Cognitive dysfunction and disability in people living with schizophrenia

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Abstract

Background: Schizophrenia is a major mental disorder characterized by positive, negative, and cognitive symptoms. Cognitive impairment is a central and enduring feature of schizophrenia and is associated with disability. It has a devastating consequence on the individuals, families, and the society. Our aim was to assess cognitive functioning, disability, and their association with sociodemographic and illness-related variables. **Methodology:** In an outpatient department of psychiatry, 82 adult patients with a diagnosis of schizophrenia were recruited. Schizophrenia Cognition Rating Scale (SCoRS), Positive and Negative Syndrome Scale (PANSS), and Indian Disability Evaluation and Assessment Scale (IDEAS) were used to assess cognitive function, psychopathology, and disability respectively. Socio-demographic and illness-related details were collected using a semi-structured questionnaire. Data were analyzed using STATA version 16.0 using appropriate statistical tests. **Results:** Approximately 93.9% of patients had at least one cognitive symptom even though not severe. The status of being married was associated with better cognitive outcome. No other socio-demographic factor was associated with cognitive dysfunction. Negative symptoms and general psychopathology scores of PANSS were positively correlated with SCoRS scores and IDEAS score. Cognitive dysfunction and disability were significantly associated suggesting higher the cognitive deficit in schizophrenia greater is the likelihood of patient experiencing disability. **Conclusion:** Cognitive deficits are commonly seen in patients with schizophrenia and are associated with disability. Therefore, treatment programs of schizophrenia should have a component to address these deficits using evidence-based cognitive remediation therapies. Family Physicians caring for those with schizophrenia should factor the cognitive deficits and simplify dosage regime and engage caregivers for supervision.

Keywords: Cognitive functions, disability, negative symptoms, schizophrenia

Introduction

Schizophrenia is a heterogeneous syndrome both clinically and etiologically. The symptoms clusters include positive psychotic symptoms, negative symptoms, cognitive symptoms, and affective symptoms. Cognitive impairment is a central and enduring feature of schizophrenia.[1] Cognitive deficit can precipitate psychotic symptoms and negative symptoms.[2] Functional deficits, similar to cognitive deficits are seen at the onset of illness. The neuro-cognitive compromise affects social competence, capacity of independent living, and vocational success.

Sustained attention, early information processing, contextual processing, memory, verbal and nonverbal ability, executive functioning, abstraction, and conceptual organization are some of the cognitive domains affected in Schizophrenia. Functional impairment and its severity are predicted by a limited set of cognitive deficits. Executive functioning and working memory are related to occupational functioning and independent living; vigilance is related to social and occupational functioning and declarative memory is related to independent living thus explaining the correlation between the cognitive domains and functioning.[3] Harvey *et al.*[4] in their study compared cognitive

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and adaptive functioning and showed that degree of declining cognition being the best predictor of functional status.

The negative symptoms added to the adipogenic risk of antipsychotic increase the rate of metabolic syndrome. The interaction between sedentary behavior and metabolic adverse effects of antipsychotics cause a direct negative influence in daily functioning, physical health and ultimately shortens the life expectancy.[5]

Studies done to assess improvement in functioning when cognition has been enhanced have found a positive result. Neuropsychological rehabilitation has been found to be useful in reducing the negative symptoms and improving the functional capacity.[6]

Even though psychiatrists may screen for medical illness in patients with schizophrenia, it is important for coordination with family physicians to ensure effective management.[7]

This study aimed to assess cognitive functioning and disability in patients with schizophrenia and to study the association of these with socio-demographic and illness-related variables

Methodology

Study design

A descriptive cross-sectional study was used to evaluate Cognitive dysfunction and disability. The study was approved by the Institutional Review Board (IRB No. 9236).

Inclusion criteria

The study population was adult patients attending OPD of the Department of Psychiatry, in a tertiary care hospital in South India. Patients with a diagnosis of schizophrenia of more than 1 year duration between the age group of 18–60 years who could read, write and converse fluently in Tamil or English and who were on stable dose of drugs for a least period of 1 month were included.

