Health-Related Quality of Life in Patients with Possible Tardive Dyskinesia Based on Patient and Clinical Assessments

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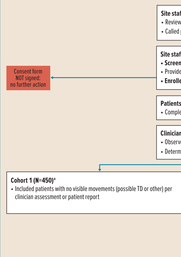
INTRODUCTION

- Tardive dyskinesia (TD) is a persistent and potentially disabling movement disorder associated with prolonged exposure to antipsychotics or other dopamine receptor blocking agents[1]
- Evidence of the negative impact of TD on health-related quality of life (HRQoL) and functioning, which has been studied primarily in patients with schizophrenia, remains limited[2-4]
- Due to the expanding use of antipsychotics in other psychiatric disorders, research is needed to better understand the effects of TD on HRQoL and functioning in a broader patient population, particularly in patients with mood disorders who may be acutely aware of involuntary movements
- RE-KINECT is a real-world screening study of involuntary movements in psychiatric outpatients in the United States who were treated with antipsychotic medications for any indication
- All enrolled patients were asked to complete the EuroQoL 5-Dimension 5-Level questionnaire (EQ-5D-5L) and Sheehan Disability Scale (SDS) before being evaluated by a clinician for possible TD
- An in-depth post-hoc analysis of the EQ-5D-5L and SDS data was conducted to assess the impact of possible TD on patient HRQoL

METHODS

- RE-KINECT included 37 outpatient psychiatry practices nationwide
- Adults (aged ≥18 years) with ≥3 months of lifetime exposure to antipsychotic(s) and ≥1 clinician-confirmed psychiatric disorder who were willing and able to provide informed consent were eligible to participate
- Patients were assigned to Cohort 1 or Cohort 2 based on their clinician's assessment of visible movements (**Figure 1**), with analyses conducted in the following groups:
  - Cohort 1: included 450 patients with no visible movements or movements consistent with TD; excluded 85 patients with involuntary movements that were not confirmed by the clinician as possible TD
  - Cohort 2: included 204 patients with visible involuntary movements that were confirmed by the clinician as possible TD; all of these patients had a clinician-rated severity of "some" or "a lot" in ≥1 body region
  - Limited Cohort 2: included 111 patients who had possible TD and a self-rated severity of "some" or "a lot" in ≥1 body region

Figure 1. Overview of Possible TD Symptom Screen and Cohort Assignment



*Excludes 85 patients who had an involuntary movement that was not confirmed by the clinician as possible TD.
EQ-5D-5L, EuroQol 5-Dimension 5-Level questionnaire; SDS, Sheehan Disability Scale; TD, tardive dyskinesia.

ASSESSMENTS

- EQ-5D-5L: visual analog scale (VAS) score, range from 0 ("worst health you can imagine") to 100 ("best health you can imagine"); utility score, range from 0 (health state equivalent to death) to 1 (perfect health); dimension scores, range from 1 (no problems) to 5 (extreme problems) for each of 5 dimensions
- SDS: domain scores, range from 0 (no disruption due to illness) to 10 (maximum disruption due to illness) for each of 3 domains; total score, defined as the sum of domain scores in patients who had a score in at least 2 of 3 domains
- Clinician- and patient-rated severity of possible TD: range from 0 ("none") to 2 ("a lot") in each of 4 body regions; summary score defined as the sum of all regions (range from 0 to 8)
- Patient-rated impact of possible TD: range from 0 ("none") to 2 ("a lot") for each of 7 daily activities; summary score defined as sum of all activities (range from 0 to 14); clinicians did not rate the impact of possible TD on patients' daily activities
- EQ-5D-5L and SDS scores were analyzed for Cohort 2 vs. Cohort 1 as follows:
  - Mean scores (EQ-5D-5L VAS and utility, SDS domains and total): analyzed using Welch's t-tests; analyses were also adjusted for age (<55 vs. ≥55 years), sex (male vs. female), and diagnosis (schizophrenia or schizoaffective disorder vs. mood or other disorder)
  - Distribution of EQ-5D-5L dimension scores: analyzed using chi-squared tests
- A generalized linear regression model was used to analyze differences between Cohort 2 and Cohort 1 for the EQ-5D-5L utility and SDS total scores, using the following covariates to adjust for other potential confounding factors:
  - Age (variable): 18 to 95 years
  - Sex (categorical): male, female
  - Overall health status (variable): 0 (no health problems) to 10 (health as bad as you can imagine) per patient report
  - Severity of psychiatric condition (variable): 0 (normal, not ill) to 6 (among the most severely ill) per clinician impression
  - Functional status of patient (variable): 0 (able to work/study independently) to 2 (unable to work/study) per clinician impression
  - Psychiatric diagnosis (categorical [2 factors]): presence/absence of schizophrenia or schizoaffective disorder; presence/absence of a mood or other disorder
- Additional regression models were conducted using Cohort 2 patients who had a rating of "a lot" on the following measures: clinician-rated severity of possible TD, patient-rated severity of possible TD, and patient-rated impact of possible TD
- In the full Cohort 2 (N=204) and limited Cohort 2 (N=111), regression analyses were conducted to evaluate the effect of the following measures on HRQoL (EQ-5D-5L utility score) and functioning (SDS total score):
  - Clinician-rated severity of possible TD: by body region and summary score
  - Patient-rated severity of possible TD: by body region and summary score
  - Patient-rated impact of possible TD: by daily activity and summary score

