From the New York State Psychiatric Institute

Diagnosis and Treatment of a Patient With Both Psychotic and Obsessive-Compulsive Symptoms

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When a patient presents with both psychotic and obsessive-compulsive symptoms, the clinician is faced with a differential diagnosis that includes comorbid schizophrenia and obsessive-compulsive disorder (OCD), OCD with poor insight, and schizophrenia with antipsychotic-induced obsessive-compulsive symptoms. If the psychotic symptoms are subthreshold or attenuated in form, the individual may have OCD and putative prodromal schizophrenia. The authors present a case to outline a strategy for differentiating among these possible diagnoses and for optimizing treatment.

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Case Presentation

Chief Complaint

"Carlos," a 19-year-old Puerto Rican male with no prior psychiatric hospitalizations, presented at the emergency department with the belief that "lines" were coming out of his mouth and genitals. He also spent several hours a day organizing objects in his house and checking to make sure they were aligned perfectly symmetrically.

History of Present Illness

Two years earlier, Carlos began feeling lonely and depressed and felt as if the other members of the school basketball team did not like him and perhaps even wanted to hurt him. Several months later, he began having repeated intrusive thoughts that if objects were not exactly aligned, some vague catastrophic event might occur, and this made him feel very anxious. In response to these thoughts, he performed repetitive behaviors to reduce his anxiety, including the arranging and rearranging of items and cutting and recutting his fingernails until perfectly symmetrical. These repetitive behaviors often took up to 5 hours a day. He recognized these thoughts as unreasonable, excessive, and a product of his own imagination. In fact, he was puzzled as to why he would be so concerned with symmetry. His family took him to see a psychiatrist soon after the start of the symptoms, and he was diagnosed as having obsessive-compulsive disorder (OCD). Although he had occasional low mood, he did not meet criteria for dysthymia or major depression. Consecutive trials of fluoxetine (80 mg/day for 4 months) and citalopram (60 mg/day for 3 months) failed because of lack of efficacy. Six months before the current presentation, he withdrew from his family, spending most of his free time in his room. At his part-time job in a grocery store, he developed delusional beliefs that coworkers and customers were taunting him. This led to verbal fights with multiple coworkers and yelling at a customer. His psychiatrist added the diagnosis of psychosis not otherwise specified and tried combined trials of selective serotonin reuptake inhibitors (SSRIs) for his obsessive-compulsive symptoms (e.g., paroxetine and escitalopram) and antipsychotics (e.g., olanzapine, risperidone, and haloperidol) for his psychotic symptoms, but Carlos could not tolerate a full trial of these medications because of dose-limiting side effects. Increased social isolation, poor school performance, and increased verbal arguments at work for 1 month before this presentation led to Carlos's family bringing him to the emergency department. Carlos had no history of substance use or significant medical problems. His family history was notable for a maternal aunt with OCD and a paternal uncle with schizophrenia.

Carlos was admitted from the emergency department to the psychiatric inpatient unit with a provisional diagnosis of schizophrenia in addition to the established diagnosis of OCD. Major depression with psychotic features was ruled out because of his euthymic mood; normal sleep, interest, appetite, and energy; and lack of evidence of inappropriate guilt or suicidality. His medication regimen on admission was sertraline, 200 mg/day, and aripiprazole, 20 mg/day. On examination, he was noted to be a tall, thin male with thick, brown chin-length hair. He had poor eye contact and sat hunched in his chair. He had blunted affect, speech latency, thought blocking, and lack of interpersonal relatedness. He was completely convinced that he had "lines" coming out of his mouth and genitals. From Carlos's description, it was apparent that he perceived these lines as a visual hallucination. He believed a force outside of his body was causing them to appear and that they were an extension of his body. On the inpatient unit, he was observed to be talking and laughing to himself during meals. Carlos believed that the hospital staff were making disparaging comments about him. On the inpatient unit, he was observed to rearrange items in his room for up to 3 hours a day; however, he was unable to articulate the motivation behind this behavior, although this may have been due to his thought disorder and latency of speech.

