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RESEARCH ARTICLE

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Botulinum Toxin for Spasticity: Real-World Effects on Patient Health-Related Quality of Life and Caregiver Burden -A Long-Term Retrospective Study

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ABSTRACT

Background: Spasticity following central nervous system lesions impairs health-related quality of life (HR-QoL) through reduced mobility, pain, sleep disturbances and loss of independence, while increasing care-giver burden. Botulinum neurotoxin type A (BoNT-A) effectively reduces muscle tone, but its real-world impact on patient HR-QoL and caregiver burden remains incompletely characterized, particularly over long-term follow-up.

Objective: To evaluate the clinical impact of BoNT-A on spasticity, patient HR-QoL, caregiver burden, pain and sleep in a real-world neurological cohort.

Methods: Retrospective observational study of 108 consecutive patients attending a spasticity clinic (Villa delle Ginestre, ASP Palermo, 2023–2025). Primary outcomes were patient HR-QoL (EQ-5D index and 5 dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and caregiver burden (Zarit Burden Interview, ZBI). Secondary outcomes included muscle tone (Modified Ash-worth Scale, MAS), pain (Numeric Rating Scale, NRS), insomnia (Insomnia Severity Index, ISI) and spasms (Penn Spasm Frequency/Severity Scale). Assessments were performed at baseline and long-term follow-up (median 16 months from first injection, IQR 8–24), with data prospectively collected in a clinical database. Inclusion criteria: confirmed central spasticity, ≥1 complete BoNT-A cycle. Statistical analysis: Wilcoxon signed-rank tests for pre-post changes, Spearman correlations for delta scores (Jamovi software).

Results: Patients (67 M/ 41F, mean age 46.2 years, range 4–85) had mixed etiologies (stroke 28%, myelopathy 17%, cerebral palsy 14%, multiple sclerosis 9%, other 32%) and were referred at median 18 months post-event (IQR 6–48). BoNT-A (mean 4 cycles/year) yielded significant improvements (all $p<0.001$): MAS 3.0→2.0 (Δmed -1.0), NRS 6→3 (Δmed -3), ISI 8→5 (Δmed -3), EQ-5D index 0.10→0.30 (Δmed +0.20), ZBI 25→18 (Δmed -7, ~25% reduction). EQ-5D gains were driven by pain/discomfort and anxiety/depression (both Δ -1 level), while mobility remained stable. Cerebral palsy caregivers showed the largest ZBI reduction (Δmed -10, $p<0.001$ vs overall).

Spearman correlations revealed ΔEQ-5D associated with ΔNRS ($\rho=0.52$, $p<0.001$), ΔISI ($\rho=0.22$, $p=0.02$) and spasms ($\rho=0.22$, $p=0.02$), but not ΔMAS ($\rho=0.16$, $p=0.09$). ΔZBI correlated with patient self-care, EQ-5D and ISI improvements ($\rho=0.18$-0.24, all $p\leq0.04$).

Conclusions: In real-world practice, long-term BoNT-A treatment significantly improves patient HR-QoL and reduces caregiver burden, primarily through non-motor benefits (pain, sleep). These effects are most pronounced in cerebral palsy families. Real-world data complement RCT limitations, supporting comprehensive spasticity management targeting motor and non-motor domains.

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Introduction

Spasticity is a frequent and disabling consequence of lesions of the central nervous system, including stroke, multiple sclerosis, spinal cord injury and cerebral palsy. It contributes to abnormal limb posture, pain, reduced mobility and loss of independence, and often requires long term physical assistance from caregivers. Beyond the motor symptoms, spasticity has a substantial impact on health related quality of life (HR QoL), by amplifying pain, anxiety and sleep disturbances and by limiting participation in daily activities. These multidimensional consequences translate into an increased caregiver burden, with many family members needing to reduce their working hours or stop working to provide care.

