

ORIGINAL REPORT

INVESTIGATING MUSCLE SELECTION FOR BOTULINUM TOXIN-A INJECTIONS IN ADULTS WITH POST-STROKE UPPER LIMB SPASTICITY

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Background: Limited empirical information exists regarding botulinum toxin-A injector decision-making practices for adult upper limb post-stroke spasticity. The design of most studies prevents such an assessment, as injection sites and dosage are mandated by researcher protocols. This contrasts to usual injector practices, where individualized decision-making is the standard of care.

Design: Secondary data analysis from an Australian randomized controlled trial of 90 adults with upper limb post-stroke spasticity where experienced clinicians followed their standard clinical injecting practice rather than a mandated injection regimen.

Methods: Clinicians were hypothesized to tailor their injection practices according to the subject's degree of spasticity and/or the type of functional gain desired. Hypothesis testing was conducted using non-parametric analysis.

Results: Muscle selection and botulinum toxin-A dosage were not significantly associated with spasticity severity or with patient-identified goals. Between-site differences in injection practices suggested that injector beliefs, rather than patient characteristics, were the dominant feature driving botulinum toxin-A injection strategy for post-stroke upper limb spasticity.

Conclusion: This result looks into the "black box" of rehabilitation, revealing significant variation in injector beliefs. Findings suggest that further scientific work is required to maximize the efficacy of botulinum toxin-A injections in post-stroke upper limb spasticity management.

Key words: Muscle spasticity; botulinum toxin A; stroke; upper limb; rehabilitation; clinical reasoning.

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INTRODUCTION

There is an accumulating body of evidence documenting the positive impact of botulinum toxin-A (BoNT-A) on reducing upper limb (UL) spasticity following adult stroke. Over the last 15 years, 12 randomized controlled trials (RCTs) have been

published indicating positive UL outcomes based on measures from a variety of assessment tools (1–12). Two-thirds of these studies have directed the clinician as to which combinations of muscles were to be injected, with the intention of creating homogeneity between active treatment and placebo groups (1–4, 8, 9, 11, 12). The most common muscle combinations used in these studies incorporated the finger flexors (flexor digitorum superficialis (FDS) and/or flexor digitorum profundus (FDP)), wrist flexors (flexor carpi radialis (FCR) and/or flexor carpi ulnaris (FCU)), and/or elbow flexors (biceps brachii (BB) and/or brachioradialis (BR)). Although RCTs remain the gold standard in biomedical research, the study protocols may not reflect clinical practice in relation to BoNT-A injection for UL spasticity (13). Only 4 of the 12 RCTs reflected true clinical practice by allowing investigator discretion in the choice of muscles to be injected (5–7, 10). From these 4 studies, details of how clinicians determined which muscles to inject and what BoNT-A dosage to use were unpublished. Such components of clinical decision-making have been referred to as the "black box of rehabilitation" (14, 15); defined as procedures that have potential to influence rehabilitation outcomes but that are difficult to evaluate formally.

One of the studies referred to above was a randomized, double-blind placebo controlled study conducted across 6 hospitals from New South Wales and Victoria, Australia (5). A detailed methodology has been published previously, reporting an intention-to-treat analysis of 96 subjects, 42 of whom received placebo and 54 who received the active agent. Patients who were treated with Dysport[®] were found to have a greater reduction in spasticity, measured using the Modified Ashworth Scale (MAS) (16), which translated into significantly greater functional improvement using goal attainment scaling (GAS) (17).

The comprehensive data recorded in McCrory et al.'s (5) study was designed to reflect the routine clinical practice of 2005 when data collection commenced. The data collected, including muscle selection, BoNT-A dosage administered and repeat treatment strategies, provides an opportunity to evaluate the injection strategy utilized in the study and thus provides insight into the "black box". This is important as current consensus recommendations for management of adult upper-limb spasticity suggest that overall treatment decisions

should be based on individual evaluation (including severity and distribution of spasticity) and the goals of treatment (18), but are imprecise regarding dosage. This contrasts to paediatric guidelines, which suggest that the injection dose for UL and lower limb spasticity should relate to the severity of spasticity/motor disorder and the goal of treatment (19, 20).