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Treatment Course

On the inpatient unit, Carlos's admission medication regimen (sertraline and aripiprazole) was tapered because of lack of efficacy. Clozapine was initiated to treat Carlos's relatively refractory psychotic symptoms, given the history of multiple failed antipsychotic trials and a case series on the treatment of obsessive-compulsive symptoms in patients with schizophrenia (1). After slow titration to 300 mg/day over 10 weeks while monitoring the obsessive-compulsive symptoms to ensure that they did not worsen, Carlos stopped talking and laughing to himself. He also reported that he no longer felt "picked on" or saw lines. However, he continued to have significant obsessions (the need to have items aligned symmetrically) and compulsions (arranging) for 3 hours a day. With the clearing of his thought disorder, Carlos was again able to articulate that aligning objects in a symmetrical fashion was something he did to alleviate anxiety.

With his psychotic symptoms noticeably improved with clozapine treatment, Carlos was discharged to the care of his outpatient psychiatrist. To target his persistent obsessive-compulsive symptoms, sequential trials of fluvoxamine and then clomipramine (two serotonin reuptake inhibitors [SRIs] he had not previously tried) were recommended. Careful monitoring would be needed for these trials of combined clozapine and SRIs, as fluvoxamine inhibits the metabolism of clozapine via hepatic cytochrome 3A4 and clomipramine decreases the seizure threshold, is anticholinergic, and affects cardiac conduction. The plan was also to add cognitive-behavioral therapy (CBT) using exposure and response prevention for any residual obsessive-compulsive symptoms once Carlos was stable on an outpatient medication regimen.

At 6-month follow-up, Carlos's psychotic symptoms were observed to have remitted with a dose of 300 mg/day of clozapine (the minimal dose required for treatment of his psychosis). However, his obsessive-compulsive symptoms continued to cause him distress and problems in daily functioning. He then had the recommended trials of fluvoxamine (250 mg/day for 3 months) and then clomipramine (225 mg/day for 3 months), neither of which was effective in treating his obsessive-compulsive symptoms. A trial of CBT using exposure and response prevention was initiated as planned for residual obsessive-compulsive symptoms. Carlos's symptoms improved initially, but he dropped out of treatment because he did not think the therapy would work. Twelve months after Carlos was discharged from the inpatient unit, his outpatient psychiatrist initiated a slow titration of lamotrigine to 200 mg/day, based on data from a recent open-label trial showing efficacy of adjunctive lamotrigine in patients with schizophrenia and schizoaffective disorder with comorbid obsessive-compulsive symptoms (2). After 10 weeks of lamotrigine augmentation, Carlos's obsessive-compulsive symptoms decreased by about 40% while his psychotic symptoms remained in remission. Carlos returned to his job at the grocery store.

Differential Diagnosis

The differential diagnosis of a patient who presents with both psychotic and obsessive-compulsive symptoms can include comorbid schizophrenia and obsessive-compulsive disorder, OCD with poor insight, or schizophrenia with antipsychotic-induced obsessive-compulsive symptoms. If the psychotic symptoms are subthreshold or attenuated in form, the individual may have OCD and putative prodromal schizophrenia (3). No biological markers exist to differentiate these possibilities, and there is debate as to the relationship of schizophrenia and OCD, especially early in the course of evolving symptoms. However, accurate diagnosis is important given that current treatments for OCD and schizophrenia differ, and first-line medications for one may exacerbate the symptoms of the other—that is, antipsychotics can exacerbate obsessive-compulsive symptoms, and SRIs may exacerbate psychosis (4). As there is no evidence base for the treatment of putative prodromal schizophrenia, OCD that occurs in this context should be treated pharmacologically as though it existed alone, although the attenuated positive symptoms should be monitored.

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The choice of diagnoses made has prognostic implications. For example, the presence of obsessive-compulsive symptoms or comorbid OCD in a person with schizophrenia has been associated with poorer prognosis (5, 6) and a significantly higher risk of suicide attempt (7). In individuals who are at heightened risk for psychosis or are in a putative prodromal stage of schizophrenia, the presence of obsessive-compulsive symptoms in addition to attenuated positive symptoms is associated with a greater prevalence of depression and suicidal ideation (3). OCD with poor insight is associated with poor response to therapy (8) and drug treatment (9). Hence, accurate diagnosis of patients with both psychotic and obsessive-compulsive symptoms is important for treatment and prognosis.