Treatment of spasticity typically relies on a combination of rehabilitation strategies, oral antispastic medications and focal treatments such as botulinum neurotoxin type A (BoNT A)

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injections. BoNT A is widely used as a first line focal treatment for focal and multifocal spasticity, with robust evidence for reducing muscle tone and improving passive care and specific functional goals. Randomized controlled trials and meta analyses have consistently shown that BoNT A reduces spastic hypertonia and facilitates individualized goals such as hygiene, dressing or limb positioning. However, its impact on broader patient centred outcomes, including HR QoL is less clear.

Health related quality of life in patients with spasticity has been increasingly assessed using generic instruments such as the EuroQol EQ 5D or EQ VAS, capturing mobility, self care, usual activities, pain/discomfort and anxiety/depression. In patients with spasticity, quality of life is often influenced more by pain, sleep problems, and difficulty with daily activities than by muscle stiffness alone. Botulinum toxin treatment may improve pain and overall health perception.

Caregiver burden in spasticity has gained growing attention in recent years. Parents and other family caregivers frequently report high levels of stress, reduced time for themselves and financial strain associated with care needs. In upper limb post stroke spasticity, a randomized controlled trial showed that BoNT A injections can significantly decrease caregiver burden compared with placebo, alongside improvements in passive function and ease of care. Real world registry data from the Adult Spasticity International Registry (ASPIRE) further indicate that BoNT A treatment is associated with reduced caregiver burden and improved caregiver QoL over time.

The burden on caregivers of patients with post-stroke spasticity can lead to significant losses in work productivity, mainly through presenteeism and, to a lesser extent, absenteeism. In a study of employed caregivers of stroke survivors with spasticity, 32% reported work-related restrictions, including 9% absenteeism and 27% presenteeism; the mean monthly indirect cost was US$835, with about 72% attributable to presenteeism. The main predictors of productivity loss were patient disability and the lack of nursing home coverage. Absenteeism, presenteeism, and work productivity loss increase with disease severity. In movement disorders associated with increased muscle tone, such as spasticity and dystonia, botulinum toxin treatment may reduce caregiver burden, with a potential indirect benefit on caregiver productivity.

In a double-blind RCT (n=55) conducted by Lam et. al, on patients with upper limb spasticity in long-term care, 60% of the treated group showed a Caregiver Burden Scale (CBS) reduction ≥4 points at 6 weeks vs 8% placebo ($p<0.001$), with persistent effect at 24 weeks, improved GAS and fewer frac-tures. Severe pre-injection impairment predicted better response.

Nevertheless, most available studies have focused either on patient reported outcomes or on caregiver burden, and few have examined both domains.

Moreover, previous randomized trials and meta analyses have often been limited by restrictive inclusion criteria, relatively small sample sizes, low baseline pain levels and short follow up periods (typically 4–12 weeks), which may underestimate the broader and longer term benefits of BoNT A on pain and HR QoL. Real world observational studies, such as ASPIRE, partly overcome these limitations by including unselected patients, multiple etiologies and flexible treatment patterns.

Against this background, there is a clear need for real world data exploring how BoNT A treatment for spasticity affects both the patient's perceived quality of life and the caregiver's perceived burden, and how non motor symptoms such as pain and sleep disturbances mediate these effects. In this study, we have assessed multiple domains, including muscle tone, pain, insomnia, spasms, patient HR QoL and caregiver burden before and after BoNT A injections in a heterogeneous neurological population.

This offers an opportunity to examine the multimodal impact of BoNT A in everyday practice, in order to better understand the non motor pathways through which BoNT A may improve the daily lives of patients with spasticity and their caregivers, and to explore the relationships between changes in clinical and patient reported outcomes.

Material and Method

Study Design and Population

This retrospective observational study analyzed data from consecutive patients with central nervous system lesions and confirmed limb spasticity, routinely assessed at the Spasticity treatment clinic of Villa delle Ginestre, ASP Palermo, Italy, between 2023 and 2025. Patients were included if they had a diagnosis of central spasticity (Modified Ashworth Scale score ≥2 in at least one major muscle group), had completed at least one full cycle of BoNT-A treatment, and had both baseline and follow-up assessments available in the clinical database. Exclusion criteria were not explicitly applied beyond routine clinical practice standards, reflecting real-world heterogeneity. Etiologies included stroke, spinal myelopathy, cerebral palsy, multiple sclerosis and other neurological conditions. No patient consent required for retrospective data analysis.

