Schizophrenia Research: Cognition 19 (2020) 100164

Contents lists available at ScienceDirect

Schizophrenia Research: Cognition

journal homepage: www.elsevier.com/locate/scog

The association of autistic traits with Theory of Mind and its training efficacy in patients with schizophrenia

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ARTICLE INFO

Keywords:
Schizophrenia
Autistic traits
Social cognition
Rehabilitation

ABSTRACT

Literature has recently identified a discrete subgroup of patients affected by schizophrenia that also present autistic traits (ATs), showing a peculiar cognitive, clinical and functional profile. Theory of Mind (ToM) represents a core, impaired feature in both schizophrenia and Autism Spectrum Disorder (ASD), ToM in patients with schizophrenia and ATs has yet to be investigated. Thus, this study aims, on the one hand, to assess differences among patients with and without ATs on clinical, cognitive and ToM abilities as well as in daily functioning; on the other hand, to compare the efficacy on mentalizing abilities of a specific ToM training in these two groups.

Ninety-six patients with schizophrenia were enrolled and underwent a broad cognitive, social-cognitive and functional assessment before and after the ToM training.

ANOVAs revealed that patients with schizophrenia and ATs are more impaired in cognition, ToM, in premorbid and daily functioning as well as in clinical features, as compared to patients without ATs. This latter group also showed a general improvement in mentalizing abilities after ToM training, while patients with schizophrenia and ATs did not, with a significant time × group interaction on ToM abilities.

These data shed new light on the relation among schizophrenia and ATs, highlighting that patients with these traits are highly impaired in ToM abilities. Thus, ATs seem to limit the effectiveness of ToM training, having implications in clinical and rehabilitative practice.

1. Introduction

Schizophrenia and Autism Spectrum Disorder (ASD) are pervasive neurodevelopmental conditions, presenting common features, both characterized by a chronic clinical course (Lai et al., 2014; Owen et al., 2016).

Although the current nosography describes schizophrenia and ASD as distinct conditions (APA, 2013), literature highlights some overlapping features between them (Barlati et al., 2016; Dell'Osso et al., 2016; Matsuo et al., 2015). The observation of impairments in cognitive, social cognitive, functional domains (Chisholm et al., 2016; Lai et al., 2014; Owen et al., 2016), and physiopathologic mechanisms suggests that ASD and schizophrenia may share similar defects in biological pathways of brain development, suggesting a disorders' phenotypic spectrum (Burbach and van der Zwaag, 2009; Kushima et al., 2018).

Noteworthy, recent research has identified a specific subgroup of patients affected by schizophrenia that reveal autistic traits (ATs), showing serious dysfunctions of social interactions, communication, emotion processing and motor abnormalities (Barlati et al., 2019; Kästner et al., 2015; King and Lord, 2011). Moreover, patients with ATs show a peculiar clinical (Barlati et al., 2019), functional (Deste et al., 2018) as well as cognitive profile (Barlati et al., 2019; Dell'Osso et al., 2016; King and Lord, 2011; Matsuo et al., 2015). In particular, patients with ATs present a longer duration of illness (Bastiaansen et al., 2011; Chisholm et al., 2016), more severe negative symptoms (Barlati et al., 2019; Sheitman et al., 2004) and an earlier disease onset (Cochran et al., 2013; Jerrell et al., 2017a). Their neurocognitive profile is

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https://doi.org/10.1016/j.scog.2019.100164
Received 28 February 2019; Received in revised form 23 September 2019; Accepted 24 September 2019
Available online 31 October 2019

characterized by more pronounced deficits in working memory, executive functions, and processing speed (Deste et al., 2018). Regarding functioning, results are still divergent: some studies report a more compromised social functioning in patients with ATs (Deste et al., 2018), while others do not show this evidence (Cochran et al., 2013; Shi et al., 2017).

