. The staff of the adolescent ward spent more time educating the parents about the course and treatment of psychotic disorders and reassuring them that their daughter was receiving the highest level of care.

On day 10 the attending psychiatrist had a peer-to-peer review with a second MCO psychiatrist to appeal the decertification. This psychiatrist agreed that Lisa needed continued hospitalization and therefore reversed the denial. By day 11 the risperidone dose had been increased to 2.5 mg in the morning and 3.0 mg at bedtime because of her persisting positive symptoms. Lisa was slowly becoming more communicative, although she still needed much prompting to perform activities of daily living. Unfortunately, her extrapyramidal side effects worsened, and she developed orthostatic hypotension; therefore, the risperidone dose was reduced to 2 mg b.i.d. On the same day, a message from the MCO social worker stated that 1) the risperidone dose was not being increased rapidly enough, 2) sertraline should be added since the case might be depression with psychotic features, and 3) the attending psychiatrist was not working as a team player with the MCO and that the chairperson of the department of psychiatry had been notified.

The MCO was unequivocally opposed to Lisa's participation in a research study despite the fact that the study would shoulder the full financial burden of treatment from the time the consent form was signed. In part, the MCO appeared concerned that study enrollment might delay discharge if Lisa did not meet the enrollment criteria. But the MCO also seemed to believe that Lisa was being referred for the study because the attending psychiatrist was unable to treat her. By communicating this belief to Lisa's parents, the MCO caused them confusion and concern and risked splitting the alliance between the treatment team and the parents. Although we felt that the MCO had breached an ethical boundary, its staff appeared to feel that their active intervention in the therapeutic relationship between the patient and treatment providers was entirely appropriate. The case highlights the influence that MCOs can exert over treatment decisions regarding severe mental illness given the increasing trend of direct communication between MCOs and patients. Since these communications cannot be monitored or easily regulated, it is important for treatment providers to have frequent contact with patients and their family members regarding

information received from MCOs about all aspects of treatment and services provided or denied.

Communicating with a reviewer should be the initial method of seeking cooperation from the MCO when one of its enrollees seeks to enter a research study. However, initial reviewers and even more experienced reviewers who handle appeals still remain unreceptive to research studies that would seem to offer the MCO advantages. This may be due to the inflexibility of the guidelines under which these reviewers operate. In such instances it can sometimes help to discuss the financial advantages of a study with persons in higher management positions, who may have greater flexibility and authority to change standard procedures. Previously this approach has been successful, and in some cases we have actually received referrals *from* MCOs for study consideration. However, in the present case we were unable to get access to MCO officials beyond the clinical reviewers.

At this stage of treatment, Lisa's medication side effects were worsening. One of the main difficulties in schizophrenia treatment is how to achieve long-term medication compliance. Medication-induced side effects have been found to account for noncompliance (13), as have poor insight, lack of family support, and comorbid substance abuse (14). There has been little research on medication compliance by adolescents, but it appears that substance abuse, side effects, and noncompliance with psychotherapy all predict medication compliance in this group (15). For Lisa, an adolescent who lacked insight, used cannabis, and was developing extrapyramidal and orthostatic side effects, efforts were made to address these barriers to compliance. Lisa received regular psychoeducation and substance abuse counseling. As extrapyramidal side effects emerged, benztropine was added. In response to the orthostatic hypotension, a transient dose reduction was felt necessary to avoid potential falls and to reduce the side effect.

Lisa had persistent hypotensive episodes over the next few days along with a low-grade fever (≤38.1°C) and malaise. A CBC revealed mild anemia (hemoglobin, 11.1 g/dl, down from 14.8 g/dl on admission). Staff of the internal medicine department were consulted. They ruled out blood dyscrasia and more severe hematologic infections but diagnosed an upper respiratory infection and recommended treatment with azithromycin. The etiology of the anemia remained unclear, but the hemoglobin level was judged stable, and periodic monitoring was recommended.

On day 14 the first MCO psychiatrist called the attending psychiatrist to state that hypotensive episodes should not prevent escalation of the risperidone dose. He again suggested that the attending psychiatrist was trying to refer Lisa to a research study because he was not able to treat her psychosis adequately and that Lisa would already be better if the MCO's recommendations had been followed. Furthermore, he stated that it was the mother's responsibility to take care of a sick child at home even if this meant quitting her job (Lisa's mother worked in a knitting mill and had limited vacation time and sick leave). This time, however, the case remained certified.

Lisa continued to improve. By day 18 she was more functional, performing most grooming and toilet-related behaviors appropriately. She was still disorganized but was able to participate in some structured group activities. She attended to internal stimuli and admitted to auditory hallucinations. Her paranoia was reduced, but she remained guarded. She stated she did not like the medications because of dizziness, muscle stiffness, and dry mouth. She then informed the staff that she would not take the risperidone after discharge. Therefore, on day 21 a cross-titration to haloperidol was initiated so that Lisa could begin treatment with a decanoate antipsychotic.