Assessments and Outcome Measures

Standardized assessments were conducted at baseline (prior to first BoNT-A injection) and at long-term follow-up, with the exact timing determined by the date of the most recent interview recorded in the clinical database for each patient. This approach captured sustained effects after multiple treatment cycles rather than acute post-injection changes.

Primary outcomes were patient health-related quality of life (HR-QoL) measured by the EQ-5D (in-dex score and five dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and caregiver burden assessed by the Zarit Burden Interview (ZBI, total score 0–88, higher scores indicating greater burden).

Secondary Outcomes Included

- Muscle Tone: Modified Ashworth Scale (MAS, 0–4 per joint/ muscle group).
- Pain: Numeric Rating Scale (NRS, 0–10).
- Insomnia: Insomnia Severity Index (ISI, 0–28).
- Spasms: Penn Spasm Frequency/Severity Scale (composite score).

Assessments were performed by trained clinic staff using validated Italian versions of all scales.

Treatment Protocol

BoNT-A injections (various formulations per clinical indication) were administered by experienced physician following Italian guidelines for adult and pediatric spasticity, targeting upper and/ or lower limb muscles based on individualized goals. Patients received a mean of four injection cycles per year, with doses and muscles selected according to response, tolerance and evolving needs. Concomitant treatments (physiotherapy, oral medications) continued as per routine care.

Statistical Analysis

Changes from baseline to follow-up were analyzed using Wilcoxon signed-rank tests for non-parametric paired data (all outcomes). Spearman rank correlations assessed associations between delta scores (Δ = follow-up minus baseline) for primary and secondary outcomes. Subgroup analyses compared etiological groups (e.g., cerebral palsy) using Mann-Whitney U tests. Statistical significance was set at $p<0.05$. Analyses were conducted with Jamovi software (version 2.3, open-source based on R).

Results

A total of 108 patients with central nervous system lesions and limb spasticity were included in the analysis. The cohort comprised 67 men and 41 women, with a mean age of 46.2 years (range 4–85 years). Patients were first referred to our spasticity clinic at a median of approximately 18 months after the index event, with an interquartile range of 6–48 months. On average, patients received about four BoNT A injection cycles per year, and the mean follow up from the first injection was 16 months (in-terquartile range 8–24 months). The main etiologies were stroke (28%), myelopathy (17%), cerebral palsy (14%) and multiple sclerosis (9%), with the remaining 32% representing other neurological con-ditions (Table 1).

BoNT A treatment was associated with significant improvements in spasticity and non motor symp-toms at 4–6 weeks after injection and at long term follow up (median 16 months from first injection). Muscle tone, assessed by the MAS, decreased from a median of 3.0 at baseline to 2.0 at follow up (median change −1.0, $p<0.001$). Pain intensity on the Numeric Rating Scale declined from a median of 6 to 3 points (median change −3, $p<0.001$), indicating a clinically meaningful reduction in pain. Insomnia severity, measured by the Insomnia Severity Index, improved from a median of 8 to 5 (median change −3, $p<0.001$). Similarly, the frequency and severity of spasms, assessed by the Penn Spasm Scale, showed significant reductions, consistent with better control of spastic tone . Patient health related quality of life improved substantially over the treatment period. The EQ 5D index increased from 0.10 at baseline to 0.30 at follow up (median change +0.20, $p<0.001$), reflecting a relevant gain in perceived health status (Table 2).

Analysis of the individual EQ 5D dimensions showed that this improvement was mainly driven by reductions in pain/discomfort and anxiety/depression, each improving by approximately one level on the 5 point scale (both $p<0.001$). In contrast, the dimensions of mobility, self care and usual activities remained overall stable, with no significant change in the mobility item. These findings indicate that, in this cohort, perceived QoL gains were largely related to amelioration of non motor symptoms rather than to changes in gross motor function (Table 3).

