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Association of Laryngeal Botulinum Neurotoxin Injection With Work Productivity for Patients With Spasmodic Dysphonia

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IMPORTANCE A disordered voice can affect an individual across both work and non–work-related life domains. There is insufficient research testing on the effect of spasmodic dysphonia or its treatment with botulinum neurotoxin (BoNT) injections on work productivity.

OBJECTIVE To assess whether employed patients with spasmodic dysphonia experience voice-related work productivity impairment before BoNT injection, and had a 10% or greater improvement in productivity 1 month after treatment with BoNT injection.

DESIGN, SETTING, AND PARTICPANTS This prospective case series carried out in 2 laryngology outpatient clinics from November 1, 2015, to August 30, 2018 included a consecutive sample of adult employed patients diagnosed with spasmodic dysphonia. Analysis was conducted between November 1, 2015, to July 31, 2018.

EXPOSURES Treatment with BoNT injection into the intrinsic laryngeal musculature.

MAIN OUTCOMES AND MEASURES Eligible participants completed the following validated outcomes instruments immediately before and 1 month after outpatient laryngeal BoNT injection: the Work Productivity and Activity Impairment instrument (WPAI), Voice Handicap Index (VHI), and WorkHoarse. Demographic, comorbidity, and occupational voice use data were also collected at baseline. The changes in outcome measures (primary, WPAI Work Productivity Impairment domain) were tested using a paired 2-tailed *t* test. Exploratory subgroup analyses were analyzed with multivariable linear regression, adjusting for demographic, comorbidity, and voice use variables.

RESULTS Of the 101 patients enrolled, 75 completed the study. The mean (SD) age of the 75 completing participants was 55.7 (11.8) years and 53 (71%) were women. The participants who completed the study had mean (SD) voice-related work productivity impairment of 43% (27%) at baseline and 22% (23%) at 1 month after BoNT injection (difference, 20% [27%] improvement; 95% CI, 14%-27%; effect size, 0.74).

CONCLUSIONS AND RELEVANCE This case series study found that employed patients with spasmodic dysphonia reported voice-related work productivity impairment, which improved significantly 1 month after treatment with BoNT injection. The association of spasmodic dysphonia with voice-related work productivity appeared greater in women than men with comparable outcomes with BoNT treatment, but this exploratory sex-associated difference requires independent validation.

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A disordered voice can significantly affect an individual's work productivity, especially presenteeism (reduced productivity while at work due to health condition).[1-3] The Work Productivity and Activity Impairment (WPAI) instrument has been used to measure dysphonia-related absenteeism and presenteeism; the rationale for use of this instrument has been discussed in previous studies.[1,4,5] Our group performed a cross-sectional analysis of self-reported voice-related work productivity impairment in individuals with spasmodic dysphonia treated with botulinum neurotoxin (BoNT) injections, showing a 30% improvement in work productivity impairment between best and worse weeks.[1] The cross-sectional nature limited causal inference because of possible recall bias, unconfirmed temporal association between BoNT injections and vocal improvement, and other uncontrolled confounding variables.

The purpose of the present study was to prospectively evaluate the association of laryngeal BoNT injections for employed patients with spasmodic dysphonia with changes in work productivity to further extend the results of our previous study.[1] We wanted to assess an important work productivity deficit before treatment, and test the hypothesis that at 1 month after BoNT injection, employed patients would report improved work productivity as assessed by the WPAI instrument (hypothesized >10%). As secondary measures we wanted to evaluate voice-related activity impairment and changes in other voice-related functional scales. We also planned exploratory subgroup analyses to generate hypotheses on which patients are most affected by spasmodic dysphonia and its treatment.

Key Points

Question Do patients with spasmodic dysphonia (a neurologic voice disorder) experience voice-related work productivity impairment, and does treatment with botulinum toxin (BoNT) improve it?

Findings In this case series study, voice-related work productivity impairment was measured prospectively before and after BoNT treatment in 75 employed patients with spasmodic dysphonia. Participants reported a voice-related work productivity impairment of 43% before treatment and 22% 1 month after treatment.

