

## Assessing Patient and Caregiver Experiences with Symptoms and Behaviors Associated with Schizophrenia

Dana B DiBenedetti<sup>1\*</sup>, Michelle T Brown<sup>1</sup> and Natalya Danchenko<sup>2</sup>

<sup>1</sup>RTI Health Solutions, Research Triangle Park, North Carolina, USA

<sup>2</sup>Lundbeck SAS, Cedex, France

### Abstract

**Objective:** Obtaining patient and caregiver perspectives may be critical for informing disease management, particularly with conditions like schizophrenia. The primary objective of the current study was to obtain and assess patient and caregiver perspectives on associated symptoms and behaviors of schizophrenia and their impact or burden on patients and their caregivers through patient interviews and caregiver focus groups.

**Research design and methods:** Seven in-depth individual interviews were conducted with individuals with schizophrenia, and four focus groups were conducted with caregivers of adults with schizophrenia (n = 21) in two different locations in the United States. Following a discussion guide, interviewers asked open-ended questions to ascertain specific definitions and experiences related to five associated symptoms and behaviors (anxiety, irritability, agitation, impulsivity, and aggression), the impact of these symptoms, and how they were associated with schizophrenia. Additionally, patients completed the 8-item Birchwood Insight Scale developed to assess insight in patients with schizophrenia.

**Results:** The impacts of anxiety were the most widespread and persistent for the patients, primarily relating to social and family interactions and relationships. For both patients and caregivers, patients' anxiety comprised a mental and a physical component and contributed to escalation of other emotions and behaviors. Other significant or debilitating impacts, such as emotional functioning, legal issues, and financial distress, were attributed to aggression and impulsivity for both the patients and the caregivers.

**Conclusion:** This study provides evidence of the impact of anxiety in the lives of patients with schizophrenia and their caregivers, and the potential relationship of and escalation from anxiety to aggression. Additionally, the study reinforces the importance of ensuring that treatment is taking into account the highly prevalent anxiety symptoms and behavioral disturbances in patients with schizophrenia as well as the implications of these symptoms and disturbances on the caregivers.

**Keywords:** Schizophrenia; Anxiety; Caregivers; Aggression; Irritability; Agitation; Qualitative study

### Introduction

Schizophrenia is a severe, chronic mental disorder characterized by psychotic thoughts and behaviors. Diagnosis requires the presence of signs of the disorder for at least 6 months, including at least 1 month of active symptoms. These active symptoms must include at least two of the following features: delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, and negative symptoms such as diminished emotional expression or volition [1]. Individuals with schizophrenia also demonstrate significant impairment in one or more areas of functioning, such as self-care, occupational functioning, and interpersonal relationships, for a significant portion of the time [1].

In addition to the core positive symptoms associated with schizophrenia (e.g., hallucinations, delusions), patients often present with other associated and debilitating symptoms, such as anxiety, agitation, and aggression [2-4]. Although limited, the existing literature suggests that anxiety comorbidities are prevalent in patients with schizophrenia. In a study of 53 outpatients with schizophrenia, 41.5% were identified as having a comorbid anxiety disorder: social phobia (17.0%), obsessive-compulsive disorder (15.1%), and generalized anxiety disorder (9.4%) [5]. In another study, patients with schizophrenia and a comorbid anxiety disorder showed significantly poorer scores on the Sheehan Disability Scale than patients without comorbid anxiety disorders [5].

Although existing pharmacological agents are generally efficacious in treating the positive and typically primary symptoms

of schizophrenia, there is an unmet treatment need with patients with both core symptoms of schizophrenia and comorbid associated symptoms (e.g., anxiety, irritability, agitation).

Still fewer articles are published on the co-occurrence of irritability or agitation with schizophrenia. However, some research suggests that irritability and aggression are some of the primary dimensions of early signs of schizophrenia [6,7].