Caregiver burden also decreased significantly over the course of BoNT A treatment. The Zarit Burden Interview total score fell from a median of 25 at baseline to 18 after treatment (median change −7, $p<0.001$), corresponding to an approximate 25% reduction in burden. When etiological subgroups were considered, the largest improvement in caregiver burden was observed in caregivers of patients with cerebral palsy (n=24), in whom the Zarit score decreased by about 10 points ($p<0.001$ compared with the overall group) (Table 4). This pattern suggests that, in conditions requiring intensive daily assistance, the facilitation of care tasks and relief of distressing symptoms may translate into particular-ly pronounced benefits for families.

Correlation analyses further clarified the relationships between changes in clinical variables, patient HR QoL and caregiver burden. Improvements in EQ 5D index were significantly associated with reductions in pain (Spearman $\rho\approx0.52$, $p<0.001$), and showed weaker but significant correlations with improvements in insomnia and spasms ($\rho\approx0.22$, $p\approx0.02$ for both). In contrast, the correlation between change in EQ 5D and change in muscle tone (MAS) did not reach statistical significance, suggesting that HR QoL improvements were driven predominantly by non motor domains. Changes in caregiver burden (Zarit) were significantly correlated with increased patient autonomy in self care, better overall HR QoL and reduced insomnia, while no strong association emerged with changes in MAS (Table 5). Taken together, these results shows in our patient sample that the beneficial effects of BoNT A on patient QoL and caregiver burden in real world practice are mediated mainly through improvements in pain, sleep and ease of care rather than through tone reduction alone.

Discussion

In this real world retrospective study of 108 patients with central nervous system lesions and limb spasticity, BoNT A treatment was associated with significant improvements across all assessed do-mains, including muscle tone, pain, insomnia, patient HR QoL and caregiver burden. The median EQ 5D index increased

by 0.20, while the Zarit Burden Interview score decreased by 7 points, corresponding to an approximate 25% relative reduction in caregiver burden. These findings support the multimodal efficacy of BoNT A beyond its established antispastic effects, and highlight that both patient centred and caregiver centred outcomes can improve meaningfully in routine clinical practice.

A key result of our analysis is that improvements in HR QoL were more closely related to changes in non motor symptoms than to changes in muscle tone. The increase in EQ 5D index was largely driven by improvements in the pain/discomfort and anxiety/depression dimensions, whereas mobility, self care and usual activities remained overall stable. Consistently, change in EQ 5D showed a strong correlation with reductions in pain (NRS) and weaker, but significant, correlations with improvements in insomnia and spasms, while it did not correlate significantly with changes in MAS. This pattern aligns with previous real world and registry data suggesting that pain relief and better sleep may be critical determinants of perceived health status in patients with spasticity, sometimes more than further gains in motor function. Our results thus reinforce the concept that BoNT A should be considered not only as a focal antispastic intervention, but also as a therapy capable of modulating sensory and non motor pathways that impact HR QoL.

The impact on caregiver burden observed in our cohort was also clinically relevant. Overall, Zarit scores decreased significantly after treatment, and the reduction in burden correlated with improvements in patient self care, global HR QoL and insomnia. This suggests that caregivers may feel less overwhelmed when patients are better able to participate in personal care and when nocturnal symptoms are alleviated, potentially resulting in more restorative sleep for both patients and caregivers. Our findings are consistent with randomized evidence showing that BoNT A can reduce caregiver burden in upper limb post stroke spasticity, as well as with registry data from ASPIRE indicating sustained improvements in caregiver burden over time under individualized BoNT treatment. Importantly, by measuring both EQ 5D and Zarit concurrently, our study provides additional insight into how patient reported HR QoL and caregiver burden move in parallel in real world practice.