Meaning Patients with spasmodic dysphonia reported clinically important voice-related work productivity impairment, which significantly improved 1 month after BoNT treatment.

Methods

Consecutive patients with a diagnosis of spasmodic dysphonia and who had appointments for therapeutic laryngeal BoNT injections were invited to participate in this study. Participants were recruited from 2 institutions: University of Washington in Seattle, Washington, and the New York Center for Voice and Swallowing Disorders in New York, New York, during the study period of November 2015 to July 2018. This study was approved by the institutional review board at the University of Washington (HSD 49562-EA), and all data were collected in compliance with the Health Insurance Portability and Accountability Act, and written informed consent was obtained from participants.

Participants were approached at the time of their clinic visit. Eligibility criteria included a diagnosis of spasmodic dysphonia (adductor, abductor, with and without tremor), receiving regular treatment with BoNT injections, aged 18 years or older, currently employed, and ability to complete questionnaires in English. Exclusion criteria included diagnosis of a concurrent voice disorder (such as laryngeal cancer). Treated laryngopharyngeal reflux was allowed. Enrolled patients completed the following outcome instruments on paper or through a Research Electronic Data Capture system (REDCap) at enrollment and at 1 month after BoNT injection:

- WPAI[6] quantifies the self-reported effect of a specific disease using 4 measures: hours of working time lost (absenteeism), impairment while at work (presenteeism), impairment while doing activities outside of work (activity impairment), and overall work impairment as a combination of absenteeism + presenteeism. Scores were rated from 0% to 100% (0% indicating no impairment and 100% indicating complete impairment).
- Voice Handicap Index 10 (VHI)[7,8] measures self-perceived voice disability and handicap. Scores range from 0 to 40 (0 indicates no handicap, 40 indicates maximum handicap).[9] The minimal important difference for the VHI is 6.[10]
- WorkHoarse[5,11] is an instrument that was specifically developed to address voice disability at work and measures dimensions unique from the more global VHI. Scores range from 0 to 32 (0 indicates no disability, 32 indicates maximum disability).
- Self-reported voice quality was rated on a scale of 0% to 100% (0% indicating complete absence of functional voice and 100% indicating normal voice) and has been used locally at both institutions to determine BoNT dosing and treatment effectiveness. Note that this is the only scale where a higher score indicates better function.

Participants completed questionnaires of covariate variables at baseline:

- Demographics: age, sex, annual income, and education level.
- Functional Comorbidity Index (FCI)[12,13] is an 18-item index of chronic comorbid conditions that specifically affect daily function. A higher score indicates a greater burden of comorbid diseases negatively affecting functional status. The index score ranges from 0 to 18.
- Occupational voice use: scored as low, moderate, or high/essential.

Statistical Analysis

The sample size was estimated to detect a change in work productivity impairment of 10% from baseline to 1 month after BoNT injection. The standard deviation (SD) was estimated as 32% from our prior cross-sectional study.[1] To test at a 2-tailed significance level of .05 ($\alpha = .05$) with 80% power ($\beta = .20$), we calculated a sample size of 81 study participants. To account

for up to 20% missing data or lost to follow-up, we targeted enrollment of 102 participants.

Descriptive data are reported as mean (SD) for continuous variables and as percentage for binary variables. The differences in outcome measures between baseline and 1 month after BoNT injection were tested with the paired 2-tailed *t* test. Change scores were calculated for each participant by subtracting the 1-month score from the baseline score, where a positive change in score denotes improvement after treatment because a lower posttreatment score represents improvement for all outcome variables except the self-reported voice quality rating. Mean (SD) outcome change scores, 95% confidence intervals (CIs), and effect sizes were calculated for each outcome in the whole sample. Effect sizes of change scores were calculated for each outcome as the mean change score divided by the baseline SD.[14] A positive effect size indicated an improved outcome at 1 month after BoNT injection; a negative effect size indicated a worse outcome. A minimal clinically important effect size was defined as 0.20 or greater, and a large effect size was defined as 0.80 or greater.[14]