To our knowledge, literature does not offer data regarding social cognitive performance in patients with ATs. Nevertheless, it is well known that a severe impairment in social cognitive abilities, especially in Theory of Mind (ToM, i.e., the ability to attribute mental states to other individuals) is a core and overlapping cognitive symptom (Frith and Corcoran, 1996), and it is related to similar neural abnormalities in the medial prefrontal and the superior temporal sulcus in both ASD and schizophrenia (Bliksted et al., 2016; Völlm et al., 2009). Many patients affected by schizophrenia show compromised ToM abilities after their illness onset and this is considered one of the main factor causing daily functioning impairment (Fett et al., 2011; Tas et al., 2013). Moreover, ToM deficit is widely heterogeneous in schizophrenia. Indeed, although many patients get a poor performance on ToM tasks, a non-negligible group of subjects displays a quite normal or close to normal performance on mentalizing tasks (Bechi et al., 2018; Brune and Schaub, 2012; Rocca et al., 2016). Therefore, we may hypothesize that ToM heterogeneity among patients with schizophrenia may be linked to ATs, since the degree of ToM impairments may be higher in patients with ATs. In line with this hypothesis, the study of ToM functioning in patients with ATs could represent a central issue and may open new debates about this clinical subgroup.

Given the main role of ToM impairment, innovative interventions have been developed in order to improve ToM abilities and, consequently, daily functioning in schizophrenia (Bechi et al., 2012; Bechi et al., 2013; Green et al., 2008; Mazza et al., 2010; Roberts and Penn, 2009). Literature demonstrated trainings' effectiveness in enhancing ToM (Kurtz et al., 2016; Vass et al., 2018) and showed the generalization of ToM gain on daily, social and work functioning (Bechi et al., 2015; Bechi et al., 2017b; Pino et al., 2015). Moreover, Eack and colleagues demonstrated that the benefit achieved in daily functioning after ToM trainings is maintained for at least one year (Eack et al., 2010; Bechi et al., 2019). Although research showed the effectiveness of the different interventions on ToM in schizophrenia, the size of improvement is variable, from small to moderate mean effect sizes (d: 0.46, 95% CI: 0.15–0.78) (Kurtz and Richardson, 2012). We can suggest that the presence of ATs may be a contributing factor to the great variance in ToM improvement. Nevertheless, to our knowledge, no studies explored the impact of social cognitive trainings in patients with ATs in order to establish if autistic features may be a limiting factor of rehabilitation efficacy.

Given this scenario, the current study is two-fold. First, it aims to estimate differences between patients with and without autistic features, on demographic and clinical features, cognitive and ToM abilities as well as on daily and premorbid functioning in a sample of patients affected by schizophrenia. Then, it aims to evaluate the efficacy of a ToM training in patients with ATs compared to patients without ATs.

2. Materials and methods

2.1. Participants

We enrolled ninety-six outpatients with schizophrenia. All patients met DSM-5 criteria for schizophrenia, as determined by trained psychiatrists using clinical interviews, and did not present relapse or hospitalization in the past 6 months. All patients underwent a ToM training (see Bechi et al., 2015). Exclusion criteria were: co-morbid psychiatric diagnoses, substance dependence or abuse in the past year, perinatal trauma and major neurological illness.

All subjects provided a written informed consent to a protocol approved by the local Ethical Committee, which followed the principles of the Declaration of Helsinki.

2.2. Design

Before ToM training (see (Bechi et al., 2015)), all enrolled patients were assessed for cognition, intellectual level, ToM, ATs, premorbid and current daily functioning and, after the training, they were re-assessed for ToM abilities.

2.3. Assessments

ATs severity was assessed with the PANSS Autism Severity Score (PAUSS) (Kästner et al., 2015). Three scores are derived from the sum of specific items of the PANSS: a “Difficulties in Social Interaction” Score (items 1 ‘blunted affect’, 3 ‘poor rapport’, and 4 ‘social withdrawal’ from the Negative Scale); a “Difficulties in Communication” Score (items 5 ‘difficulties in abstract thinking’, and 6 ‘lack of spontaneity and flow of conversation’ from the Negative Scale); and a “Stereotypies/Narrowed Interests” Score (item 5 ‘mannerism’ and 15 ‘preoccupation’ from the General Scale, and item 7 ‘stereotyped thinking’ from the Negative Scale). PAUSS is a reliable tool for the measure of autistic traits in patients; indeed constructs and criterion-related validity of the task were first assessed in a sample of high-functioning ASD patients (Kästner et al., 2015). Patients were not assessed with full PANSS, but they were evaluated only with the PAUSS. The scale has been used to provide a measure of autistic features among patients with schizophrenia (Barlati et al., 2019; Kästner et al., 2015).