Patients are not the only individuals affected by schizophrenia and its associated symptoms. Results from interviews conducted with caregivers of individuals with schizophrenia confirm that patients are largely dependent upon their caregivers for their care, and subsequently, caregivers report having less time for themselves and other responsibilities, such as family and work. The burden of caring for an individual with schizophrenia can have physical (e.g., fatigue, sickness) and/or emotional (e.g., depression and anxiety) effects [8].

Although effective treatment of these symptoms theoretically

**\*Corresponding author:** Dana Britt DiBenedetti, PhD, Head, Patient-Reported Outcomes, RTI Health Solutions, 200 Park Offices Drive, Research Triangle Park, NC 27709 USA, Tel: +19193163764; Fax: +19193411960; E-mail: [ddibenedetti@rti.org](mailto:ddibenedetti@rti.org)

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could improve functioning and quality of life in both patients and their caregivers, the relationship of these symptoms to schizophrenia is not well understood. Obtaining patient and caregiver perspectives may be critical for informing disease management, particularly with conditions like schizophrenia. Thus the primary objective of the current study was to obtain and assess patient and caregiver perspectives on associated symptoms and behaviors of schizophrenia and their impact or burden on patients and their caregivers through patient interviews and caregiver focus groups.

## Participants and Methods

Seven in-depth individual interviews were conducted with individuals with schizophrenia, and four focus groups were conducted with caregivers of adults with schizophrenia in two locations in the United States (Raleigh, NC, and Boston, MA). Participants were screened for eligibility by trained medical recruiters from two qualitative research firms. All patient interviews and caregiver focus groups were conducted by two PhD-level psychologists, both experienced in qualitative research in this therapeutic area, using a semi-structured discussion guide. Institutional review board approval for this study was obtained prior to any participant recruitment.

### Patient interviews

Potentially qualified participants were identified either by the medical recruiters, who contacted individuals within their databases to assess eligibility and determine interest for the study, or by local clinicians, who referred interested patients to the qualitative research firms. Patients who were not clinician-referred were required to provide a diagnosis verification form to recruiters.

Screening prior to interviews assessed patient report of the following inclusion criteria:

1. Being aged 18 to 75 years
2. Having received a diagnosis of schizophrenia from a physician or other health care professional at least 3 months earlier
3. "Often" experiencing anxiety, impulsivity, agitation, irritability, and/or aggression
4. Taking one or more medications for schizophrenia

Exclusion criteria included diagnosis of bipolar disorder, current hospitalization, or participation in a related qualitative research study in the past 6 months.

Following screening and provision of written informed consent and using the semi-structured interview guide, participants were asked to list symptoms and behaviors they thought might be related to their schizophrenia. They were then asked about their experiences, if any, with the targeted symptoms and behaviors (anxiety, irritability, agitation, impulsivity, and aggression), including how they described each of the targeted symptoms, how the symptoms were related to each other, the frequency in which they experienced them, and the impact of the targeted symptoms. Participants were also asked to describe how treatment for schizophrenia affected targeted symptoms, if at all.

At the end of the interview, patients were asked to complete the eight-item Birchwood Insight Scale (IS), developed to assess insight in patients with schizophrenia [9]. The Birchwood IS comprises three insight domains measured on a scale of 0 to 4: Awareness of Symptoms, Awareness of Illness, and Need for Treatment. Together these provide a total score (0 to 12). A score of 3 or greater on each domain indicates the patient is aware of his or her own relationship to that particular

domain (symptoms, illness, or need for treatment), and a total score of 9 or greater indicates the patient's awareness of all three domains [9].

### Caregiver focus groups

Potentially qualified caregivers of patients with schizophrenia were identified by trained medical recruiters from the same two qualitative research firms that recruited for the patient interviews to assess eligibility and determine interest in participating in the focus groups.

To be eligible for caregiver focus group participation, an individual needed to self-report all of the following at screening:

1. Being aged 18 years or older
2. Being responsible for the care and well-being of an adult (aged 18 years or older) with a diagnosis of schizophrenia
3. Providing care for 5 or more hours per week for the individual with schizophrenia
4. The person for whom they provide care "often" experiences anxiety, impulsivity, agitation, irritability, or aggression

Although some of the caregivers provided care for one or more of the patients interviewed, this relationship with an interview participant was not a study requirement.