Exclusion criteria

Patients who had received electro convulsive therapy (ECT) within past 6 months (ECT can affect cognition and those effects can last for 6 months),[8] patient with co-morbid alcohol use in dependence pattern (as alcohol dependence can independently affect cognitive function), patient with Acquired and/or Traumatic Brain Injury (as various domains of cognition can be affected depending on the region involved in the trauma), patient with independent Dementia, patient with medication and dose changes in past 1 month (these being considered a proxy indicator for recent change in mental state) were excluded.

Sample size

We estimated the sample size based on an anticipated prevalence that at the least seventy percent of patients with schizophrenia had at least one cognitive deficit.[9]

The sample size (n) estimated with anticipated prevalence of 70% and 10% level of precision was 81. Eighty two consecutive eligible patients were recruited.

Consent

An informed written consent from both patient and their caregiver was obtained.

Assessment tools

Socio-demographic details and illness-related details were obtained using a semi-structured questionnaire.

Assessment of cognitive functioning: Schizophrenia Cognition Rating Scale (SCoRS)[10] was used to assess the cognitive functioning: which is scored subjectively by the patient, objectively by the caregiver and by the principal investigator (PI). The SCoRS score has a range of 0-80, with higher score indicating greater dysfunction. It also has a global assessment made by the interviewer in a scale of 1 to 10.

Assessment of psychopathology: It was measured using Positive and Negative Syndrome Scale for schizophrenia (PANSS) which has three subscales of positive, negative and general psychopathology. The maximum possible score for positive and negative symptoms were 49 and for general psychopathology were 98.

Assessment of disability: The disability score was assessed using Indian Disability Evaluation and Assessment Scale (IDEAS) which is an interviewer administered scale. The scores can range from 0-20 with higher scores reflecting greater disability.

Statistical methods

Data were analyzed using STATA version 16.0.[11] the prevalence rate is presented with 95% confidence interval. The frequency of demographic and clinical variables which were categorical such as gender, marital status, and subtype was presented along with percentage. Descriptive statistics for continuous variables was presented as mean, median, standard deviation and interquartile range. We used penalized logistic regression as compared to ordinary logistic regression analysis in order to avoid sparse data problem (i.e. few cell values) to find out the risk factors for having "high" SCoRS score and "Moderate/Severe" Disability score. Initially, univariate risk factor analyses were done to find the relationship between clinical variables such as severity of disease, duration of illness and so on and the demographic factors such as age, and gender by considering each variable in the model. In order to avoid false negative findings at the univariate analyses, the potential variables for multivariable analyses were identified based on $P <=0.20$. We used Shapiro Wilk test for testing the normality of the data. By considering the cognitive scores, disability scores and PANSS scores as continuous variable we found out the relationship between them, by using Spearman's rank correlation coefficient as the scores were not normally distributed. Statistical significance was based on $P < 0.05$ level.

Results

This study was designed to assess the cognitive functioning in schizophrenia and to assess for correlation between cognitive symptoms and disability. The details of socio-demographic and descriptive statistics of clinical variables are described in Table 1.

Descriptive statistics of the clinical variables

Cognitive functioning: The SCoRS score was not normally distributed and hence a median cutoff was used as a descriptive statistic for central tendency and it has been used to divide subjects with high SCoRS score and low SCoRS score. The mean score was 34.1 with standard deviation was 11.1. The distribution was skewed to right. The median was 31.5.

Disability assessment: The scores obtained were normally distributed. The mean score was 6.4 with standard deviation of 3.05.

Table 1: Socio-demographic and clinical variables of sample

Variable	n (%)
Male Gender	48 (58.54)
Socio Economic Status	
Upper	30 (36.59)
Middle	30 (36.59)
Lower	22 (26.83)
Marital Status	
Single	39 (47.56)
Married	36 (43.90)
Others	7 (8.54)
Nuclear type of Family	69 (84.15)
Living in a rural Habitat	46 (56.09)
Education:	
Up-to X grade	21 (25.61)
Beyond X grade	61 (74.4)
Employed gainfully	20 (24.39)
Paranoid subtype	75 (91.46)
Psychotic episode more than once	42 (51.22)
Positive history of in-patient treatment	31 (37.80)
Good compliance with Medications	60 (73.17)
Past history of treatment with ECT	4 (4.88)
Medical history of Diabetes Mellitus	5 (6.10)
Use of tobacco -harmful use/dependence	12 (14.63)
Positive family history of psychiatric illness	28 (34.15)
	Mean (SD)/ Median (IQR)
Age	35.05 (8.99)
Age at onset	26.55 (7.37)
Duration of illness (months)	78.00 (42.0, 138.0)
Duration of untreated illness (months)	6.00 (2.00, 36.00)
Total years of antipsychotic exposure	4.67 (2.00, 9.00)
SCoRS- Interviewer score	34.12 (11.10)
IDEAS score	6.40 (3.05)
PANSS Positive subscale score	7.57 (2.34)
PANSS Negative subscale score	12.84 (6.39)
PANSS General Psychopathology subscale score	21.74 (5.63)