Cognition was assessed with the Italian version of the Brief Assessment of Cognition in Schizophrenia (BACS) (Anselmetti et al., 2008; Keefe et al., 2004), assessing verbal memory, working memory, psychomotor speed and coordination, processing speed, verbal fluency and executive functions.

Intellectual level was assessed by means of the Wechsler Adult Intelligence Scale–Revised (WAIS-R) Italian Version (Wechsler, 1997). WAIS-R estimates the intelligence quotient (IQ) and its both verbal and performance components.

ToM abilities were assessed with the ToM Picture Sequencing Task (PST) (Brune, 2003) which is composed by a Sequencing Task (i.e., a measure of affective ToM processes) and a Questionnaire (i.e., a measure of cognitive ToM). A previous study by Bechi and colleagues (Bechi et al., 2012) confirmed the reliability and the good internal consistency (Cronbach's α coefficient = 0.86). The variables of interest were: First Order Beliefs Total Score, Second Order Beliefs Total Score, Third Order False Beliefs Score, Total Questionnaire Score, Total Sequencing Score, and Total Score.

Premorbid functioning was assessed with the Premorbid Adjustment Scale (PAS) (Cannon-Spoor et al., 1982), a retrospective interview focused on the individual's social and academic achievements preceding illness onset. The PAS assesses premorbid adjustment (PA) during childhood (up to 11 years), early adolescence (12 to 15 years), late adolescence (16 to 18 years) and adulthood (19 years and above). Five domains are assessed (i.e., sociability and withdrawal, peer relationships, scholastic performance, adaptation to school and social-sexual functioning) and rated from 0 (normal adjustment) to 6 (severe impairment).

Functioning was assessed with the Quality of Life Scale (QLS) (Heinrichs et al., 1984), a 21-items semi-structured interview, balancing subjective questions regarding life satisfaction and objective indicators of social and occupational role functioning. As in previous studies (Bechi et al., 2017a; Cavallaro et al., 2009), we analyzed three subscores: Interpersonal relations (items 1–8), Instrumental role (items 9–12), Personal autonomy (items 13–2).

All tasks were administered by trained psychologists, except for the PAUSS, which was administered by trained psychiatrists. All data were collected at patients' enrollment.

2.4. Intervention

The ToM Intervention consists of five modules divided into 18 sessions (1-h session, twice a week), using comic strips, cartoons and clips depicting human social interactions. The modules were executed in an ascending order of complexity, with the first three modules focusing on cognitive ToM and the last two on affective ToM. Patients were request to recognize mental states and emotions, in order correctly comprehended ToM. A guided discussion of hypotheses follows each session (see more details in Bechi et al., 2015).

2.5. Data analysis

In line with the previous literature (Deste et al., 2018; Kästner et al., 2015), we set a PAUSS cut-off score of 30, in order to compare patients with and without ATs. This cut-off yields a specificity of 95%, leading to consider patients with PAUSS > 30 as patients with ATs (ATs+ group) (Kästner et al., 2015).

Analyses of variance (ANOVAs) were performed on demographic, clinical, cognitive, intellectual, ToM (at T0), functional and premorbid variables, in order to evaluate differences among patients' groups (ATs + group and ATs− group).

The size of changes, in each PST subdomains and Total Score, were estimated using Cohen's d effect sizes (Cohen, 1988).

Pre- to post-treatment changes between groups were analyzed with repeated-measures ANOVA (2×2, $p < .05$, two-tailed) entering ToM measures (i.e., PST total score at T0 and T1) as dependent variables, time as within subjects factor, and patients' group (i.e., ATs+ group and ATs− group) as independent variable. Fisher LSD post hoc test followed.

3. Results

Table 1 shows demographic and clinical characteristics of the sample.

Seventy-three patients (76.04% of the total sample) showed a PAUSS Total Score < 30 (ATs− group), while 23.95% (23 patients) had a PAUSS Total Score > 30 (ATs+ group).

Table 2 summarizes ANOVAs results. Significant between groups differences emerged in many areas. ATs+ group presented an earlier age of onset and a longer duration of illness. Concerning cognitive abilities, ATs+ group had a more impaired cognitive functioning, characterized by a lower intellectual level and more impaired performances in working memory, verbal memory, processing speed and executive functions tasks. As for ToM, ATs+ group resulted more impaired than ATs− group in PST Total Questionnaire Score and Total Score. Differences between groups were also found for premorbid functioning, indeed patients with ATs presented a more impaired premorbid functioning, especially during childhood and adolescence. As for actual daily functioning, ATs+ group resulted more impaired than ATs− group in QLS Self-directedness Score and Total Score.