After providing written informed consent and following the caregiver semi-structured discussion guide, participants were asked to list all of the symptoms and behaviors they have observed in individuals with schizophrenia, how they defined or described each of these, how these symptoms were related to each other, and the impact of these symptoms and behaviors on their lives as caregivers. Caregivers were also asked to describe how they felt that treatment for schizophrenia affected targeted symptoms, if at all.

## Results

### Participant demographics

**Patients:** A total of 7 patients with schizophrenia, with a mean age of 44.1 years, were screened and participated in the interviews. Five participants were male, and 4 were white. The mean time since diagnosis was 9.1 years. Table 1 presents the demographic and clinical characteristics of the interview participants collected by telephone at screening. As part of the telephone screening, patients were asked to indicate which of the target feelings or symptoms they experienced "often." As seen in Table 1, 6 of the 7 participants reported feelings of agitation, irritability, and sadness/emptiness at screening; and 5 reported feelings of anxiety and anhedonia.

The mean Birchwood IS score across all patients with schizophrenia ( $N = 7$ ) was 9.9 (standard deviation [SD] 2.3), with 5 patients (71.4%) scoring a total of 9 or higher on the Birchwood IS, indicating good insight. The domain scores were as follows: Awareness of Symptoms, 3.3 (SD 0.95); Awareness of Illness, 3.0 (SD 1.0); and Need for Treatment, 3.6 (SD 0.8).

**Caregivers:** A total of 21 caregivers for individuals with schizophrenia participated in the focus groups. Caregivers had a mean age of 51.3 years, were mostly female, and about half were white. All but one participant cared for a family member with schizophrenia (the one caregiver worked as a social worker in a group home for individuals with schizophrenia), and almost half were parents of a

child with schizophrenia. Fifteen of the participants (71%) reported living in the same residence with the patients some or all of the time. Table 2 presents the combined demographic characteristics collected by telephone at screening for the focus group participants. During the screening process, caregivers were asked if their family member or individuals for whom they provide care exhibit pre-identified feelings or symptoms “on a regular basis.” As seen in Table 2, all caregivers reported observing anxiety, followed by irritability, sadness/emptiness, anhedonia, agitation, and impulsivity.

Characteristics	Raleigh (N = 4)	Boston (N = 3)	Total (N = 7)
<b>Sex, n (%)</b>			
Male	3 (75.0)	2 (66.7)	5 (71.4)
Female	1 (25.0)	1 (33.3)	2 (28.6)
Mean age, years (range)	40.3 (20-54)	49.3 (45-54)	44.1 (20-54)
<b>Race, n (%)</b>			
White	1 (25.0)	3 (100.0)	4 (57.1)
Black	2 (50.0)	0 (0.0)	2 (28.6)
Hispanic/Latino	1 (25.0)	0 (0.0)	1 (14.3)
Mean time since diagnosis, years (range)	7.0 (4-12)	12.0 (6-23)	9.1 (4-23)
<b>Living situation, n (%)</b>			
Alone/independently	2 (50.0)	1 (33.3)	3 (42.9)
With adult family member(s)	1 (25.0)	2 (66.7)	3 (42.9)
With child(ren)/minor(s)	1 (25.0)	0 (0.0)	1 (14.3)
<b>Associated feelings/symptoms, n (%)</b>			
Agitation <sup>a</sup>	3 (75.0)	3 (100.0)	6 (85.7)
Irritability <sup>a</sup>	4 (100.0)	2 (66.7)	6 (85.7)
Sad/empty	4 (100.0)	2 (66.7)	6 (85.7)
Anxiety <sup>a</sup>	2 (50.0)	3 (100.0)	5 (71.4)
Loss of interest/pleasure	3 (75.0)	2 (66.7)	5 (71.4)
Impulsivity <sup>a</sup>	1 (25.0)	1 (33.3)	2 (28.6)
Aggression <sup>a</sup>	0 (0.0)	1 (33.3)	1 (14.3)
<b>Comorbidities, n (%)</b>			
Depression	3 (75.0)	2 (66.7)	5 (71.4)
Diabetes	3 (75.0)	0 (0.0)	3 (42.9)
High blood pressure	2 (50.0)	0 (0.0)	2 (28.6)
<b>Antipsychotic medication, n (%)<sup>b</sup></b>			
Quetiapine	0 (0.0)	1 (33.3)	1 (14.3)
Aripiprazole	2 (50.0)	1 (33.3)	3 (42.9)
Clozapine	0 (0.0)	1 (33.3)	1 (14.3)
Fluphenazine	1 (25.0)	0 (0.0)	1 (14.3)
Lurasidone	1 (25.0)	0 (0.0)	1 (14.3)
Ziprasidone	1 (25.0)	0 (0.0)	1 (14.3)
Olanzapine	1 (25.0)	0 (0.0)	1 (14.3)
<b>Antidepressant medication, n (%)</b>			
Venlafaxine	1 (25.0)	2 (66.7)	3 (42.9)
Duloxetine	0 (0.0)	1 (33.3)	1 (14.3)
Doxepin	1 (25.0)	0 (0.0)	1 (14.3)
<b>Antianxiety medication, n (%)</b>			
Clonazepam	1 (25.0)	0 (0.0)	1 (14.3)
<b>Anticonvulsant medication, n (%)</b>			
Lamotrigine	1 (25.0)	0 (0.0)	1 (14.3)
<b>Other medication, n (%)</b>			
Zolpidem	0 (0.0)	1 (33.3)	1 (14.3)
Clonidine	0 (0.0)	1 (33.3)	1 (14.3)
Atomoxetine HCl	0 (0.0)	1 (33.3)	1 (14.3)