Analysis of risk factors

Factors affecting cognition

The risk factors for higher cognitive dysfunction were studied by dividing the sample into two groups based on higher score (cases) and lower score (controls) using the median cutoff of SCoRS score. It was found that marital status has been shown to be protective with the odds ratio of 0.12 (0.02-0.79). Multivariate analysis was done using these variables and the effects still persisted. They have been tabulated in Table 2.

Risk factors for higher disability

Disability Median score of 6.0 was used as a cut-off point to divide the subpopulation into groups of high (cases) and low disability (controls). It was found, male gender and lower socioeconomic status were the socio-demographic variables associated with high disability with odds ratio of 3.09 (95% confidence interval (OR) 1.21-7.84) and 3.50 (1.10- 11.09) respectively. Among the clinical variables, age of onset and the duration of illness have been found to be a risk factor for increased disability with odds ratio of 3.43 (1.37-8.57) and 4.05 (1.58-10.36), respectively. These have been described in Table 3.

Relationship between cognitive functioning and disability

Correlation between cognitive functioning using interviewer score in SCoRS and disability was done. Spearman's rho was calculated to be 0.616 which was significant with a *P* value less than 0.001 in 2 tailed test, showing cognitive dysfunction to be positively associated with disability.

Relationship between psychopathology and cognitive functioning and relationship between disability and psychopathology

Correlation between disability and the three subscales of PANSS showed a significant positive correlation, however, the correlation between negative symptoms and disability was strongest with a correlation coefficient of 0.765. Correlation between cognitive functioning and the three subscales of PANSS showed a significant positive correlation. The Spearman's rho between negative symptoms and cognitive dysfunction was more than twice that of the Spearman's rho between positive symptoms and cognitive dysfunction. General psychopathology was even more strongly correlated. These correlations are tabulated in Table 4.

Discussion

This cross-sectional study aimed to look at the cognitive functioning in patients with schizophrenia and to study its relationship with disability and identify the risk factors. Our study population was predominantly male and single (never married) from all socioeconomic strata with various levels of educational achievement. About half of the subjects were employed and stable in jobs before the onset of illness. More than half of this subgroup had become unemployed after the onset of illness making about three-fourths of this subgroup unemployed at the

Table 2: Factors associated with Cognition- Bivariate (Penalized logistic regression) analysis Definition: Interviewer SCoRS score: Control: <= 31 score & Case: > 31 score