Exploratory subgroup analyses were performed for each baseline covariate. Differences in the work productivity impairment change scores (primary outcome) were tested between women and men using the unpaired 2-tailed *t* test with unequal variances. The effect size of difference between change scores for women and men was calculated as the difference in means divided by the pooled change SD (change SD in the whole cohort). A positive effect size for this analysis indicates greater improvement of the Work Productivity Impairment score in women over men. Simple linear regression was used to calculate the unadjusted differences and 95% CIs for subgroups defined by each of 6 variables: age, sex, annual income, education level, functional comorbidity index, and occupational voice use level. Multivariable linear regression was used to calculate the independent differences and 95% CIs for each subgroup while simultaneously adjusting for the others. Adjusted effect sizes of differences between change scores for each subgroup were calculated as the adjusted difference divided by the pooled change SD for the whole cohort. A positive effect size indicates greater improvement in the subgroup relative to its defined reference. All analyses were performed with Stata/SE (version 16, Stata Inc).

Results

The consecutive sample consisted of 101 adult employed participants with the diagnosis of spasmodic dysphonia and receiving BoNT injections, of which 75 completed this study. The cohort was middle-aged and consisted mostly of women with incomes lower than $100 000 per year and at least some college education (**Table 1**). About half of the participants had any functional comorbid conditions. The most commonly reported comorbidities were upper gastrointestinal disease (7 individuals), arthritis (6 individuals), anxiety (5 individuals), and degenerative disc disease (5 individuals). Most participants reported high occupational voice use. Withdrawn participants consisted of individuals who enrolled in clinic but never returned electronic or paper-based questionnaires: 14 (54%) were women, mean (SD) age was 55.1 (11.1) years. No participants experienced unexpected adverse effects from the BoNT injections.

Table 1. Baseline Characteristics in 75 Patients[a]

Characteristic	Finding
Age, mean (SD), y	55.7 (11.8)
Duration of disease, mean (SD), y	13.6 (8.6)
Adductor +/− tremor	73 (97)
Women	53 (71)
Income ≥$100 000	22 (37)
Education: at least some college	53 (84)
Functional Comorbidity Index, at least 1 comorbidity	30 (48)
Voice use high	65 (87)

[a] All findings are presented as No. (%) unless otherwise specified.

The primary outcome of work productivity impairment (combined presenteeism and absenteeism) was improved by a mean of 20% (hypothesized to be >10%) at 1 month after BoNT injection, with a medium-to-large effect size (**Table 2**). The lower bound of the 95% CI remained above the 10% a priori threshold for a clinically important effect. The effect on work productivity was related to presenteeism, whereas absenteeism did not change with treatment. Voice-related nonwork activity impairment also showed a clinically important and statistically significant improvement 1 month after BoNT injection. The other secondary voice outcome measures all showed clinically important and statistically significant improvements with medium-to-large effect sizes (Table 2).

Exploratory subgroup analysis suggested that women had a worse baseline work productivity impairment than men, and they experienced a greater improvement than men to a comparable outcome at 1 month after BoNT injection (**Table 3**). Multivariable exploratory subgroup analyses suggest that women, those with lower annual income, and college-educated participants may be more likely to experience a clinically important improvement in work productivity from BoNT injection, but these exploratory analyses were not statistically powered for definitive analysis and require independent validation (**Table 4**).

Discussion

This study supports the hypothesis that treatment of spasmodic dysphonia with laryngeal BoNT injections was associated with improvement in the primary voice-related WPAI Work Productivity Impairment outcome and the secondary activity impairment and other voice-related functional outcomes to a clinically important degree in this sample of patients. Subgroup analysis suggests that women may have greater pretreatment work productivity impairment and treatment effect than men with comparable work productivity impairment at 1 month after BoNT injection. This sex-based finding is new and requires independent validation. Annual income

Table 2. Work Productivity and Activity Impairment and Secondary Voice Outcome Changes Between Baseline and 1 Month After Botulinum Neurotoxin Injection