Therefore, this paper explores how these recommendations may relate to muscle selection and dosing in a previously published RCT aiming to achieve optimal anti-spasticity benefit. This secondary analysis examines 3 hypotheses formed from the international consensus recommendations: (i) presence and severity of muscle spasticity will be associated with muscle selection; (ii) patient-identified goals will be associated with muscle selection and injection dosage; and (iii) injector practices and treatment effects will show minimal between-site variability.

METHODS

Participants

Efficacy data for primary and secondary end-points of the primary study were analysed by McCrory et al. (5), using an intention-to-treat population, defined as all patients who were randomly assigned and who received at least one cycle of study medication. Six patients did not complete the study as allocated; leaving 90 participants for analysis per protocol (52 BoNT-A, 38 placebo). This *post-hoc* analysis was performed on the 90 per protocol participants. Inclusion and exclusion criteria of this sample are outlined elsewhere (5, 17).

Injectors

The physicians involved in the study (3 rehabilitation physicians, 3 neurologists) were experienced BoNT-A injectors who performed 2 serial UL injections for participants with post-stroke UL spasticity across a 12-week interval. Participants were injected with a maximum of 1000 units of placebo or active BoNT-A (Dysport®, Ipsen Pty Ltd, Paris, France), as a previous dose-ranging study demonstrated this to be the most effective total dose for UL spasticity (12).

Post-hoc data preparation

Each of the 6 study sites was randomly assigned a site number (sites 1–6). Injection practices were evaluated in a two-stage process. First, individual UL muscles were coded as injected or not injected for each participant. Secondly, to assess injection dosages, muscles were grouped on the basis of their principal function, i.e. elbow flexion (BB, brachialis (B), BR), wrist flexion (FCU, FCR) and finger/hand flexion (FDS, FDP, flexor pollicis longus (FPL and the intrinsic hand and thumb muscles). BoNT-A or placebo dosage was calculated as the total number of units injected into these functional muscle groups at Injection 1 (Inj1) and Injection 2 (Inj2). Injections were not given into the shoulder girdle muscles in this study.

The MAS was used to indicate presence and severity of muscle spasticity as this was accepted clinical practice at the time of protocol development in the primary study (5). MAS scores vary from 0 to 4 with each rating category representing a higher level of resistance to passive movement noted by the examiner at each joint of the limb being tested (16). This *post-hoc* analysis utilized MAS scores for elbow, wrist and finger flexors collected in weeks 0 and 12 of the study (immediately prior to Inj1 and Inj2). Study participants were grouped into MAS < 2 or MAS ≥ 2, indicating lower and higher levels of resistance to passive movement, respectively.

Patient-identified goals were recorded to identify expectations for functional outcome following BoNT-A injections. A baseline GAS score, weighted for importance and difficulty, was calculated prior to

Inj1 and again prior to Inj2 using previously reported methods (21). Each study participant was categorized as having a goal directly related to hand function or not. Hand goals were further categorized according to whether they required active movement and control of the affected hand (active goals) or not (passive goals). Where the participant had both a passive and an active goal, the active goal was given priority in the analysis. Some participants receiving UL BoNT-A injections did not have specific hand function related goals, instead citing general UL goals (e.g. shoulder abduction to enable axilla cleaning), improvement in independence, or mobility as anticipated outcomes from UL injections.

Data analysis

Descriptive analysis of clinical outcomes, including MAS and GAS, were conducted, frequency of muscle selection, and injection dose mean and range were also calculated. The results of statistical tests were considered to be significant when $p \leq 0.05$.