Among the etiological subgroups, in patients with infantile cerebral palsy is evident the largest reduction in caregiver burden, with a 10 point median decrease in the Zarit score. This finding is particularly relevant in a population in which caregiving is often provided by young parents who, daily demands and may experience a high cumulative burden. In this group, BoNT A facilitates care by reducing resistance to passive movements, easing hygiene and dressing, and attenuating pain and spasms that can trigger behavioural distress. While our study was not powered for detailed subgroup analyses, the prominent effect on caregiver burden in cerebral palsy supports the clinical perception that focusing on comfort and ease of care can have substantial downstream benefits for families, even when gross motor function changes are limited in this kind of patients.

Our results also need to be interpreted in light of previous controlled studies and meta analyses. Earlier randomized trials and systematic reviews have demonstrated robust effects of BoNT A on spasticity, but have reported inconsistent or limited effects on pain and generic QoL, partly due to short follow up, low baseline pain levels and strict inclusion criteria. In contrast, our cohort reflects the heterogeneity of routine practice, with mixed etiologies, variable chronicity and a broader spectrum of baseline symptoms, and with repeated treatment cycles over a median follow up of 16 months. In this context, the significant improvements in pain, insomnia, HR QoL and caregiver burden may indicate that the real world therapeutic impact of BoNT A on non motor outcomes is larger than what early trials suggested. Assessments were conducted at baseline and long term follow up, reflecting sustained effects over multiple treatment cycles in time. In everyday clinical practice, systematically assessing pain, sleep and caregiver strain may help clinicians identify patients and families who are most likely to benefit from BoNT A in terms of overall well being, and to monitor meaningful changes beyond muscle tone reduction.

Limitations

Our study has several limitations inherent to its retrospective observational design. First, the lack of a control group precludes definitive causal attribution of the observed improvements to BoNT A treatment alone, as concurrent rehabilitation, natural recovery processes or adaptive strategies may have contributed to changes in outcomes. Second, while the sample size of 108 patients is reasonable for a single centre real world study, it may have been underpowered for robust subgroup analyses beyond the main etiological categories, particularly for less common conditions. For instance, the cerebral palsy subgroup (n=24) showed a striking reduction in caregiver burden, but larger multicentre studies are needed to confirm this finding and to explore rarer etiologies.

Third, although follow up assessments were conducted at long term intervals (median 16 months), reflecting sustained effects after multiple BoNT A cycles, the timing of individual interviews varied according to clinical routine, and we did not standardize the exact interval or number of cycles between baseline and final evaluation for all patients. Additionally, the retrospective nature limited the availability of some data, such as detailed goal attainment scales or patient specific treatment goals, which could have provided further insight into functional impacts. Future prospective studies with larger samples and longer follow up are warranted to confirm these results, to clarify the mechanisms linking spasticity control, non motor symptoms and caregiver burden, and to define optimal assessment batteries for capturing the full impact of BoNT A in real world spasticity care [1-21].

Table 1: Baseline Characteristics of the Study Population (n=108). Baseline Characteristics showing Mixed Etiologies and Long-Term Follow-Up Design. Data are n (%), Mean (SD), or Median (IQR) as Appropriate

Characteristic	Value
Sex, n (%)	Male 67 (62%), Female 41 (38%)
Age, mean (SD), years	46.2 (22.1)
Age range, years	4–85
Time from index event to first referral, median (IQR), months	18 (6–48)
BoNT-A cycles per year, mean	4
Follow-up from first injection, median (IQR), months	16 (8–24)
Etiology, n (%)	
Stroke	30 (28%)
Myelopathy	18 (17%)
Cerebral palsy	15 (14%)
Multiple sclerosis	10 (9%)
Other	35 (32%)

Table 2: Changes in Clinical and Patient-Reported Outcomes (Pre- vs Long-Term Follow-Up, n=108). All outcomes showed Statistically Significant improvements at long-term follow-up. Abbreviations: BoNT-A, Botulinum Toxin type A; MAS, Modified Ashworth Scale; NRS, Numeric Rating Scale (0-10); ISI, Insomnia Severity Index; EQ-5D, EuroQol 5-Dimension Questionnaire; IQR, INTERQUARTILE Range. ** p<0.001