Note: <sup>a</sup> Agitation, irritability, anxiety, impulsivity and aggression were the target symptoms of this study  
<sup>b</sup> Percentages sum to more than 100% due to multiple responses.

Table 1: Characteristics of interview patients at screening.

Characteristic	Raleigh (N = 16)	Boston (N = 5)	Total (N = 21)
<b>Sex, n (%)</b>			
Male	3 (18.8)	3 (60.0)	6 (28.6)
Female	13 (81.3)	2 (40.0)	15 (71.4)
Mean age, years (range)	49.5 (25-69)	57.2 (46-73)	51.3 (25-73)
<b>Race, n (%)</b>			
White	6 (37.5)	4 (80.0)	10 (47.6)
Black	9 (56.3)	1 (20.0)	10 (47.6)
Hispanic/Latino	0 (0.0)	0 (0.0)	0 (0.0)
Other	1 (6.3)	0 (0.0)	1 (4.8)
<b>Relationship to patient, n (%)</b>			
Parent	8 (50.0)	2 (40.0)	10 (47.6)
Other family member	7 (43.8)	3 (60.0)	10 (47.6)
Paid professional/not a relative	1 (6.3)	0 (0.0)	1 (4.8)
<b>Observed associated feelings/symptoms of patient, n (%)<sup>a</sup></b>			
Anxiety <sup>b</sup>	16 (100.0)	5 (100.0)	21 (100.0)
Irritability <sup>b</sup>	14 (87.5)	5 (100.0)	19 (90.5)
Sad/empty	13 (81.3)	4 (80.0)	17 (81.0)
Loss of interest/pleasure	14 (87.5)	3 (60.0)	17 (81.0)
Agitation <sup>b</sup>	12 (87.5)	3 (60.0)	17 (81.0)
Impulsivity <sup>b</sup>	13 (81.3)	3 (60.0)	16 (76.2)
Aggression <sup>b</sup>	7 (43.8)	1 (20.0)	8 (38.1)
<b>Time lived in same residence with patient, n (%)</b>			
All of the time	8 (50.0)	2 (40.0)	10 (47.6)
Some of the time	2 (12.5)	3 (60.0)	5 (23.8)
None	6 (37.5)	0 (0.0)	6 (28.6)

Note: <sup>a</sup> Percentages sum to more than 100% due to multiple responses.  
<sup>b</sup> Anxiety, irritability, agitation, impulsivity, and aggression were the target symptoms of this study.