RESULTS

- Based on unadjusted analyses, mean EQ-5D-5L utility and VAS scores indicated worse HRQoL and overall health state in Cohort 2 (with possible TD) vs. Cohort 1 (without possible TD or other movement) (**Table 1**)
  - A significant difference between cohorts was still found for EQ-5D-5L utility when the analysis was adjusted for age, sex, and psychiatric diagnosis
  - Mean SDS scores were not significantly different between cohorts (both unadjusted and adjusted)

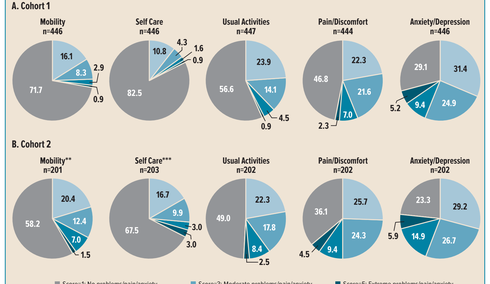
Table 1. Mean EQ-5D-5L and SDS Scores at Baseline

	Cohort 1		Cohort 2		*P*-value	Adjusted *P*-value[a]
	n	Mean (SD)	n	Mean (SD)		
EQ-5D-5L scores[b]						
Health state VAS	446	70.4 (21.4)	204	66.8 (25.1)	0.0613	0.0134
Utility score	442	0.78 (0.18)	197	0.71 (0.21)	<0.0001	<0.0001
SDS scores[c]						
Work/school	310	3.5 (3.4)	111	4.2 (3.4)	0.0609	0.0727
Social life	446	3.5 (3.2)	203	4.0 (3.4)	0.1010	0.1200
Family/home life	445	3.4 (3.2)	203	3.8 (3.3)	0.2460	0.2041
Total score[d]	445	10.5 (8.8)	203	11.7 (9.3)	0.0931	0.0693

[a]Adjusted for age (<55 vs. ≥55 years), sex (male vs. female), and diagnosis (schizophrenia or schizoaffective disorder vs. other).
[b]Higher EQ-5D-5L scores indicate better HRQoL.
[c]Higher SDS scores indicate greater disruption due to health condition.
[d]Calculated for patients who had a score on ≥2 domains. When only 1 domain was missing, the average of the participant's observed score was imputed.
EQ-5D-5L, EuroQol 5-Dimension 5-Level questionnaire; HRQoL, health-related quality of life; SD, standard deviation; SDS, Sheehan Disability Scale; VAS, visual analog scale.

- Compared to Cohort 1, a higher percentage of Cohort 2 patients reported moderate problems (score=3), severe problems (score=4), or extreme problems (score=5) in all EQ-5D-5L dimensions (**Figure 2**)

Figure 2. EQ-5D-5L Dimension Scores at Baseline



**P<0.01, ***P<0.001 (Cohort 1 vs. Cohort 2; not adjusted for age, sex, and psychiatric diagnosis).
EQ-5D-5L, EuroQol 5-Dimension 5-Level questionnaire.