Variable	Cases n=41 (50%)	Controls n=41 (50%)	Bivariate		
			OR	95% CI	P
Gender Male	27 (65.85)	21 (51.22)	1.81	(0.75, 4.35)	0.186
Socio-Economic Status: Middle	12 (29.27)	18 (43.90)	0.77	(0.28, 2.10)	0.609
Lower	15 (36.59)	7 (17.07)	2.35	(0.77, 7.22)	0.135
Marital Status					
Single	23 (56.10)	16 (39.02)	0.33	(0.05, 2.16)	0.247
Married	12 (29.27)	24 (58.54)	0.12	(0.02, 0.79)	0.027**
Nuclear type of Family	32 (78.05)	37 (90.24)	0.41	(0.12, 1.38)	0.151
Living in a rural habitat	22 (53.66)	24 (58.54)	0.82	(0.35, 1.95)	0.660
Education: up-to Grade X.	11 (26.83)	10 (24.39)	1.67	(0.54, 5.11)	0.371
beyond Grade X	19 (46.34)	14 (34.15)	2.05	(0.75, 5.61)	0.164
Occupational Status Unemployed	32 (78.05)	30 (73.17)	1.29	(0.48, 3.48)	0.615
Paranoid Subtype	38 (92.68)	37 (90.24)	1.32	(0.30, 5.73)	0.711
Psychotic episode more than once	17 (41.46)	25 (60.98)	0.46	(0.19, 1.11)	0.083
No hospitalization in the past	27 (65.85)	24 (58.54)	1.35	(0.56, 3.28)	0.501
Poor Compliance with medications	12 (29.27)	10 (24.39)	1.27	(0.49, 3.33)	0.625
No past history of treatment with ECT	39 (95.12)	39 (95.12)	1.00	(0.16, 6.10)	1.00
Medical history of Diabetes Mellitus	2 (4.88)	3 (7.32)	0.70	(0.13, 3.75)	0.673
Use of tobacco Harmful use/dependence pattern	7 (17.07)	5 (12.20)	1.44	(0.44, 4.76)	0.548
Positive family history of psychiatric illness	16 (39.02)	12 (29.27)	1.53	(0.62, 3.78)	0.360
Age*	33.73 (8.25)	36.37 (9.59)	0.97	(0.92, 1.02)	0.198
Age at onset <=25 yrs	23 (56.10)	19 (46.34)	1.47	(0.62, 3.46)	0.383
Duration of illness >6 yrs	22 (53.66)	23 (56.10)	0.91	(0.38, 2.15)	0.826
Duration of untreated illness >6 months	21 (51.22)	18 (43.90)	1.33	(0.56, 3.14)	0.513
Total years of antipsychotic exposure >5 yrs	18 (43.90)	19 (46.34)	0.91	(0.38, 2.15)	0.826

OR: Odds ratio; *Mean (SD); **Significant with *P*<0.05

time of assessment. The shift in the employment status from having a stable job to becoming unemployed after the onset of illness could be secondary to the decline in cognitive functioning as also reported in the study by Trivedi *et al*.[12] or due to the negative symptoms in the study by Srinivasan *et al*.[13]

In our study, we chose patients who were clinically stable which ensured not to pick up deficits due to new-onset psychopathology and deficits due to adverse drug reactions like sedation which are usual early on in treatment.

Cognitive functioning: Cognitive functioning was assessed using the Schizophrenia cognition rating scale. The interviewer's final score was the SCoRS score, and it was used for measuring the cognitive functioning which showed that most of the study population had milder levels of cognitive dysfunction. However, to study the risk factors for higher cognitive dysfunction the sample was divided into two groups. The groups were based on higher and lower cognitive functioning using the median cutoff of SCoRS score. Our study showed the status of living in marriage serves as a protective factor against higher cognitive dysfunction. This is in consistent with the fact that being married is a good prognostic factor in schizophrenia.[14] However, this could also signify that people who have greater cognitive deficits have lesser chances of getting married or have higher chances of being separated or divorced. Current age, age of onset of illness, gender, socioeconomic status, educational status, occupation, number

of hospitalizations, compliance, duration of illness, duration of untreated illness, total years of antipsychotic exposure were not associated with risk of higher cognitive deficits.

Psychopathology: When the mean scores of PANSS was analyzed as a whole, the mean scores fell on the lower end. This could probably be due to the selection of patients who were clinically stable. Patients with acute disturbance, necessitating the need for change in dose of the antipsychotic medication, are likely to have higher scores on PANSS. However, as patients with such profile were excluded from the study the scores were skewed to the right.

Risk factors of higher disability

Socio-demographic and psychopathologic characteristics were studied using appropriate statistical tests as described in results section. Various factors like male gender, lower socio-economic status, age of onset less than 25 years, and the duration of illness were associated with higher disability. The status of being married has offered protection against higher disability. It can be argued that people with greater disability were at risk for not finding partners or being abandoned or divorced by spouses. In our study, male gender came out to be risk factor a well-known poor prognostic factor in schizophrenia.[13] This effect persisted in multivariate analysis also.