Measure	Mean (SD)		Change[a]		
	Baseline	Post-Tx	Mean (SD)	(95% CI)	Effect size[b]
Work productivity impairment[c]	43 (27)	22 (23)	20 (27)	(14 to 27)	0.74
Presenteeism[d]	41 (26)	21 (22)	20 (27)	(14 to 26)	0.77
Absenteeism[e]	3 (7)	1 (8)	1 (8)	(-1 to 3)	0.14
Activity impairment[f]	32 (25)	17 (20)	15 (26)	(9 to 21)	0.60
Voice Handicap Index[g]	25 (8)	19 (9)	7 (8)	(5 to 9)	0.88
Voice quality, self-reported[h]	55 (28)	76 (20)	-21 (27)	(-28 to -13)	0.75
WorkHoarse[i]	16 (7)	10 (7)	5 (8)	(4 to 7)	0.71

Abbreviations: Post-Tx, 1 month after treatment with botulinum neurotoxin injection.

[a] Change = Baseline minus Post-Tx (1 month after botulinum neurotoxin injection). Positive denotes improvement after treatment for all measures except for Voice Quality, Self-reported in which it denotes worsening of this measure.

[b] Effect size = change over baseline SD. A positive effect size indicated an improved outcome at 1 month after botulinum neurotoxin injection; a negative effect size indicated a worse outcome. A minimal clinically important effect size was defined as 0.20 or greater, and a large effect size was defined as 0.80 or greater.

[c] Work productivity impairment percentage (includes presenteeism and absenteeism), higher is worse impairment.

[d] Presenteeism percentage, higher is worse presenteeism.

[e] Absenteeism percentage, higher is worse absenteeism.

[f] Activity impairment percentage, higher is worse impairment.

[g] Voice Handicap Index score, 0 to 40, with higher being worse. Minimal important difference = 6.[10]

[h] Voice quality, self-reported 0% to 100%, with higher being better.

[i] WorkHoarse score 0 to 32, with higher being worse.

Table 3. Subgroup Analysis by Sex: Work Productivity Impairment[a] Between Baseline and 1 Month After Botulinum Neurotoxin Injection

Group	No.	Mean (SD)		Change[b]		
		Baseline	Post-Tx	Mean (SD)	(95% CI)	Effect size[c]
Whole cohort	70	43 (27)	22 (23)	20 (27)	(14 to 27)	0.74
Women	48	47 (26)	23 (25)	24 (29)	(16 to 33)	0.92
Men	21	33 (25)	19 (17)	14 (16)	(6 to 21)	0.56
Difference[d]	69[e]			10	(-1 to 21)	0.37[f]

Abbreviation: post-Tx, 1 month after treatment with botulinum neurotoxin injection. [a]Work Productivity Impairment percentage, higher is worse impairment.

[b] Change = baseline minus post-Tx (1 month after botulinum neurotoxin injection). Positive denotes improvement after treatment.

[c] Effect size = change over baseline SD. A positive effect size indicated an improved outcome at 1 month after botulinum neurotoxin injection; a negative effect size indicated a worse outcome. A minimal clinically important effect size was defined as 0.20 or greater, and a large effect size was defined as 0.80 or greater.

[d] Difference in the mean work productivity impairment change between women and men, tested with the unpaired 2-tailed *t* test with unequal variances. A positive difference indicates that work productivity impairment improved after botulinum neurotoxin injection in the women more than men.

[e] Sex variable missing on 1 participant.

[f] Effect size of difference = difference over pooled change SD (change SD in whole cohort). A positive effect size indicated greater improvement in women over men. A minimal clinically important effect size was defined as 0.20 or greater, and a large effect size was defined as 0.80 or greater.