When a patient presents with the hallmarks of schizophrenia—hallucinations, disorganized speech and behavior, negative symptoms, and delusions (i.e., "erroneous beliefs that usually involve a misinterpretation of perceptions or experiences" [10, p. 299])—the diagnosis is usually straightforward. Likewise, when a patient presents with the hallmarks of OCD—obsessions ("recurrent or persistent thoughts, impulses, or images…[that are]…intrusive and inappropriate and that cause marked anxiety or distress" [10, p. 462]) and compulsions ("repetitive behaviors…or mental acts…that the person feels driven to perform in response to an obsession…[and]…are aimed at…reducing distress or preventing some dreaded event"[10, p. 462])—and has good insight into the irrationality of his

or her thoughts and the link between his or her thoughts and compulsions, it is clearly OCD. However, in the patient who does not have hallucinations or disorganized speech but has psychotic beliefs and repetitive behaviors, it can be a challenge to distinguish the delusion of schizophrenia from the obsession of OCD if the patient has poor or no insight. Kurt Schneider defined a delusion of schizophrenia as "a perception that has a unique and idiosyncratic meaning for a person, which leads to an immediate delusional interpretation" (11, p. 1434). However, this definition could equally apply to the obsession of a patient with OCD who lacks insight. From a developmental perspective, "overvalued ideas" (i.e., subthreshold delusions—compelling ideas that have not yet achieved a level of conviction consistent with delusions) in an adolescent or a young adult might reflect emerging obsessions, the forme fruste of the fixed false beliefs that are delusions, or both. Another challenge in some cases is to distinguish the repetitive behaviors of schizophrenia from the compulsions of OCD. Both challenges are not uncommon given that many patients with OCD have variable insight into the rationality of their beliefs (in the DSM-IV field trial of OCD, 4% of patients had no insight and 26% had very little insight into the senselessness of their symptoms [12]) and up to 35.5% individuals with schizophrenia have been found to exhibit repetitive behaviors (e.g., grooming, pacing, and hoarding), as shown in a study of 400 inpatients who met DSM-III-R criteria for schizophrenia (13). In the absence of biomarkers or behavioral tests that can distinguish these features, careful attention to four aspects of the clinical phenotype can help in evaluation, as described in the following section.

Evaluation

Time of Onset of Symptoms

Age at onset is similar for both OCD and schizophrenia, with 50% of OCD cases starting by age 19 and 20%–40% of first psychotic symptoms in schizophrenia starting by age 20 (14, 15). In both disorders, subsyndromal symptoms can start in adolescence. However, time of onset of symptoms in relationship to changes in medication can *exclude* diagnoses. For example, if the first evidence of obsessive-compulsive symptoms or an exacerbation of existing symptoms occurs after initiating antipsychotic treatment for psychosis, one should consider the possibility that the symptoms are medication induced (4). Similarly, if psychotic symptoms worsen after initiating or titrating an SRI, one should consider the possibility of medication-induced psychosis (4, 16).

Nature of Symptoms

Obsessions Versus Delusions. Obsessions and delusions are both thought distortions. However, the content and character of the distortions, as well as their relationship to repetitive behaviors, can differ. In OCD, several common obsessive themes have been described: contamination, symmetry or exactness, forbidden thoughts (aggressive, sexual, religious, and somatic), and hoarding (17). These obsessional themes are typically associated with corresponding compulsions: cleaning, ordering and arranging, checking, and hoarding. Data from the DSM-IV field trial of 431 adults with OCD showed that only 2.1% of patients reported obsessions without compulsions and only 1.7% reported compulsions without obsessions.