- In the regression model (**Table 2**), EQ-5D-5L utility and SDS total scores were significantly worse in Cohort 2 patients who self-reported "a lot" of severity (n=53) or "a lot" of impact (n=33) than in Cohort 1 patients (N=450), regardless of whether the analysis was unadjusted or adjusted
  - In the analyses that included all Cohort 2 patients (N=204) or those with a clinician rating of "a lot" for severity (n=68), significant differences from Cohort 1 were found for EQ-5D-5L utility score but not SDS total score

Table 2. Mean Differences in EQ-5D-5L Utility and SDS Scores (Cohort 2 vs. Cohort 1)

Cohort 2 Analysis Populations[a]	EQ-5D-5L Utility Score Mean Difference (SE)		SDS Total Score Mean Difference (SE)	
	Unadjusted	Adjusted[b]	Unadjusted	Adjusted[b]
All Cohort 2 patients (N=204)	-0.066 (0.016)***	-0.037 (0.015)*	1.278 (0.760)	0.267 (0.756)
With a clinician-rating of "a lot" for severity of possible TD (n=68)	-0.092 (0.024)***	-0.044 (0.023)	1.083 (1.153)	-0.732 (1.139)
With a patient-rating of "a lot" for severity of possible TD (n=53)	-0.128 (0.027)***	-0.087 (0.025)***	5.093 (1.294)***	3.179 (1.234)*
With a patient-rating of "a lot" for impact of possible TD (n=33)[c]	-0.175 (0.034)***	-0.121 (0.031)***	7.667 (1.587)***	5.401 (1.509)***

*P<0.05; ***P<0.001.
[a]All Cohort 2 populations were compared to Cohort 1 (N=450).
[b]Adjusted using the following covariates: age, sex, overall health status, severity of psychiatric condition, patient's functional status, and psychiatric diagnosis.
[c]Excludes patients who did not have a self-rating of "some" or "a lot" for possible TD severity.
EQ-5D-5L, EuroQol 5-Dimension 5-Level questionnaire; SDS, Sheehan Disability Scale; SE, standard error; TD, tardive dyskinesia.

- Mean scores for severity of possible TD (clinician- and patient-rated) and impact of possible TD (patient-rated) were generally higher (worse) in the limited Cohort 2 (N=111) than in the full Cohort 2 (N=204) (**Tables 3 and 4**)
- In Cohort 2 (limited and full), significant associations were found between patient-rated impact scores and the EQ-5D-5L utility score (**Table 3**)
  - In the limited Cohort 2, significance was found in the patient-rated severity summary score
  - No significant association was found with clinician-rated severity
- A similar pattern of results was found for SDS total score (**Table 4**), although significance for the patient-rated severity summary score was found in the full Cohort 2 (rather than in the limited Cohort 2)