In the Indian cultural context, there is an expectation for women to perform all the household chores despite being unwell and men to earn money by working outside the home. In, IDEAS

Table 3: Factors associated with disability- Bivariate (Penalized logistic regression) analysis. Definition: Disability score: Control: <= 6 score & Case: > 6 score

Variable	Cases *n*=37 (45.12%)	Controls *n*=45 (54.88%)	Bivariate		
			OR	95% CI	*P*
Male Gender	27 (72.97)	21 (46.67)	2.98	(1.19, 7.47)	0.019**
Socio-Economic Status					
Middle	13 (35.14)	17 (37.78)	1.51	(0.54, 4.21)	0.435
Lower	14 (37.84)	8 (17.78)	3.33	(1.08,10.3)	0.036**
Marital Status					
Single	23 (62.16)	16 (35.56)	1.11	(0.24, 5.13)	0.896
Married	10 (27.03)	26 (57.78)	0.31	(0.06, 1.48)	0.141
Nuclear type of family	30 (81.08)	39 (86.67)	0.67	(0.21, 2.12)	0.494
Living in a rural habitat	19 (51.35)	27 (60.00)	0.71	(0.30, 1.69)	0.437
Education:	12 (32.43)	9 (20.00)	1.32	(0.43, 4.01)	0.629
up-to Grade X. beyond Grade X	11 (29.73)	22 (48.89)	0.51	(0.18, 1.41)	0.196
Occupational Status: Unemployed	27 (72.97)	35 (77.78)	0.77	(0.29, 2.08)	0.613
Paranoid subtype	36 (97.30)	39 (86.67)	4.00	(0.64, 25.00)	0.138
Psychotic episode more than once	16 (43.24)	26 (57.78)	0.56	(0.24, 1.35)	0.197
No history of hospitalization in the past	27 (72.97)	24 (53.33)	2.30	(0.92, 5.75)	0.075
Poor Compliance with medications	9 (24.32)	13 (28.89)	0.80	(0.30, 2.12)	0.657
No past history of treatment with ECT	34 (91.89)	44 (97.78)	0.33	(0.05, 2.37)	0.271
Medical history of Diabetes Mellitus	4 (10.81)	1 (2.22)	3.99	(0.60, 26.68)	0.154
Use of tobacco in Harmful use/Dependence pattern	6 (16.22)	6 (13.33)	1.25	(0.38, 4.10)	0.708
Positive family history of psychiatric illness	14 (37.84)	14 (31.11)	1.34	(0.54, 3.31)	0.525
Age*	35.19 (9.67)	34.93 (8.49)	1.00	(0.96, 1.05)	0.895
Age at onset <=25 yrs	25 (67.57)	17 (37.78)	3.32	(1.35, 8.18)	0.009**
Duration of illness >6 yrs	27 (72.97)	18 (40.00)	3.89	(1.55, 9.80)	0.004**
Duration of untreated illness >6 months	17 (45.95)	22 (48.89)	0.89	(0.38, 2.11)	0.794
Total years of antipsychotic exposure >5 yrs	21 (56.76)	16 (35.56)	2.33	(0.97, 5.62)	0.06

OR: Odds ratio; *Mean (SD); **Significant with *P*<0.05

Table 4: Correlation between psychopathology and IDEAS score and SCoRS Interviewer score

	Total IDEAS Score	SCoRS Interviewer score
PANSS Positive subscale Score	0.284**	0.321**
PANSS Negative subscale Score	0.765**	0.663**
PANSS General Psychopathology subscale score	0.670**	0.683**

**Significant with *P*<0.05

credit for work is given for employment, household activities, and education equally. There is a possibility that women got credit for lesser work done at home but men failing to meet tougher standards outside were unemployed and failed to get credit. It also could indicate that gender roles persist in our society and men may not be taking active household maintenance tasks even if they possibly could. Disability due to this domain needs further exploration.

Lower socio-economic status was associated with greater disability. It can be argued that lower socioeconomic status is a consequence of greater disability. This is the idea behind the downward drift hypothesis.[15] However, in a cross-sectional study, directionality of the cause cannot be ascertained. The other technical issue in IDEAS assessment that can be impacted by socio economic status is in the domain of self-care. Many

non-mentally ill poor people have poor self-care. We noticed that the informants who came with patient as caregivers did not differ greatly from the patient in self-care. However, when interviewer rates in IDEAS, self-care is seen independently and not relative to the caregiver. This domain has 20% weight-age of the total score. Therefore, low social status patients would receive high score for poor self-care and can thereby have high disability scores.