Table 4. Exploratory Subgroup Analyses of Work Productivity Impairment Change With Botulinum Neurotoxin Injection

Subgroups	Reference	Unadjusted difference (95% CI)[a]	Adjusted difference (95% CI)[b]	Adjusted effect size[c]
Sex: women	Men	10 (-3 to 24)	14 (-3 to 31)	0.52
Income: <$100k	>$100k	12 (-3 to 28)	13 (-4 to 30)	0.48
Education: college	No college	3 (-16 to 21)	13 (-11 to 37)	0.48
Age: 20 y, younger	Older	2 (-9 to 13)	3 (-11 to 17)	0.11
Functional comorbidity index: any	None	2 (-12 to 17)	2 (-14 to 19)	0.07
Voice use: high use	Mod/low use	1 (-17 to 19)	0 (-24 to 24)	0

[a] Difference in the mean work productivity impairment change within each subgroup. A positive difference indicates that work productivity impairment improved in the subgroup compared to the reference. Unadjusted difference and 95% CI calculated with simple linear regression. Change = baseline minus 1 month results (positive denotes improvement).

[b] Adjusted for all a priori covariates listed: sex, income level, education level, age, functional comorbidity index, and occupational voice use level.

[c] Adjusted effect size of difference = adjusted difference/pooled change SD (Table 2). A positive effect size indicated greater improvement in the subgroup compared with the reference. A minimal clinically important effect size was defined as 0.20 or greater, and a large effect size was defined as 0.80 or greater.

and education levels may also be associated with the effect of BoNT injection therapy.

This prospective study supports the main results of our previous cross-sectional retrospective study,[1] although there are

important expected differences in result trends. In our original study, all reported change measures demonstrated a larger magnitude of change[1] than in the current study. By recall, participants reported an improvement in total work productivity impairment of 29% with BoNT injections, as compared with an improvement of 20% in the current prospective study. This result may reflect an upward recall bias,[15] which was one of the reasons motivating the current prospective analysis. Furthermore, the prior study inquired about the differences between best and worst levels of voice, whereas the current study tested the effect at a set time of 1 month when results might not have been maximum for some participants.

A few other studies have attempted to quantify voice-related work productivity impairment. Cohen et al[2] used a nationally representative administrative claims database (MarketScan Commercial Claims and Encounters and Medicare Supplemental and Coordination of Benefits data set) and reported that individuals with *International Classification of Diseases, Ninth Revision* diagnosis codes identifying dysphonia showed a mean of 39.2 work days absent in 12 months. That study did not measure presenteeism but showed that laryngeal disorders were associated with work-related absenteeism.

Rosow et al[3] measured the economic effect of vocal dysfunction using the WPAI instrument among teachers in Miami-Dade county, Florida. They showed a presenteeism impairment between 25% to 50% for their cohort that reported dysphonia, which is consistent with our presenteeism impairment of 41% before treatment. They extrapolated a yearly presenteeism cost of $11 913 375 to the county, which was 11.5 times the calculated cost of absenteeism. In our study the baseline presenteeism effect was approximately 14-fold greater than absenteeism (41%/3%) which is an effect discrepancy of a similar magnitude. The study by Rosow et al[3] was uniquely suited to monetize the work productivity impairment due to dysphonia because they looked at a cohort of individuals within a single job type (teacher) and with a similar salary structure. Their results further highlight the significant cost to society of the presenteeism effect in voice disorders and is congruent with other studies on work productivity[16-18] demonstrating that presenteeism is the major driver of cost to society of disease.

Another study measured presenteeism in Colombian teachers[19] using a 1-to-10 presenteeism scale similar to that of the WPAI instrument. The authors reported that 64% of the monthly cost of voice symptoms is due to presenteeism. They also estimated direct health care costs and absenteeism costs at 3% and 33% respectively. This study again confirmed the importance of presenteeism cost.

Our research design distinguished this study from other work productivity studies in voice disorders. We evaluated work productivity impairment by disease as opposed to by profession (teachers) or by symptom (dysphonia). Spasmodic dysphonia is suited to measure the effects of dysphonia on life functions because of the cyclical voice treatment schedule related to the BoNT injections with subsequent cycling of vocal quality as the injection loses efficacy. In addition, spasmodic dysphonia is not generally treated with voice therapy or voice rest that would add to presenteeism or absenteeism, so our measure of work productivity impairment is isolated to the disorder itself and the improvements to the therapy itself. For these reasons our study design had the potential to isolate the effects of dysphonia on work productivity in a unique format.