Table 3. Effects of Possible TD on the EQ-5D-5L Utility Score

	Full Cohort 2 (N=204)[a]			Limited Cohort 2 (N=111)[b]		
	Mean Score (SD)[c]	Unadjusted Regression Coefficient (SE)	Adjusted Regression Coefficient (SE)[d]	Mean Score (SD)[c]	Unadjusted Regression Coefficient (SE)	Adjusted Regression Coefficient (SE)[d]
Clinician-rated severity						
Head/face	0.86 (0.72)	-0.015 (0.020)	0.001 (0.019)	0.84 (0.76)	-0.005 (0.026)	0.007 (0.026)
Neck/trunk	0.25 (0.53)	0.016 (0.027)	0.014 (0.026)	0.27 (0.57)	0.008 (0.035)	-0.010 (0.035)
Upper extremities	0.69 (0.65)	-0.022 (0.023)	-0.007 (0.021)	0.77 (0.67)	-0.036 (0.030)	-0.027 (0.028)
Lower extremities	0.50 (0.64)	-0.033 (0.023)	-0.039 (0.021)	0.55 (0.67)	-0.037 (0.030)	-0.038 (0.029)
Summary	2.3 (1.4)	-0.013 (0.010)	-0.007 (0.010)	2.4 (1.5)	-0.015 (0.013)	-0.013 (0.013)
Patient-rated severity						
Head/face	0.52 (0.73)	-0.021 (0.021)	-0.009 (0.019)	0.96 (0.76)	-0.034 (0.027)	-0.026 (0.025)
Neck/trunk	0.17 (0.47)	-0.003 (0.031)	0.002 (0.030)	0.32 (0.60)	-0.001 (0.033)	-0.001 (0.032)
Upper extremities	0.46 (0.69)	-0.028 (0.022)	-0.008 (0.021)	0.85 (0.74)	-0.042 (0.027)	-0.031 (0.026)
Lower extremities	0.32 (0.60)	-0.050 (0.025)*	-0.040 (0.023)	0.58 (0.72)	-0.061 (0.028)*	-0.061 (0.026)*
Summary	1.5 (1.8)	-0.014 (0.008)	-0.007 (0.008)	2.7 (1.6)	-0.029 (0.012)*	-0.028 (0.012)*
Patient-rated impact						
Usual activities	0.43 (0.66)	-0.105 (0.021)***	-0.076 (0.021)***	0.57 (0.70)	-0.119 (0.027)***	-0.097 (0.027)***
Talking	0.41 (0.65)	-0.064 (0.022)**	-0.043 (0.021)*	0.52 (0.70)	-0.044 (0.029)	-0.033 (0.027)
Eating	0.37 (0.64)	-0.096 (0.022)***	-0.071 (0.022)**	0.41 (0.65)	-0.095 (0.030)**	-0.069 (0.030)*
Breathing	0.11 (0.35)	-0.099 (0.041)*	-0.085 (0.038)*	0.11 (0.34)	-0.071 (0.058)	-0.065 (0.054)
Being productive	0.45 (0.64)	-0.103 (0.022)***	-0.077 (0.022)***	0.59 (0.69)	-0.097 (0.028)***	-0.078 (0.027)**
Self care	0.33 (0.59)	-0.134 (0.024)***	-0.110 (0.023)***	0.35 (0.60)	-0.141 (0.032)***	-0.118 (0.032)***
Socializing	0.48 (0.68)	-0.086 (0.021)***	-0.068 (0.020)**	0.67 (0.74)	-0.077 (0.026)**	-0.075 (0.025)**
Summary	2.6 (3.0)	-0.027 (0.004)***	-0.021 (0.004)***	3.2 (3.1)	-0.028 (0.006)***	-0.024 (0.006)***

*P<0.05; **P<0.01; ***P<0.001 for the regression coefficient (i.e., effect on EQ-5D-5L utility).
[a]Includes all 204 patients with clinician-confirmed possible TD, all of whom had clinician-rated severity of "some" or "a lot" in at least 1 body region.
[b]Limited to 111 patients with clinician-confirmed possible TD who also had a self-rated severity of "some" or "a lot" in at least 1 body region.
[c]Mean scores based on clinician- or patient-ratings of 0 ("none"), 1 ("some"), or 2 ("a lot"). For missing values (e.g., patients with no severity or impact assessment), a score of 0 was assumed.
[d]Adjusted using the following covariates: age, sex, overall health status, severity of psychiatric condition, patient's functional status, and psychiatric diagnosis.
SD, standard deviation; SDS, Sheehan Disability Scale; SE, standard error; TD, tardive dyskinesia.