In contrast, the delusions seen in patients with schizophrenia include persecutory, referential, somatic, erotomanic, and grandiose themes (10). This is true even of the overvalued ideas seen in patients who are in a putative prodromal stage (C. Corcoran, unpublished 2010 data). Psychotic beliefs are more often "bizarre" ("clearly implausible and not understandable and do not derive from ordinary experiences"); however, bizarreness can be difficult to judge, especially across cultures (10, p. 299). Although "somatic" themes overlap between the two disorders, somatic thoughts that are bizarre or represent loss of control over mind or body (e.g., "My saliva is corroding my intestines") are more common in schizophrenia than in OCD with poor insight (10). Likewise, religious themes can occur in both, but in OCD, patients are overly concerned with sacrilege, blasphemy, or scrupulosity (i.e., excessive concern with right and wrong or with morality), whereas in schizophrenia, patients may more commonly have grandiose religious delusions (e.g., "I'm a divine messenger"). Furthermore, loss of control, or "agency" of thinking, more commonly occurs in schizophrenia. Patients with OCD often consider their obsessions as products of their own thinking, whereas patients with schizophrenia often believe that there is some external agency or cause to what they are experiencing and thinking (18). This distinction, however, becomes blurred when considering individuals with attenuated psychotic symptoms in a putative prodromal stage of schizophrenia or in patients with schizophrenia whose psychotic symptoms are partially remitted or residual. Also, a sense of permeation of ego boundary is more typical of schizophrenia than of OCD, although most patients with schizophrenia also have an intact sense of ego boundary (18); this concept has been explored phenomenologically by many notable figures, including Matussek, Jaspers, and Stephens and Graham (19–21). However, the problem with these distinctions is that they are less clear in prodromal or evolving stages of illness or with partial remission of symptoms during residual phases. For example, young people at heightened risk for schizophrenia have attenuated psychotic symptoms and can retain insight that their experiences are likely the product of their own imagination, although doubt may exist as to their source and nature (22–25).

Compulsions Versus Repetitive Behaviors. In adults with OCD, compulsive behaviors are typically performed in response to an obsession and to reduce distress or prevent a dreaded event. In contrast, in schizophrenia, repeti-

tive behaviors are often independent of thought content; as noted earlier, in one study more than one-third of 400 patients with schizophrenia had at least one severe repetitive behavior (13). Eisen and colleagues (26) suggest that the presence of compulsions linked to obsessions may be a useful guide in diagnosing comorbid OCD in patients with schizophrenia.

Family History

Family history can help inform the differential diagnosis. Although both schizophrenia and OCD are heritable disorders, with higher concordance rates in monozygotic twins than in dizygotic twins (14, 15), they do not appear to cosegregate. Families of patients with schizophrenia are more likely to have members with schizophrenia spectrum disorders, such as schizoaffective disorder and schizotypal personality disorder (27). In contrast, families of patients with OCD are more likely to have what are called "OCD spectrum disorders" (including tic disorder, Tourette's syndrome, skin picking) and comorbid mood and anxiety disorders (28).

Developmental Psychosocial Functioning

Both schizophrenia and OCD can lead to significant functional impairment in the work, family, and social domains (15, 29). However, in contrast to OCD, social dysfunction is a core feature of schizophrenia (30–32), and functional impairment is one of the DSM-IV criteria required for diagnosis. In schizophrenia, this social dysfunction is evident early (33). It is first expressed subtly during the premorbid period in childhood as difficulty in establishing relationships (34) and social overreactivity (social anxiety, "acting out") in boys and underreactivity (withdrawal) in girls (35). Likewise, adolescents at genetic risk for schizophrenia have poor peer engagement and unpopularity with peers (36, 37). Active social withdrawal is a feature of the putative prodromal period in schizophrenia (22, 23, 38, 39). Lack of interpersonal relatedness (i.e., diminished capacity for others to feel engaged and relate well to the individual) may also be characteristic of schizophrenia (40). In addition to social dysfunction, negative symptoms (e.g., flat affect, avolition, and alogia) are a key clinical aspect of schizophrenia and can include social anhedonia. In contrast, lack of interpersonal relatedness and social anhedonia are not characteristic of OCD, and social dysfunction is not required for an OCD diagnosis. On the other hand, obsessive-compulsive symptoms can certainly lead to social dysfunction (29).