The effects of spasmodic dysphonia and its treatment on work productivity may be different in women and men, which is a pattern seen across other health conditions. In our cohort, the difference between women and men appeared to be clinically important. Both women and men achieve a similar final result with regard to level of reported work impairment, but women report an initially greater level of work productivity impairment at baseline, which accounts for the greater magnitude of change with treatment. The absenteeism scores were similar between gender groups (both groups reported less than 3% absenteeism at baseline). Although in this study absenteeism was not different between sexes related to spasmodic dysphonia, many studies of sickness have shown that women have a higher rate of both presenteeism[20,21] and absenteeism[22,23] than men. The reasons why women report more presenteeism and demonstrate more absenteeism are unclear and warrant further study, as existing studies show inconsistent support of potential underlying mechanisms. Among patients presenting for the evaluation of dysphonia, most tend to be women.[24]

It is notable that the study participants reported greater effects of spasmodic dysphonia and its treatment on work productivity (especially presenteeism) than on nonwork activity. For the current study, the work presenteeism was approximately 30% higher than nonwork activity impairment, which is a trend carried over from the previous cross-sectional study where participants had a similar difference.[1] On a smaller scale, Rosow et al[3] also showed this cohort of teachers reporting dysphonia rated presenteeism due to hoarseness as greater than activity impairment due to hoarseness, although this was not a trend that was discussed in the article. The validity of this finding is supported by other studies. Using qualitative research methods, Baylor et al[25] showed that, although patients with spasmodic dysphonia reported a restriction of social roles, they described a loss of professional and occupational roles, such as quitting jobs they would have otherwise continued, avoiding pursuit of new career paths, and giving up leadership activities. That 4 independent studies have shown this trend is compelling evidence to support the notion that individuals with dysphonia feel that their vocal impairment during work affects them more than during personal activities. In contrast, for other disease-specific work productivity studies using the WPAI instrument (insomnia,[26] asthma,[27] anxiety[28]), activity impairment is often rated greater than the presenteeism effect.

Limitations

There are several limitations to the current study. There were 26 participants that enrolled but did not complete the study. Participants who did not complete the questionnaires may have experienced worse outcomes, and this attrition may bias our results.[15] We enrolled all subtypes of SD but almost all had the adductor subtype with or without coexisting tremor. Differ-

ent subtypes of dystonia may respond differently to treatment.[29] This group of patients return consistently for treatment and may not allow the effects of their laryngeal BoNT to completely dissipate, which would decrease the reported change magnitude. The study design did not include a no-treatment group to control for natural course or variation; however, spasmodic dysphonia is not known to improve spontaneously, so this lack of control probably introduced little bias. The optimal treatment effect might occur at different times for different patients, so our 1-month outcome might have missed the optimal outcome for some participants. These results are all self-reported without an objective standard, which is a limitation common to most presenteeism scales.[30] The WPAI is not specifically validated for spasmodic dysphonia; however, it is validated for a number of chronic health conditions and has been used in the spasmodic dysphonia population previously.[1]

The findings of this study support the hypothesis that treatment of spasmodic dysphonia with BoNT injections into the intrinsic laryngeal musculature improves work productivity. Treatment with BoNT injections are still not approved by the US Food and Drug Administration for spasmodic dysphonia, so some patients have difficulty getting coverage for this treatment at the necessary intervals. This study adds to the body of literature supporting the efficacy of BoNT treatment for this patient group and suggests that BoNT therapy may have a net favorable economic effect despite its cost, by improving work productivity. Examples of next steps in research include testing the potential sex-related differences in baseline work productivity and treatment effects with BoNT injections in an independent cohort, quantifying the cost-effectiveness of BoNT injections, and exploring the perceived communication benefits of BoNT therapy of patients with SD through qualitative interviews of coworkers.