Table 2: Characteristics of focus group participants at screening.

### Associated symptoms and behaviors

During the interviews/focus groups, in both patients’ and caregivers’ initial (and exhaustive) listings of symptoms and behaviors associated with schizophrenia, all five target symptoms and behaviors (anxiety, irritability, agitation, impulsivity, and aggression) were spontaneously reported by at least one patient and one caregiver as part of this exercise, either using the exact word or an associated concept (e.g., anger, argumentative, frustration). A majority of both patients and caregivers reported anxiety, irritability, and agitation as “often” occurring. Slightly more caregivers than patients reported aggression and impulsivity.

**Anxiety:** All patients reported frequently experiencing anxiety, and most patients reported anxiety on a daily basis. Even though on medications to treat their schizophrenia, patients noted they still frequently experienced anxiety and at uncomfortable levels. Each patient expressed an understanding of anxiety and could easily describe it from his or her own perspective. However, patients’ descriptions of anxiety varied slightly. The experience of anxiety was physical (e.g., physical changes, shaking, tense), mental for some (e.g., fear, worry), or both. Patients also frequently described anxiety as a discomfort or even an inability to be with or in close proximity to other people. Additionally, most patients were unable to distinguish their anxiety (physical or mental) from their paranoia, delusional thinking, or hallucinations. Specifically, participants described their anxiety, especially their worries and fears, and even their discomfort with others, as related to their paranoid thoughts.

Of the five associated symptoms and behaviors, anxiety was the

most frequently reported by caregivers. Caregivers reported that nearly all of the individuals for whom they provide care appeared to experience anxiety on a regular basis, either as observed or as reported from the individuals themselves. Caregivers had no difficulty describing anxiety. Their descriptions were similar to those provided by patients, although descriptions from the caregivers tended to be more consistent from caregiver to caregiver and encompassed both physical and mental components.

**Irritability:** Most patients said that they experienced irritability regularly, although the concept of or state of irritability was difficult for some patients to articulate. For the patients able to express this concept, it was a generally a state of bother or annoyance—the “inability to get along with people”. Additionally, patients described irritability in physical terms (e.g., “wanting to calm down”, “something on the inside of you that is just bouncing around”, “a physical reaction”) with less of a focus on the way irritability feels emotionally.

Caregivers reported observing irritability in most of those for whom they care. Although the caregivers’ descriptions of this concept were brief, they did not state any difficulties in describing or understanding it. To caregivers, irritability was generally defined as a state of impatience with feelings of bother and annoyance, similar to the descriptions provided by the few patients able to clearly articulate this emotion and behavior.

**Agitation:** Patients seemed better able to articulate and define agitation than irritability, although their definitions of agitation tended to include elements of or reference to anxiety and even aggression. In general, for patients, agitation was slightly more physical than irritability, and it was this physical state that patients could easily understand and express. About one-third of the patients described agitation as being similar to aggression, or they actually interchanged the words when they spoke of one or the other of these concepts. One patient was not familiar with the term “agitation”. When a definition of the concept was provided to him (“feeling like you have to move or cannot sit still”), he said that it sounded like anxiety to him. The majority of patients stated that they regularly experience agitation.

Caregivers seemed to have a good understanding of agitation as a concept very similar to irritability, albeit in a more physical form, akin to restlessness. Just like patients, caregivers were able to articulate and define agitation more easily than irritability. The frequency of agitation was also similar to that of irritability, reported for the majority of the individuals for whom the caregivers provided care.

**Aggression:** About half of the patients reported experiencing aggression, although they reported experiencing it infrequently. Patients attributed this infrequency to their ability to suppress aggression when regularly taking their antipsychotic medications. Aggression often occurred when there was a lapse in their medication and symptoms were not well controlled. All patients were able to easily discuss and expound on the meaning of aggression, which was generally described as an act or desire to act with physical or verbal behavior (e.g., violent behavior, getting into arguments, being confrontational).