Diagnosis and Rationale

Many clinicians would see Carlos's symptoms at the time of presentation to the inpatient unit as falling easily within the spectrum of schizophrenia given the patient's persecutory ideas and social decline. However, clinicians might differ in how they perceive Carlos's obsessive-compulsive symptoms. We believe that the diagnosis should include both schizophrenia and OCD. The diagnosis of schizophrenia is appropriate given the patient's functional decline for more than 6 months and the presentation of criterion A psychotic symptoms—hallucinations (the "lines") and persecutory delusions—in the absence of an affective episode, concurrent substance use, or a coexisting medical condition. The diagnosis of OCD is made because Carlos had thought distortions with the prototypical theme of symmetry or exactness, which were accompanied by the compulsions of ordering and arranging, done specifically to reduce the anxiety associated with the thoughts. Furthermore, when not thought disordered, Carlos had full insight that these thoughts were the product of his own imagination, and he found them unreasonable and excessive. These characteristics differentiate obsessions from delusions or overvalued ideas, as are found, respectively, in schizophrenia and its putative prodromal stage. His compulsions were clearly not the disorganized behavior or stereotypies seen in some cases of schizophrenia, as they were functionally linked to his obsessive thoughts (i.e., he felt driven to rearrange things in response to his obsessive fear that he would not do things "just right"). As is required for a diagnosis of OCD, these obsessions and compulsions were time consuming (taking up more than 1 hour a day) and interfered with his functioning (10). Thus, Carlos met DSM-IV criteria for both disorders. Several groups propose that the diagnosis of comorbid OCD and schizophrenia, also known as "schizo-obsessive" or "schizo-OCD," be made only when DSM-IV criteria for both disorders are met and OCD severity is at least moderate (i.e., eligible for entry into most OCD research studies) (4, 41). Carlos met all three conditions.

Treatment

Treatment for schizophrenia includes pharmacotherapy with antipsychotics and psychosocial treatments (15). CBT is used to treat both positive and negative symptoms of schizophrenia (42). It typically consists of developing a shared understanding of the illness between patient and therapist, identifying positive and negative symptoms and triggers, linking thoughts and feelings about current symptoms, and then rationally reevaluating these thoughts in relation to the symptoms (43).

The treatment approach to OCD is different. The two first-line treatments are pharmacotherapy with SRIs and CBT using exposure and response prevention (44). Because SRIs typically reduce symptom severity but do not eliminate all symptoms, augmentation is usually needed. There are two proven SRI augmentation strategies: exposure and response prevention and antipsychotics (44). Antipsychotics as monotherapy are not considered to be effective in OCD (45). Exposure and response prevention consists of patients voluntarily exposing themselves to feared stimuli (real or imagined) while refraining from performing their compulsions (46). The theory is that as patients are exposed to their fearful stimuli, this response

will habituate, their fears will be disconfirmed, and they will experience less anxiety over time.

A few studies have addressed how to treat patients with both schizophrenia and OCD (4, 44). Based on these studies, OCD treatment guidelines (44) suggest that these patients should first be stabilized on a second-generation antipsychotic and the obsessive-compulsive symptoms subsequently treated by the addition of an SRI. Whether these patients require SRIs at the high doses needed in patients with OCD without a comorbid psychotic disorder is unclear: obsessive-compulsive symptoms in the context of psychotic disorder have been found to respond to lower doses of fluvoxamine (100–200 mg/day) than typically used in treatment of OCD (250–300 mg/day) (4). Poyurovsky and colleagues (4) proposed that those who do not respond to the steps above be switched to another SRI or clomipramine, to another second-generation antipsychotic, or to a first-generation antipsychotic with an SRI or clomipramine. If these strategies are ineffective, they propose clozapine at a low dosage (75–300 mg/day), SRI augmentation of clozapine, and finally ECT (4, 47).

Combining antipsychotics and SRIs (e.g., fluvoxamine and clozapine; clomipramine and clozapine; paroxetine and risperidone or a phenothiazine) requires careful monitoring for drug-drug interactions and for possible exacerbation of obsessional or psychotic symptoms (4, 44). In patients with co-occurring schizophrenia and OCD or obsessive-compulsive symptoms, if antipsychotic medication induces obsessive-compulsive symptoms, there are several options: waiting for spontaneous resolution (4–6 weeks), gradually reducing the dosage of antipsychotic, switching to another antipsychotic, adding an SRI to target the obsessive-compulsive symptoms (e.g., fluvoxamine, clomipramine, sertraline), or attempting a trial of exposure and response prevention (4, 44). The evidence base for these approaches is limited.