Table 4. Effects of Possible TD on the SDS Total Score

	Full Cohort 2 (N=204)[a]			Limited Cohort 2 (N=111)[b]		
	Mean Score (SD)[c]	Unadjusted Regression Coefficient (SE)	Adjusted Regression Coefficient (SE)[d]	Mean Score (SD)[c]	Unadjusted Regression Coefficient (SE)	Adjusted Regression Coefficient (SE)[d]
Clinician-rated severity						
Head/face	0.86 (0.72)	0.515 (0.899)	0.196 (0.879)	0.84 (0.76)	0.485 (1.149)	0.347 (1.161)
Neck/trunk	0.25 (0.53)	-0.493 (1.222)	-0.868 (1.182)	0.27 (0.57)	-0.936 (1.512)	-0.461 (1.590)
Upper extremities	0.69 (0.65)	0.997 (1.000)	0.684 (0.970)	0.77 (0.67)	1.531 (1.278)	0.971 (1.261)
Lower extremities	0.50 (0.64)	0.092 (1.017)	0.242 (0.803)	0.55 (0.67)	-0.157 (1.295)	0.341 (1.289)
Summary	2.3 (1.4)	0.219 (0.453)	0.027 (0.440)	2.4 (1.5)	0.221 (0.572)	0.259 (0.578)
Patient-rated severity						
Head/face	0.52 (0.73)	2.992 (0.868)***	2.412 (0.845)**	0.96 (0.76)	2.298 (1.125)*	2.115 (1.110)
Neck/trunk	0.17 (0.47)	0.556 (1.398)	-0.418 (1.388)	0.32 (0.60)	-0.860 (1.443)	-1.084 (1.481)
Upper extremities	0.46 (0.69)	2.681 (0.929)**	1.677 (0.930)	0.85 (0.74)	1.627 (1.158)	1.002 (1.166)
Lower extremities	0.32 (0.60)	1.662 (1.077)	1.036 (1.049)	0.58 (0.72)	0.323 (1.203)	0.641 (1.193)
Summary	1.5 (1.8)	1.152 (0.361)**	0.794 (0.363)*	2.7 (1.6)	0.845 (0.543)	0.742 (0.552)
Patient-rated impact						
Usual activities	0.43 (0.66)	4.600 (0.940)***	4.004 (0.943)***	0.57 (0.70)	4.911 (1.156)***	4.469 (1.212)***
Talking	0.41 (0.65)	2.683 (0.997)**	2.317 (0.969)*	0.52 (0.70)	2.246 (1.223)	1.970 (1.214)
Eating	0.37 (0.64)	2.404 (1.020)*	1.932 (1.021)	0.41 (0.65)	2.233 (1.313)	1.933 (1.381)
Breathing	0.11 (0.35)	4.461 (1.833)*	3.608 (0.043)*	0.11 (0.34)	2.446 (2.536)	2.852 (2.487)
Being productive	0.45 (0.64)	4.775 (0.971)***	4.054 (0.968)***	0.59 (0.69)	4.411 (1.178)***	3.946 (1.215)**
Self care	0.33 (0.59)	4.372 (1.082)***	4.049 (1.061)***	0.35 (0.60)	5.035 (1.374)***	4.702 (1.416)**
Socializing	0.48 (0.68)	4.890 (0.904)***	4.125 (0.910)***	0.67 (0.74)	3.209 (1.126)**	2.934 (1.146)*
Summary	2.6 (3.0)	1.129 (0.201)***	0.984 (0.202)***	3.2 (3.1)	1.089 (0.261)***	1.011 (0.271)***

*P<0.05; **P<0.01; ***P<0.001 for the regression coefficient (i.e., effect on SDS total score).
[a]Includes all 204 patients with clinician-confirmed possible TD, all of whom had clinician-rated severity of "some" or "a lot" in at least 1 body region.
[b]Limited to 111 patients with clinician-confirmed possible TD who also had a self-rated severity of "some" or "a lot" in at least 1 body region.
[c]Mean scores based on clinician- or patient-ratings of 0 ("none"), 1 ("some"), or 2 ("a lot"). For missing values (e.g., patients with no severity or impact assessment), a score of 0 was assumed.
[d]Adjusted using the following covariates: age, sex, overall health status, severity of psychiatric condition, patient's functional status, and psychiatric diagnosis.
SD, standard deviation; SDS, Sheehan Disability Scale; SE, standard error; TD, tardive dyskinesia.

CONCLUSIONS

- Mean EQ-5D-5L and SDS scores indicated that possible TD had a negative impact on HRQoL independent of age, sex, and psychiatric diagnosis, especially in patients who self-rated themselves as having "a lot" of severity or "a lot" of impact on daily activities
- In the full Cohort 2 (i.e., 204 patients with clinician-confirmed possible TD) and limited Cohort 2 (i.e., 111 patients who self-rated the severity of their movements as "some" or "a lot"), the summary score for patient-rated impact was significantly associated with HRQoL (EQ-5D-5L utility) and functioning (SDS total)
- The summary score for patient-rated severity was significantly associated with EQ-5D-5L utility in the limited Cohort 2 and with SDS total score in the full Cohort 2
- No significant association was found between clinician-rated severity and EQ-5D-5L utility or SDS total in either Cohort 2 (full or limited)
- These data suggest that clinicians should consider including specific questions (at usual care visits) regarding possible TD symptoms' impact on daily activities to better determine the health-related impact
- More research is needed to better understand the impact of TD on HRQoL in different psychiatric patient populations

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