Table 1
Demographic and clinical characteristics of the sample.

	Mean	Standard deviation (SD)
Age (years)	45.51	± 11.11
Education (years)	11.71	± 2.82
Age at onset (years)	23.91	± 6.30
Duration of illness (years)	21.51	± 9.86
Sex (% male)	68.22	–
PAUSS – difficulties in social interaction	10.44	± 3.59
PAUSS – difficulties in communication	6.30	± 2.99
PAUSS – stereotypies/narrowed interests	9.31	± 4.71
PAUSS – total score	26.05	± 10.63

PAUSS = PANSS Autism Severity Score (total score: range 0–56).

Effect-sizes of improvements on PST subscales and Total Score in both groups are depicted in Table 3.

Repeated-measures ANOVA showed significant time (pre vs post treatment) × group (ATs+ group and ATs− group) interactions on PST Total Score ($F(1, 94) = 4.57$, $p = .03$). As revealed by Fisher LSD post hoc test, ATs− group improved significantly from pre to post treatment (T0-T1), while ATs+ group did not (see Table 4).

4. Discussion

The present study was conceived to identify cognitive, sociocognitive and functional differences between patients with and without ATs, and to evaluate the different efficacy of ToM training in these two groups.

Our work supports previous literature, showing that there is a subgroup of patients with ATs (Barlati et al., 2019; Deste et al., 2018), characterized by a more deficitary cognitive, sociocognitive and functional profile. This is the first study that observed a more limited ToM improvement after a socio cognitive training in patients with ATs.

In detail, the use of the cut-off of PAUSS Total Score at 30 allowed to identify patients with ATs (23.95% of the sample) and without ATs. Our results confirm the rates found in previous studies for ATs in schizophrenia, which are highly variable, from 0.78% to 61% (Chisholm et al., 2016; Kincaid et al., 2017), according to the assessment employed.

As demonstrated in literature (Barlati et al., 2019; Chisholm et al., 2016; Jerrell et al., 2017), ATs+ group is characterized by a significant earlier onset of the disease and a longer illness duration. As for cognition, ANOVA showed significant differences between groups in I.Q. (Verbal, Performance and Total Scores), verbal memory, working memory, processing speed, and executive functions. Thus, ATs+ group showed a more severe impairment in cognitive abilities, which affects specific domains, as already seen in previous works (Barlati et al., 2019; Deste et al., 2018).

To our knowledge, this is the first study that evaluates ToM functioning in patients with schizophrenia showing autistic traits. Results suggest that ATs+ group has a more pronounced ToM impairment, which mostly affects Cognitive ToM. Indeed, ANOVA shows significant differences between groups in PST Questionnaire Score and PST Total Score, while there is not a significant difference in PST Sequencing Score, which is considered a measure of Affective ToM. As observed by Bechi (Bechi et al., 2018), Affective and Cognitive ToM deficits are differently distributed in schizophrenia. While Cognitive ToM resulted globally impaired compared with a healthy control group, Affective ToM seems to be more preserved in schizophrenia. Therefore, we could speculate that also patients with ATs are less impaired in Affective ToM then in cognitive ToM domain. Recently, a ToM functioning heterogeneity was also observed in ASD, with a different impairment of Affective and Cognitive ToM that can contribute to explain the severity of the illness (Altschuler et al., 2018). Our results are in line with this evidence, and we can hypothesize that ATs may contribute to explain the ToM functioning heterogeneity in schizophrenia, since ATs+ group presents a more pronounced impairment of ToM abilities.

Additionally, an intriguing result concerns functioning. As known, literature suggests multiple functional trajectories before schizophrenia onset, indeed during childhood and adolescence some patients do not show premorbid impairments, while others show a poor premorbid adjustment (Chang et al., 2013; Horton et al., 2015). Noteworthy, using PAS scale, we found significant differences between groups in premorbid paths and, in particular, a worse functioning during childhood and early adolescence in ATs+ group. These different functional trajectories are also observed, using QLS scale, in the current daily functioning. Indeed, ATs+ group shows a worse daily functioning, especially in Self-directedness. Surprisingly, we did not find differences in relationships domain; we can hypothesize that social skill differences did not emerge because it was assessed with the QLS task, which

Table 2
ANOVA of demographical, clinical, cognitive, ToM, functional variables in both groups.