Conclusions

Patients with spasmodic dysphonia who received BoNT injections into the intrinsic laryngeal musculature reported a significant improvement in voice-related work productivity impairment and nonwork activity impairment. Women may have a larger magnitude baseline deficit in work productivity and greater improvement after BoNT injections than men, but this finding requires independent validation. Spasmodic dysphonia appeared to have a greater effect on work productivity impairment than on nonwork activity impairment, and BoNT injection appeared to improve work productivity more than nonwork activity.

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REFERENCES

1. Meyer TK, Hu A, Hillel AD. Voice disorders in the workplace: productivity in spasmodic dysphonia and the impact of botulinum toxin. *Laryngoscope*. 2013;123(suppl 6):S1-S14. doi:10.1002/lary.24292

2. Cohen SM, Kim J, Roy N, Asche C, Courey M. The impact of laryngeal disorders on work-related dysfunction. *Laryngoscope*. 2012;122(7):1589-1594. doi:10.1002/lary.23197

3. Rosow DE, Szczupak M, Saint-Victor S, Gerhard JD, DuPont C, Lo K. The economic impact of vocal attrition in public school teachers in Miami-Dade County. *Laryngoscope*. 2016;126(3):665-671. doi:10.1002/lary.25513

4. Isetti D, Meyer T. Workplace productivity and voice disorders: a cognitive interviewing study on presenteeism in individuals with spasmodic dysphonia. *J Voice*. 2014;28(6):700-710.

5. Giliberto JP, Zhu Q, Meyer TK. Development of a voice disorder work productivity inventory utilizing cognitive interviewing technique. *Laryngoscope Investig Otolaryngol*. 2016;1(6):180-184. doi:10.1002/lio2.40

6. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics*. 1993;4(5):353-365. doi:10.2165/00019053-199304050-00006

7. Jacobson BH, Johnson A, Grywalski C, et al. The Voice Handicap Index(VHI): development and validation. *Am J Speech Lang Pathol* 1997; 63:66-70. doi:10.1044/1058-0360.0603.66

8. Rosen CA, Murry T, Zinn A, Zullo T, Sonbolian M. Voice handicap index change following treatment of voice disorders. *J Voice*. 2000;14(4):619-623. doi:10.1016/S0892-1997(00)80017-X

9. Rosen CA, Lee AS, Osborne J, Zullo T, Murry T. Development and validation of the voice handicap index-10. *Laryngoscope*. 2004;114(9):1549-1556. doi:10.1097/00005537-200409000-00009

10. Misono S, Yueh B, Stockness AN, House ME, Marmor S. Minimal important difference in Voice Handicap Index-10. *JAMA Otolaryngol Head Neck Surg*. 2017;143(11):1098-1103. doi:10.1001/jamaoto.2017.1621

11. Zhu Q, Hu A, Giliberto JP, et al. Development of an instrument to assess work productivity in individuals with voice disorders: the Work Hoarse. *Ann Otol Rhinol Laryngol*. 2019;128(1):5-12. doi:10.1177/0003489418803961

12. Levine CG, Weaver EM. Functional comorbidity index in sleep apnea. *Otolaryngol Head Neck Surg*. 2014;150(3):494-500. doi:10.1177/0194599813518164

13. Groll DL, To T, Bombardier C, Wright JG. The development of a comorbidity index with physical function as the outcome. *J Clin Epidemiol*. 2005;58(6):595-602. doi:10.1016/j.jclinepi.2004.10.018

14. Kazis LE, Anderson JJ, Meenan RF. Effect sizes for interpreting changes in health status. *Med Care*. 1989;27(3)(suppl):S178-S189. doi:10.1097/00005650-198903001-00015

15. Vetter TR, Mascha EJ. Bias, confounding, and interaction: lions and tigers, and bears, oh my! *Anesth Analg*. 2017;125(3):1042-1048. doi:10.1213/ANE.0000000000002332