Also on day 21 another peer-to-peer review occurred. The first MCO psychiatrist was quite hostile and made derogatory remarks about Lisa's treatment. He insisted that she be discharged that same day. The case was decertified for a second time, but Lisa was not discharged. At this time a complaint was filed with the state insurance commissioner regarding the difficulties experienced in receiving approval for services and the behavior of the first MCO psychiatrist in particular.

Given MCOs' relative immunity in today's health care system, there is no easy recourse against an MCO that may have breached an ethical boundary or interfered with clinical care. However, when such situations arise, complaints can be filed with state insurance commissioners, who then decide whether to pursue an investigation. Therefore, it is important that all communications with MCOs are well documented in patient charts to facilitate any such investigation. In this case, we filed a complaint with the insurance commissioner based on the potential interference that the first MCO psychiatrist could have had in Lisa's treatment rather than on actual harm or interference. The treatment team had fostered a sufficiently strong alliance with the parents that they did not respond adversely to the MCO's direct communications about the care their daughter was receiving. It was also a concern that the MCO reviewer attempted to dictate care so adamantly given his distance from an actual patient-physician relationship. The insurance commissioner decided not to launch a formal investigation into this case on the basis that no actual harm was done. Nevertheless, just as Bailey (12) suggested that psychiatrists should establish a track record of appealing denials for the certification of care, we also feel that consistent (if not necessarily frequent) filing of complaints to state insurance commissioners for actual or potential harm to patient care is important for several reasons. First, even if an investigation is not pursued, the insurance commissioner's office can be alerted to patterns of behavior of particular MCOs that may over time reach a threshold for investigation. Second, it sends a clear message to the MCO that physicians and/or hospitals will take an active role to protect their patients' interests. This may deter MCOs from repeating

similar behaviors in the future, since sanctions from state regulators could harm an MCO's reputation and have financial repercussions.

On day 22, although unaware of the latest decertification, Lisa's parents were reconsidering the study. On day 24 a meeting between the parents, Lisa, and the research staff was held to discuss the study further. Lisa seemed to be gaining some insight into her illness by indicating her willingness to take medication. On day 25 Lisa gave assent and her parents provided informed consent for her participation in the study.

Lisa began the study screening phase, which included administration of a broad array of structured psychiatric rating scales to verify her diagnosis and to assess the current severity of her symptoms, as well as a battery of blood and urine tests to rule out any exclusionary criteria. During the screening period Lisa continued to take haloperidol, 2 mg b.i.d. On day 28 the laboratory results revealed a positive serum β-HCG test (repeated and confirmed), excluding her from the study. As noted earlier, the result of her admission urine β-HCG test was negative. On day 32 a consultation with the obstetrics and gynecology department demonstrated a 7.5-week intrauterine pregnancy by ultrasound. In retrospect, the pregnancy likely accounted for the unexplained anemia and intermittent malaise.

Lisa was not surprised to learn that she was pregnant. She had continued to take haloperidol during the screening phase and had continued to improve, interacting more socially, becoming less disorganized, and attending less to internal stimuli. Her insight into having schizophrenia remained limited, but she agreed to continued taking medication after discharge. Given her pregnancy, it was decided not to administer haloperidol decanoate. She would take haloperidol, 2 mg b.i.d., and prenatal vitamins and would have frequent follow-up appointments in both the psychiatry department and the high-risk obstetrics and gynecology clinic. Her mother would monitor Lisa's medication compliance. Lisa was discharged into her mother's care 35 days after admission.

Lisa and her parents were disappointed that she was ineligible for the study. However, it was fortunate that her pregnancy was discovered before discharge so that appropriate prenatal care could be arranged. The decision of whether to administer haloperidol decanoate to Lisa was influenced by many factors. Although haloperidol is not known to have teratogenic effects, efforts should always be made to minimize the exposure to and dose of all medications during pregnancy (16). Furthermore, even schizophrenic patients who firmly deny having a mental illness often remain fully compliant with oral medication regimens. In first-episode psychosis it can be difficult to assess the future level of compliance. The conversion to haloperidol was undertaken to facilitate the use of the decanoate form of medication. When that option was discounted because of Lisa's pregnancy, another option would have been to switch to a different atypical antipsychotic. However, this alternative raised the concern that Lisa might experience adverse effects or less therapeutic response and would not comply. In order to maximize our alliance with Lisa, who continued to have limited insight but was pledging to take her medication after discharge, low-dose oral haloperidol was continued.