Because aggression is an outward expression of behavior, caregivers easily discussed this concept as they observed it among the individuals for whom they provide care. As noted by patients, caregivers indicated that patients experienced aggression more often when they were not taking their medication regularly. In the focus groups, about half of the caregivers reported observing aggression in the individuals for whom they provide care. Also similar to patients’ definition, aggression was

defined by caregivers as some sort of overt physical or verbal behavior, often involving feelings of anger.

**Impulsivity:** Impulsivity was reportedly experienced by about half of the patients but only infrequently and usually when patients were off their medication. Patients were able to easily and consistently describe and define this behavior as an action that occurred without a known reason or previous thought or without consideration of consequences. For some patients, their delusional thinking likely played a role in their impulsivity, and for others, their memory of the impulsive behavior was limited. Most patients acknowledged their lack of insight prior to or during the actual impulsive behavior, but a few patients also commented on their inability to remember the event. In the latter case, patients knew about the event only as a result of the consequences of their impulsive behavior (e.g., large credit card bill due) or details from those involved or affected (e.g., family members having to go get them).

Because impulsivity is a behavior that is observable (like aggression), caregivers could clearly describe and define this concept in the individuals for whom they provide care as not thinking through their actions before acting or not thinking about the consequence of this behavior. Also, like aggression and consistent with the patients’ report, caregivers stated that patients usually experienced impulsivity only when they were not taking their medication regularly. Slightly more than half of the caregivers reported observing impulsive behavior in those for whom they provided care.

### Symptom impact and bother

**Anxiety:** All patients reported experiencing some level of anxiety (physical and/or mental). The anxiety impact areas were relatively consistent, largely referencing distress around or limitations related to being around other people and in crowds (e.g., not going to theaters, church, restaurants) as well as having debilitating fears and worries (e.g., taking a shower when alone in the house, inability to drive). Although patients noted that the fears and worries were likely associated with their delusional thinking, the impact areas related to both physical and mental anxiety.

The impact of the patients’ anxiety on caregivers, as reported by the caregivers, was more challenging to depict than for patients. Caregivers indicated difficulty isolating the impact of anxiety itself from many of the other symptoms and behaviors that patient’s exhibit (e.g., hallucinations, delusions). Similar to the report by patients, most of the caregiver impacts of anxiety related to their own social, family, and emotional functioning (e.g., limiting social engagements with friends and family, adapting outings to accommodate the patient).

**Irritability and agitation:** Irritability and agitation were reported frequently (by the majority of both patients and caregivers). However, for both patients and caregivers, the impacts of irritability and agitation were difficult to differentiate from each other, from anxiety, and from other symptoms of schizophrenia. Also, some patients and caregivers referred to the impacts of agitation as aggressive behaviors in the immediate escalation from agitation to aggression.

**Aggression:** The impacts of aggression largely related to patients’ relationships with others, as well as the impact related to legal issues such as divorce and consequences of assaulting others. Caregivers noted job loss resulting from aggressive behavior as another example of impact to a patient.

From the caregivers’ perspectives, the effects of aggression were largely related to the caregivers’ emotional, social, and family functioning, including managing patient disruptions during family

gatherings and stress over decisions to commit family members to institutional care. Caregivers also indicated impacts related to their sleep and legal ramifications (e.g., requiring police involvement) because of a patient’s aggression.

**Impulsivity:** While only one-third of patients reported impulsivity (and those that did reported it infrequently), the impact of impulsivity was easily identified. Patients primarily referred to the financial and relational impacts of their impulsive behaviors and actions, such as spending money allotted for bills and hurting family members’ feelings, respectively.

Caregiver reports of the impacts of patient impulsivity on the caregivers were similar to those reported by patients. The impacts were significant and usually financial, including the caregivers’ need to miss work (e.g., to retrieve patient from another state or jail).