16. Vo P, Fang J, Bilitou A, Laflamme AK, Gupta S. Patients' perspective on the burden of migraine in Europe: a cross-sectional analysis of survey data in France, Germany, Italy, Spain, and the United Kingdom. *J Headache Pain*. 2018;19(1):82. doi:10.1186/s10194-018-0907-6

17. McDonald M, DiBonaventura Md, Ullman S. Musculoskeletal pain in the workforce: the effects of back, arthritis, and fibromyalgia pain on quality of life and work productivity. *J Occup Environ Med*. 2011;53(7):765-770. doi:10.1097/JOM.0b013e318222af81

18. Enns MW, Bernstein CN, Kroeker K, et al; CIHR Team in Defining the Burden and Managing the Effects of Psychiatric Comorbidity in Chronic Immunoinflammatory Disease. The association of fatigue, pain, depression and anxiety with work and activity impairment in immune mediated inflammatory diseases. *PLoS One*. 2018;13(6):e0198975. doi:10.1371/journal.pone.0198975

19. Cantor Cutiva LC, Burdorf A. Medical costs and productivity costs related to voice symptoms in Colombian teachers. *J Voice*. 2015;29(6):776.e15-776.e22.

20. Gustafsson Sendén M, Schenck-Gustafsson K, Fridner A. Gender differences in reasons for sickness presenteeism—a study among GPs in a Swedish health care organization. *Ann Occup Environ Med*. 2016;28:50. doi:10.1186/s40557-016-0136-x

21. Aronsson G, Gustafsson K, Dallner M. Sick but yet at work: an empirical study of sickness presenteeism. *J Epidemiol Community Health*. 2000;54(7):502-509. doi:10.1136/jech.54.7.502

22. Leinonen T, Viikari-Juntura E, Husgafvel-Pursiainen K, et al. Labour market segregation and gender differences in sickness absence: trends in 2005-2013 in Finland. *Ann Work Expo Health*. 2018;62(4):438-449. doi:10.1093/annweh/wxx107

23. Laaksonen M, Mastekaasa A, Martikainen P, Rahkonen O, Piha K, Lahelma E. Gender differences in sickness absence--the contribution of occupation and workplace. *Scand J Work Environ Health*. 2010;36(5):394-403. doi:10.5271/sjweh.2909

24. Remacle A, Petitfils C, Finck C, Morsomme D. Description of patients consulting the voice clinic regarding gender, age, occupational status, and diagnosis. *Eur Arch Otorhinolaryngol*. 2017;274(3):1567-1576. doi:10.1007/s00405-016-4332-7

25. Baylor CR, Yorkston KM, Eadie TL. The consequences of spasmodic dysphonia on communication-related quality of life: a qualitative study of the insider's experiences. *J Commun Disord*. 2005;38(5):395-419. doi:10.1016/j.jcomdis.2005.03.003

26. Bolge SC, Doan JF, Kannan H, Baran RW. Association of insomnia with quality of life, work productivity, and activity impairment. *Qual Life Res*. 2009;18(4):415-422. doi:10.1007/s11136-009-9462-6

27. Chen H, Blanc PD, Hayden ML, Bleecker ER, Chawla A, Lee JH; TENOR Study Group. Assessing productivity loss and activity impairment in severe or difficult-to-treat asthma. *Value Health*. 2008;11(2):231-239. doi:10.1111/j.1524-4733.2007.00229.x

28. Erickson SR, Guthrie S, Vanetten-Lee M, et al. Severity of anxiety and work-related outcomes of patients with anxiety disorders. *Depress Anxiety*. 2009;26(12):1165-1171. doi:10.1002/da.20624

29. Blitzer A. Spasmodic dysphonia and botulinum toxin: experience from the largest treatment series. *Eur J Neurol*. 2010;17(suppl 1):28-30. doi:10.1111/j.1468-1331.2010.03047.x

30. Schultz AB, Chen CY, Edington DW. The cost and impact of health conditions on presenteeism to employers: a review of the literature. *Pharmacoeconomics*. 2009;27(5):365-378. doi:10.2165/00019053-200927050-00002