	ATs+ group	ATs− group	ANOVA	
	Mean (SD)	Mean (SD)	F	*p*
Age (years)	45.30 (± 12.42)	45.40 (± 10.73)	0.001	.97
Education (years)	11.26 (± 2.43)	11.84 (± 2.95)	0.716	.39
Age at Onset (years)	20.09 (± 2.91)	25.05 (± 6.65)	12.055	.0008*
Duration of illness (years)	25.21 (± 12.59)	20.34 (± 8.61)	4.421	.03*
Sex (% male)	52.17	65.75		
PST (T0)				
First Order Beliefs Total Score	3.30 (± 1.55)	3.82 (± 1.08)	3.202	.07
Second Order Beliefs Total Score	3.13 (± 1.18)	3.51 (± 1.32)	1.485	.22
Third Order False Beliefs	1.17 (± 0.83)	1.49 (± 1.00)	1.914	.16
Total Questionnaire Score	14.70 (± 4.09)	16.68 (± 3.94)	4.370	.03*
Total Sequencing Score	21.96 (± 7.08)	25.41 (± 7.44)	3.858	.052
Total Score	36.65 (± 10.13)	42.10 (± 10.06)	5.103	.02*
I.Q.				
Verbal score	81.35 (± 10.49)	90.26 (± 14.02)	6.817	.01*
Performance score	75.95 (± 10.00)	84.53 (± 13.43)	6.903	.01*
Total score	78.81 (± 9.53)	86.58 (± 12.99)	6.388	.01*
BACS				
Verbal memory	30.74 (± 12.53)	36.58 (± 10.05)	5.208	.02*
Working memory	13.43 (± 4.30)	16.55 (± 3.35)	12.971	.0005*
Psychomotor speed and coordination	66.52 (± 17.39)	68.87 (± 15.73)	0.348	.55
Verbal fluency	35.00 (± 13.57)	36.96 (± 13.39)	0.370	.54
Processing speed	31.96 (± 13.13)	37.49 (± 10.14)	4.414	.03*
Executive functions	10.04 (± 3.95)	13.37 (± 3.83)	12.904	.0005*
PAS				
Childhood	0.46 (± 0.18)	0.32 (± 0.17)	7.584	.007*
Early adolescence	0.51 (± 0.14)	0.38 (± 0.16)	7.338	.008*
Late adolescence	0.55 (± 0.12)	0.46 (± 0.18)	3.621	.06
Adulthood	0.50 (± 0.24)	0.42 (± 0.22)	1.442	.23
General score	0.51 (± 0.11)	0.49 (± 0.13)	0.237	.62
Total score	0.48 (± 0.07)	0.39 (± 0.11)	8.307	.005*
QLS				
Relationships	16.70 (± 8.68)	19.41 (± 6.75)	2.205	.14
Work	3.30 (± 4.77)	3.20 (± 4.77)	0.007	.93
Self-directedness	19.20 (± 9.41)	26.77 (± 7.98)	12.983	.0005*
Total score	39.20 (± 20.90)	49.38 (± 14.64)	6.178	.01*

Data are given as mean and (standard deviation).
ANOVA = analysis of variance.
PST = Picture Sequencing Task (Total Questionnaire Score: range 0–23; Total Sequencing Score: range 0–36; Total Score: range 0–59). I.Q. = Intelligence Quotient. BACS = Brief Assessment for Cognition in Schizophrenia (verbal memory: range 0–75; working memory: range 0–28; psychomotor speed and coordination: range 0–100; verbal fluency: 0–60; processing speed:0–110; executive functions: range 0–22). PAS = Premorbid Adjustment Scale (Total Score: range 0–1). QLS = Quality of Life Scale (Total Score: range 0–126).
* = $p < .05$

Table 3
Effect-sizes of improvements on PST in both groups.