One of the MCO's earlier concerns was that participation in the research study would delay discharge if Lisa did not meet the entry criteria, thereby increasing the MCO's costs. Clinical studies are often designed to maintain prestudy pharmacotherapy during the screening phase, reducing concern that clinical deterioration or relapse will occur if subjects do not meet entry criteria. In this case, Lisa's clinical care was not altered or delayed as part of the screening process. Admittedly, if Lisa had qualified and started taking the study medication, it is possible that clinical deterioration could have occurred, forcing study withdrawal. However, the risk of deterioration during treatment of psychosis always remains, even when patients are maintained with stable doses of medication.

It is recognized that MCOs affect clinical research in general and that this influence will continue to escalate (17). Moy et al. (18) demonstrated an inverse relationship between growth in National Institutes of Health funds during the past decade and MCO penetration within U.S. medical schools. Although causality for this correlation has not been established, possible reasons include 1) clinically derived funds for research may be reduced, 2) clinician researchers must spend more time in clinical care with less time for research, and 3) access to patients may be falling as a result of MCO enrollment (18, 19). Although many MCOs view research as yet another impediment to financial profitability, research represents a means to develop improved treatments that can reduce morbidity and mortality. These advances can ultimately lead to reduced health-related costs in the treatment of severe mental illnesses, which currently are costly to treat because of inadequate treatment options for many patients. Stronger efforts must be made by academicians to demonstrate the benefits of research to MCOs in reducing costs and improving patient care (20). If MCOs can recognize research as a necessary element in their success, then the relationship between academic research centers and MCOs can become more productive.

Discussion

The treatment of schizophrenia has advanced in several areas over the past decade. Since their introduction, atypical antipsychotic medications have been shown to have lower levels of side effects than are produced by conventional neuroleptics and to be more effective for multiple dimensions of the illness (21, 22). The effectiveness of lower doses of antipsychotic medication has been demonstrated, particularly for first-episode psychosis (4). Also, research on first-episode psychosis has shown that the first treatment intervention for the initial episode of illness is a critical opportunity to influence the long-term course

and outcome of the illness. Studies have demonstrated correlations of better long-term outcome to 1) short duration of active psychosis and 2) fewer relapses (10, 23). This is a compelling argument for ensuring adequate treatment response before hospital discharge and taking steps to enhance medication compliance. Furthermore, this approach should lead to long-term cost savings by reducing the risk of rehospitalization.

The case described in this report highlights an emerging trend: the demand by MCOs for standardized treatment regimens and the expectation of rapid therapeutic response of severe mental illness. Research has clearly demonstrated that schizophrenia is a heterogeneous illness with tremendous variations in symptoms and treatment response. Expectations of defined remission times for individual patients are not possible with the currently available treatments. The course of recovery for first-episode patients is often prolonged, and treatment that is rushed or truncated can unnecessarily lead to incomplete recovery, subsequent relapses, other complications in patients' social and vocational situations, and potentially even suicide. For third-party payers, framing schizophrenia as an illness with a standardized course and treatment may have short-term financial advantages. However, possible consequences include 1) compromise of patient outcomes through incomplete inpatient treatment, 2) loss of trust in physicians and the mental health care system by patients and their families, 3) acceptance throughout the insurance industry of standards that are not based on scientific evidence, and 4) vulnerability of physicians, especially trainees, who are in frequent communication with MCOs to assimilate such standards into their own understanding and treatment of schizophrenia. It may be understandable, if not acceptable, that MCOs give higher priority to cost-reduction measures than to best clinical practice, since their ultimate responsibility is the fiscal health of their companies and shareholders. Therefore, the onus falls on physicians and academic leaders to educate MCOs, legislators, and the public at large about standards of care for serious illnesses so that arbitrary standards are not adopted solely on the basis of cost.

Finally, clinical research is integrated into the patient care enterprises of most academic medical centers in the United States. MCOs can benefit both in the short and long run from this research. Short-term benefits include the substantial savings in patient care costs (e.g., medications, physician visits) while a patient remains enrolled in a study. Long-term benefits may be considerably more significant, particularly for an illness such as schizophrenia, which is associated with $20 billion in annual direct costs and about which knowledge remains limited. Nevertheless, many MCOs remain to be convinced of these benefits. In part, this situation is related to the need for cost-reducing measures in the intensely competitive managed care industry. But we also believe that MCOs lack sufficient knowledge about the long-term course and treatment of chronic mental illnesses to recognize the potential gains (therapeutic and financial) that may be achieved through clinical research studies. Through effective communication and a better understanding of the other's mission, MCOs and clinical researchers alike can achieve their goals. Ultimately, patients and society as a whole would be the beneficiaries.

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