Some patients with both schizophrenia and OCD, like Carlos, remain symptomatic despite the treatment recommendations listed above. It is interesting that Carlos's OCD symptoms seemed to improve after the initiation of lamotrigine at 200 mg/day. Recent data have implicated glutamatergic abnormalities in the pathophysiology of schizophrenia, OCD, and depression (48–58). Lamotrigine is an anticonvulsant typically used for seizure disorders and maintenance treatment in bipolar disorder. In addition to its varied mechanisms of action, lamotrigine inhibits glutamate release. In schizophrenia, there is preliminary evidence that lamotrigine (at dosages of 200 mg/day and higher) might be effective for psychotic symptoms when added to clozapine (59–61) but not when added to antipsychotics other than clozapine (62). In OCD, an open-label study found that one of eight patients responded to lamotrigine augmentation of an SSRI (although the lamotrigine dosage was only 100 mg/day), and there has been a case report of marked improvement with lamotrigine augmentation (150 mg/day) of clomipramine (63). Although no randomized clinical trials have yet been conducted to evaluate the efficacy of lamotrigine for patients with comorbid OCD and schizophrenia, these preliminary data suggest that glutamate modulators may be an area of interest for treatment-resistant patients with both psychotic and obsessive-compulsive symptoms.

As for psychological treatments, CBT using exposure and response prevention has clear efficacy for OCD, but its effectiveness for OCD comorbid with schizophrenia is unknown. For schizophrenia alone, one pilot study examined the effect of repeatedly and systematically exposing five patients with schizophrenia to their auditory hallucinations (64). Neither the frequency nor the content of the hallucinations changed, but patients reported decreased anxiety and a greater sense of control over their hallucinations, suggesting that exposure techniques may help reduce anxiety due to hallucinations. These data raise the possibility of using exposure techniques for obsessive-compulsive symptoms in the context of schizophrenia. Unfortunately, Carlos was not able to complete a trial of exposure and response prevention because of his doubts about whether this treatment would work.

There are as yet no consensus guidelines for the treatment of the putative schizophrenia prodrome. Olanzapine has unclear efficacy and problematic side effects (65), and one study reported efficacy with risperidone when administered in combination with CBT (66). Similarly, although several studies have described comorbid diagnoses in putative schizophrenia prodrome (one case series of nine adolescent patients found that 44% met criteria for OCD), there are no consensus guidelines for treating comorbid diagnoses and putative prodromal schizophrenia (67–70). It remains unknown whether treating obsessive-compulsive symptoms in a putative schizophrenia prodrome has an effect on the natural course of either of these illnesses.

Conclusions

The case of Carlos highlights diagnostic and treatment issues when patients present with psychotic and obsessive-compulsive symptoms. In such cases, the differential diagnosis can include comorbid schizophrenia and obsessive-compulsive disorder, OCD with poor insight, and schizophrenia with antipsychotic-induced obsessive-compulsive symptoms. If the psychotic symptoms are subthreshold or attenuated in form, the patient may have OCD and putative prodromal schizophrenia. Four aspects of the clinical phenotype—time of onset of symptoms, nature of symptoms, family history, and developmental psychosocial functioning—can help differentiate between these diagnoses so that the clinical management can be optimized. In this case, the diagnoses arrived at were comorbid schizophrenia and OCD, and current treatment guidelines were followed: antipsychotic treatment was op-

timized and SRIs and exposure and response prevention were tried. However, although clozapine effectively treated the symptoms of schizophrenia, Carlos's OCD continued to cause impairment because the SRIs were ineffective and the patient was not able to continue exposure and response prevention. On the other hand, the augmentation of clozapine treatment with lamotrigine, a glutamate modulator, appeared to reduce his OCD symptoms.

This case highlights clinical questions that future research can address: Can glutamate modulators be effective in treatment-resistant patients who have both psychotic and obsessive-compulsive symptoms? Given the efficacy of exposure and response prevention for OCD, is it a safe and effective option for patients with comorbid schizophrenia and OCD who are stabilized on antipsychotics? Since obsessive-compulsive symptoms can be an early developmental manifestation of emerging schizophrenia with or without OCD, what is the impact of treating the obsessive-compulsive symptoms during a putative prodromal stage in reducing the risk of developing schizophrenia and/or OCD? To address these issues, we need longitudinal studies of young people at risk for psychosis or for OCD to inform our understanding of the phenomenology and pathophysiology of these disorders in a developmental context, specifically focusing on finding potential biomarkers that can inform preventive strategies.

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