Outcome Measure	Baseline median (IQR)	Follow-up median (IQR)	Median Change (IQR)	p-value (Wilcoxon)
MAS (tone)	3.0 (2.0–3.5)	2.0 (1.5–2.5)	-1.0 (-1.5 to -0.5)	<0.001**
NRS (pain)	6 (4–7)	3 (2–5)	-3 (-4 to -2)	<0.001**
ISI (insomnia)	8 (5–12)	5 (3–8)	-3 (-5 to -2)	<0.001**
Penn Spasm Scale	12 (8–16)	8 (5–12)	-4 (-6 to -2)	<0.001**
EQ-5D index	0.10 (0.00–0.30)	0.30 (0.20–0.50)	+0.20 (+0.10 to +0.30)	<0.001**
Zarit Burden	25 (18–35)	18 (12–25)	-7 (-12 to -4)	<0.001**

Table 3: Changes in EQ-5D-5L Dimensions (n=108). EQ-5D-5L Dimensional Analysis Showing HR-QoL Gains Driven Primarily by Improvements in Pain/Discomfort and Anxiety/Depression domains. ** p<0.001

Dimension	Baseline level, n (%)	Follow-up level, n (%)	Median change in level	p-value
Mobility	Level 3: 72 (67%)	Level 3: 68 (63%)	0	0.12
Self-care	Level 2: 58 (54%)	Level 2: 52 (48%)	0	0.08
Usual activities	Level 3: 65 (60%)	Level 3: 60 (56%)	0	0.15
Pain/disconfort	Level 3: 70 (65%)	Level 2: 45 (42%)	-1	<0.001**
Anxiety/Depression	Level 3: 62 (57%)	Level 2: 40 (37%)	-1	<0.001**

Table 4: Subgroup Analysis - Changes in Zarit Burden by Etiology. Caregivers of Cerebral Palsy patients showed largest burden Reduction (10-point Median decrease, **p<0.001 vs overall). MS: Multiple Sclerosis

Etiology (n)	Baseline Zarit median (IQR)	Follow-up Zarit median (IQR)	Median ΔZarit (IQR)	p vs Overall
Overall (108)	25 (18–35)	18 (12–25)	-7 (-12 to -4)	-
Stroke (30)	24 (17–32)	19 (14–26)	-5 (-9 to -3)	0.15
Myelopathy (18)	28 (20–38)	22 (16–28)	-6 (-10 to -4)	0.42
Cerebral Palsy (15)	**35 (25–45)**	**25 (15–32)**	**-10 (-15 to -7)**	**<0.001**
MS (10)	22 (16–30)	17 (12–23)	-5 (-8 to -3)	0.28
Other (35)	23 (17–33)	17 (11–24)	-6 (-10 to -4)	0.35

Table 5: Spearman Correlations Between Delta Scores (ρ, p-value; n=108). Strongest associations link pain reduction (ΔNRS) to HR-QoL improvement (ΔEQ-5D, ρ=0.52, p<0.001). Muscle tone changes (ΔMAS) showed weak/non-significant correlations with primary outcomes. *p<0.05, **p<0.001. Abbreviations: MAS, Modified Ashworth Scale; NRS, Numeric Rating Scale; ISI, Insomnia Severity Index; Penn, Penn Spasm Scale

	ΔMAS	ΔNRS	ΔISI (insomnia)	ΔPenn Spasm	ΔEQ-5D index	ΔZarit
ΔMAS	-	0.12 (0.22)	0.10 (0.30)	0.18 (0.06)	0.16 (0.09)	0.08 (0.41)
ΔNRS		-	*0.25 (0.009)	*0.28 (0.003)	**0.52 (<0.001)	*0.23 (0.01)
ΔISI			-	*0.20 (0.04)	*0.22 (0.02)	*0.18 (0.04)
ΔPenn				-	*0.22 (0.02)	0.15 (0.12)
ΔEQ-5D					-	*0.24 (0.01)
ΔZarit						-

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