### Comparison of impacts

The impacts of anxiety were the most widespread and continuous for the patients. Both patients and caregivers attributed the most significant or debilitating impacts to aggression and impulsivity. Patients and caregiver expressed similar impacts from the target symptoms, especially for aggression (i.e., legal impact). Table 3 summarizes the impacts of the associated symptoms and behaviors as reported by the patients and caregivers.

### Relationship among target symptoms

For both patients and caregivers, anxiety includes both a mental and a physical component. As described by patients and caregivers, mental components include the fears and worries associated with the patients’ delusional thinking and paranoia, and physical components include restlessness, tension, and fidgeting (psychomotor agitation). Either or both components can contribute to the escalation of other emotions and behaviors.

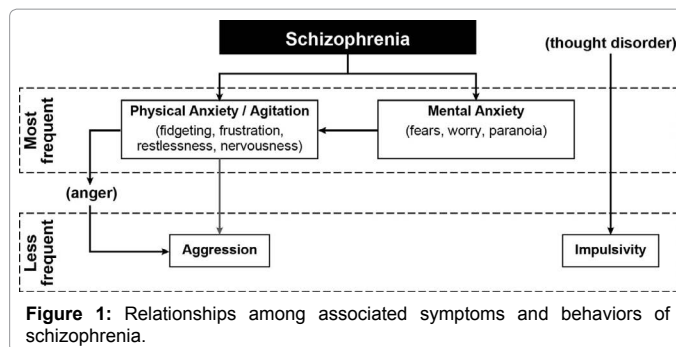
Mental anxiety can lead to physical anxiety and/or agitation (e.g., feeling like you cannot sit still). Patients more easily described the physical aspects of anxiety/agitation than the more emotional or mental symptoms. Caregivers also tended to focus on the physical symptoms of anxiety/agitation (as these were observed).

Both patients and caregivers described relationships between some of the symptoms and aggression. Specifically, anxiety and/or agitation may escalate into anger, which may then proceed to aggression. Additionally, physical anxiety may lead directly to aggression without an observed progression.

Impacts	Anxiety		Aggression		Impulsivity	
	P	C	P	C	P	C
Social and family interactions and relationships: avoid crowds/leaving home, interacting with people	P	C	P	C	P	C
Emotional health, well-being	P	C	-	C	-	-
Self-care and daily tasks (e.g., showering, shopping)	P	-	-	-	-	-
Romantic relationships	-	-	P	-	-	-
Legal involvement (jail)	-	-	P	C	-	-
Sleep	P	-	-	C	-	-
Driving	P	-	-	-	-	-
School/work	P	-	P	-	-	C
Financial	-	-	-	-	-	C

Note: C = caregiver; P = patient.

**Table 3:** Summary of symptom and behavior impacts on patients and caregivers.



The concept of irritability was difficult for patients to describe or define. Furthermore, both patients and caregivers generally did not significantly distinguish between anxiety, irritability, and agitation. In fact, physical anxiety and agitation were considered synonymous to both patients and caregivers.

While most patients were able to easily define impulsivity, they were unable to comment on its relationship to any of the target symptoms. Patients being off of their medication were the only behavior in which patients and caregivers could identify a clear relationship between impulsivity and schizophrenia.

Figure 1 depicts the relationship, as reported by patients and caregivers, among the associated symptoms and behaviors.

### Discussion

Of the associated symptoms examined in this study, anxiety was reported most often and was chosen by the most patients and caregivers as the symptom and behavior they would most like a new treatment to address. As defined by patients and their informal (unpaid) caregivers, anxiety is a broad concept, encompassing both physical (agitation) and mental (fears, worry, paranoia) elements. The impact of anxiety on patients with schizophrenia is extensive, both in terms of prevalence (e.g., experienced by all patient participants) and in its impact (e.g., limitations related to being around other people and in crowds and debilitating fears and worries about common activities like showering and driving). For patients, the importance they placed on reducing their level of anxiety was partly related to their ability to get along with other people, while most caregivers acknowledged the role they thought anxiety plays as a precursor to symptom escalation. Specifically, anxiety was thought to be the source of other associated symptoms and behaviors and sometimes led to the progression to or escalation of aggression. Caregivers indicated a belief that patients’ thoughts and fears, such as perceived threats to safety, were often the drivers of the aggressive behavior.