Age of onset of illness below 25 years has three times the risk of having higher disability strongly suggesting that earlier the age of onset, higher is the disability. This is also known as a poor prognostic factor in schizophrenia[8] Early age of onset of illness interferes with the development of a person. It does not allow for adequate training in any vocation and leads to difficulty in interpersonal relationships thereby leading to difficulties in work and thereby disability. The total duration of illness has come out as a risk factor associated with higher disability. However, a multivariate analysis of the same did not show the effect. This effect was tending towards significance and would probably become significant if a larger sample were assessed.

Our study also found that, longer the duration of illness, higher is the disability. This is understandably so, as duration of illness *per se* increases the IDEAS score independently to 3 and above in the duration of illness criteria thus increasing

the global score of IDEAS. This association persisted on multivariate analysis indicating it to be a significant risk factor for higher disability.

Duration of antipsychotic use has also been found to have a risk of increasing the disability. However, the treatment duration being associated with duration of illness ceased to be an independent risk factor on multivariate analysis.

In our study, a positive correlation was obtained between cognitive functioning and disability which means that greater the cognitive deficit, higher is the disability. A person with an impaired attention, concentration, working memory, and executive function would have impairment in the day-to-day activities, thus leading to disability. This is consistent with the literature and in any other studies done to measure cognitive functioning and disability. However, some studies have found contrasting results of no correlation between cognitive functioning and disability as seen in Rajiv Krishnadas *et al.*[16] study and Addington *et al.*[17] study.

This study has also found a strong correlation between negative symptoms and cognitive dysfunction. The positive correlation between positive symptoms and cognitive symptoms was not strong in our study. However general psychopathology did show a positive correlation with cognitive dysfunction.

Our study has found a positive correlation between psychopathology and disability. This has been seen in various studies[18-20] done across the world.[21] However Krishnadas *et al.*[16] study had not shown any relation between psychopathology and disability.

Our study has reemphasized on the need for focus for addressing the deficit in real-world functioning of patient with schizophrenia. We can conclude cognitive deficits are commonly seen in patients with schizophrenia and are associated with disability. Therefore treatment programs of schizophrenia should have a component to address these functional deficits and incorporate psychosocial rehabilitation measures to improve the functioning level.[22] It is important for family physicians who care for those with mental illness to factor the cognitive deficits in their practice by simplifying dosage regime[23] and engaging caregivers in supervision.[24]

The cluster of negative symptoms when added to the adipogenic risk of antipsychotic, increase the rate of diabetes, obesity, hypertension, and cardiovascular disease. The vicious interaction between sedentary behavior and metabolic adverse effects of antipsychotics causes a direct negative influence in daily functioning, physical health and ultimately shortens the life expectancy. Hence, during their regular follow-up for the medical causes with the family physicians, the role of lifestyle modification, appropriate advice regarding diet and exercise could be emphasized and monitored.[25]

It has also been known that 50-90% of service users have at least one chronic medical illness. Even though psychiatrists may follow intensive screening guidelines for medical illness in patients with schizophrenia, it is important for coordination with primary care physicians to ensure effective management. Family physicians are the frontline workers who could address this issue in collaboration with psychiatrist by working out an accommodative framework of medical care.[7]

Strengths and limitations
Strengths of the study

1. The study was a cross-sectional study that has shed light on the cognitive functioning of schizophrenia patients by assessing real-life functioning in the day today life activities and not through a formal neuropsychological battery for cognitive assessment, which would have shown impairment in different domains of cognition.
2. In our study we found that SCoRS assessment tool build insight into the informant and patient regarding patient's level of functioning.

Limitations of the study

1. The sample size was calculated to suit the primary objectives. Therefore, it was underpowered for identifying secondary objectives.
2. The study was done on literate population. When about half of Indian population is illiterate, these findings cannot be generalized to whole population of schizophrenia patients.
3. Causality cannot be established with associations in a cross-sectional study. The factors that are possible risk factors could have well been the consequences of the disease.

Key points

1. Disability, cognitive dysfunction, and severity of psychopathology in schizophrenia are positively correlated
2. Lower life expectancy due to chronic medical conditions, lifestyle change, and adverse effects of drugs warrants screening by psychiatrists followed by referral and liaison with family physicians
3. Family physicians should factor the cognitive issues of patients in determining the required support of family and seek to simplify the treatment regime.

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Conflicts of interest

There are no conflicts of interest.

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