	ATs+ group	ATs− group
	Mean (SD)	Mean (SD)
PST		
First Order Beliefs Total Score	0.16 (± 1.11)	0.30 (± 0.98)
Second Order Beliefs Total Score	0.03 (± 1)	0.53 (± 1.08)
Third Order False Beliefs	0.21 (± 1.21)	0.45 (± 1.24)
Total Sequencing Score	−0.04 (± 0.86)	0.33 (± 0.89)
Total Questionnaire Score	0.02 (± 1.01)	0.49 (± 0.98)
Total Score	−0.02 (± 0.91)	0.42 (± 0.87)

Data are given as mean and (standard deviation).
PST = Picture Sequencing Task.

Table 4
Repeated measures ANOVA on ToM.

	ATs+ group	ATs− group	T		G × T	
	p (T0-T1)	*p* (T0-T1)	F	*p*	F	*p*
PST – Total Score	.89	< .0001*	3.66	.059	4.57	.03**

Repeated measures (pre- to post-treatment changes) and interactions outcomes are reported.
PST = Picture Sequencing Task.
* Significant within-group differences marked.
** Significant time and group × time interactions marked.

evaluates the subject's perception of his social functioning. It can be suggested that patients with ATs may show a different developmental trajectory since childhood, which seems to be more comparable to ASD's functional neurodevelopmental path, and a subsequent more impaired daily functioning. This relevant issue highlights the importance of early interventions for cognitive and social cognitive impairments, which may offer possible opportunity to modify the course of the disease in patients with ATs.

In sum, our results show that ATs+ group manifests lacking cognitive and ToM abilities, associated with the impairment in premorbid and current functioning. Taken together, these data suggest that patients with ATs may have specific neurodevelopmental features, which, however, do not meet diagnostic criteria for ASD.

Given this scenario, we evaluated the effect of rehabilitative interventions in patients with ATs, by estimating the effectiveness of a treatment aimed at enhancing ToM. Repeated measures ANOVA reveals a significant time × treatment interaction in the PST Total Score, and Post Hoc analyses show that the Schizophrenia group obtains a

significant improvement after the training, while there is not significant enhancement in ATs+ group. Nevertheless, results show moderate to medium effects sizes for both groups in ToM first, second and third order beliefs, but not in PST Sequencing Score. This indeed suggests that a slight degree of improvement is achievable also in ATs+ group, particularly in Cognitive ToM domains. However, results show that both groups present an impairment of Affective ToM before the training, which can be enhanced only in in ATs− group. As sustained by literature, a good performance on PST Sequencing Task could be supported by cognitive abilities, such as executive functions (Devine and Hughes, 2014; Vera-Estay et al., 2016), which resulted highly impaired in this group. The ATs+ present a wider impairment of high-level cognitive abilities which can be a limiting factor of ToM rehabilitation efficacy.

Therefore, it could be proposed that, even if ToM rehabilitative interventions produce a small improvement in ATs+ group, they do not provide the necessary building blocks for the acquirement of more complex abilities, suggesting that ATs limit the effectiveness of rehabilitation.

Indeed, this study has some limitations: the small sample size limits the generalizability of results and the study would have benefit from adding into analyses additional sociocognitive evaluations, such as Empathy and Emotion Recognition, and functional evaluations after the training. Moreover, studies suggested that ToM measures may not be sensitive enough to capture individual's ToM skills in real-life situations and thus may not be ecologically measures of mentalizing abilities.

In conclusion, this study suggests the existence of a distinct group of patients with schizophrenia exhibiting ATs that is characterized by a distinctive clinical, premorbid, functional, cognitive, and sociocognitive profile. To the best of our knowledge, few studies focused on these patients, and this is the first study specifically aimed at analyzing their sociocognitive abilities and premorbid functioning. Our results might have implications in clinical and rehabilitative practice; indeed we found that current rehabilitative interventions for ToM do not produce a significant ToM improvement, suggesting the importance of the implementation of cutting-edge, person-centered treatments, based on each subjects' clinical and sociocognitive profile. Indeed, since the larger cognitive and sociocognitive impairment in ATs+ group, we can hypothesize that an integrated rehabilitative approach, including both ToM and neurocognitive interventions, can lead a ToM enhancement in both groups. Results suggest that PAUSS should be used more extensively in clinical practice, considering that not taking into account ATs may result in some patients not receiving appropriate services, benefits, or specific treatments.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors declare that there is no conflict of interest.

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