While anxiety seemed to be the most impactful symptom to patients and their informal caregivers, other target symptoms (irritability, aggression, and impulsivity) were relevant to some patients and caregivers. Aggression and impulsivity were reported less frequently than other target symptoms, by both patients and caregivers, and when experienced, they often occurred during periods of increased positive symptoms and/or medication noncompliance. Patients reported impulsivity even less frequently than caregivers, possibly due to being less aware of or less able to recognize impulsivity than other associated symptoms.

The frequency with which patients experienced the associated symptoms and behaviors may not have been reflected in the amount of

detail and description they were able to verbalize. Patients may be able to describe more easily the physical aspects of the associated symptoms and behaviors (versus those more emotional or mental). Some patients had difficulty defining and distinguishing between some symptoms (namely, irritability, agitation, and aggression) despite reportedly experiencing many of these symptoms and behaviors with frequency. Additionally, some patients, when describing some symptoms and behaviors (especially in describing anxiety as including fear and worry), tended to relate or attribute these symptoms and behaviors to their paranoia or delusional thinking.

While patients had some difficulty describing some of the target symptoms or the differences between them, patients did seem to have an understanding of their own experiences (e.g., anxiety) and the impact of them. Birchwood IS scores (mean of 9.9) indicate that this patient sample overall had good insight. Furthermore, it was the interviewers' experience with discussing patient symptoms, behaviors, and feelings that all patients did exhibit a good level of insight and articulation in their verbalizations.

In this real-world study, patient and caregiver perspectives on emotions and behaviors associated with schizophrenia—how they are expressed by the patients and the impacts on patients and on their caregivers—contribute to the scant literature available on prevalence, relevance, and treatment of these comorbid symptoms. Additionally, this study is unique in that it provides both patient and caregiver perspectives and that, in general, these perspectives are similar. While this qualitative study included a small number of patients and their informal (unpaid) caregivers, and their representativeness to the general schizophrenic population is unclear, overall study results, including those from caregivers, suggest that the data obtained from this study can be interpreted in the manner allowed for qualitative data (i.e., for directional and explorative purposes). It is not clear how these results generalize, if at all, to formal, paid caregivers (e.g., group home or case workers) of individuals with schizophrenia.

This study reinforces the need for treatments to target a broad range of highly prevalent anxiety symptoms and behaviors in patients with schizophrenia. Treatment of the underlying anxiety could improve disease management and patient functioning, in addition to the well-being of others, such as caregivers. Further areas of research include assessing change in anxiety and these other symptoms of schizophrenia within a clinical study.

## Conclusion

The current study provides new information on the relationship of schizophrenia with other associated symptoms and behaviors, supports the pervasive impact of anxiety in the lives of patients with schizophrenia and their caregivers, highlights the potential relationship of and escalation from mental to physical anxiety and from physical anxiety to aggression, and identifies a key unmet treatment need for both patients and caregivers. However, additional research is needed to better understand the relationship of anxiety in particular to schizophrenia and to these other symptoms.

## Transparency

### Declaration of funding

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Solutions in study design, interpretation of data, the decision to submit the manuscript for publication, and approval of the final manuscript.

1. ND is an employee of Lundbeck SAS, sponsor of the study; she collaborated on study design, interpretation of study results, and development of the manuscript.

2. DBD and TMB are employees of RTI Health Solutions, contracted by Lundbeck SAS to design and implement this study. DBD designed and co-facilitated the interviews and focus groups, collaborated on the analysis and interpretation of study results, and contributed to development of the manuscript. TMB collaborated on the design of the study, co-facilitated the interviews and focus groups, analyzed the data and interpreted study results, and contributed to development of the manuscript.

### Declaration of financial/other relationships

All authors contributed equally to the work. ND is employed by Lundbeck SAS, sponsor of this study. DBD and TMB are employed by RTI Health Solutions, the organization conducting the work. The authors have no additional financial relationships or otherwise to declare.

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