Although the primary study was double-blinded, it is recognized that blinding may have failed if injectors became aware of differential treatment efficacy between the active BoNT-A and placebo groups. This potential confound was assessed using a series of χ^2 analyses to compare injection choices between placebo and active treatment groups and across injection occasions (Inj1 and Inj2). Mean injection dosage into muscle groups was analysed for between-group differences using the non-parametric Mann-Whitney *U* test, and from Inj1 to Inj2 using the Wilcoxon matched-pair signed-ranks test.

To test the first hypothesis, elbow, wrist and finger MAS scores were examined for a relationship with muscle selection using χ^2 analysis, where the likelihood of injecting a muscle was hypothesized to increase when MAS scores were higher (≥ 2). The correlation between dosage and MAS score was examined using Spearman's correlation (ρ). MAS scores at Week 0 were examined against Inj1 practices, while MAS scores in Week 12 were examined for a relationship with muscle selection and dosages choices at Inj2.

In order to test the second hypothesis, the relationship between having a self-identified hand function goal and muscle selection was examined by χ^2 analysis, where the likelihood of injecting wrist or finger flexors, thumb or intrinsic muscles was hypothesized to be greater in people with a hand function goal. Dosing practices were compared between participants with active and passive hand goals using the non-parametric Mann-Whitney *U* test. On the basis of previously published research (22), it was hypothesized that injection dosage for participants with active function goals would be more conservative than injection dosage for participants with passive function goals. Muscle selection, hand injection dose and wrist injection dose at Inj1 and Inj2 were examined against goal identification and type, which were held consistent across the study period. Only participants with hand goals were included in the analysis of goal type and dose.

The final hypothesis examined between-site differences in injection practices. With respect to muscle selection, frequencies were examined using χ^2 analysis, while between-site differences in dosage were examined using non-parametric analysis of variance (ANOVA) (Kruskal–Wallis test). To account for the potential confound of different levels of spasticity by site, MAS scores were analysed between sites using a Kruskal–Wallis test. Finally, outcomes achieved by participants injected with BoNT-A were compared between sites using a Kruskal–Wallis test to evaluate site-specific reduction in muscle spasticity (measured by MAS) and attainment of goals (measured by GAS).

RESULTS

The 90 participants comprised 36 females and 54 males, with a mean age of 59.9 years (SD = 12.9; range 21–83 years). These participants were distributed across the 6 study sites (Site 1, $n = 18$; Site 2, $n = 11$; Site 3, $n = 13$; Site 4, $n = 24$; Site 5, $n = 15$; Site 6, $n = 9$).

The efficacy of blinding was examined first. Each of the 15 muscles injected were independently assessed for a treatment group effect. At Inj2, 1 of the 15 injected muscles was more likely to be injected in the placebo group (FDP; $\chi^2=4.02$; $p=0.05$). No other muscle selections at either Inj1 or Inj2 were influenced by treatment group. The dose injected into each muscle group at Inj1 and Inj2 was not influenced by treatment group, with the exception that dosage injected into hand flexors was higher in the placebo group at Inj1 (placebo: median 450 units; BoNT-A: median 400 units, $\chi^2=-2.53$; $p=0.012$).

The general lack of difference between treatment groups suggested that blinding remained intact with regard to placebo and BoNT-A status. Active and placebo injection data were subsequently collapsed into one set for further analysis.

The second potential confounding variable, injection timing, was evaluated to determine if muscle selection and dose changed from Inj1 to Inj2 for the sample ($n=90$). There was no relationship between injection time and muscle selection for any of the 15 muscles examined. Total injected dose into muscle groups did not significantly differ from Inj1 to Inj2 (elbow flexors $z=0.97$ $p=0.33$; wrist flexors $z=-0.63$, $p=0.53$; finger flexors $z=-0.13$, $p=0.90$). The most frequently injected muscles were FDS and FDP, followed by BB, FCU and FCR (Fig. 1).

With regards to the first hypothesis, individual muscle selection was associated with higher MAS ($MAS \geq 2$) in select UL muscles. Participants with finger $MAS \geq 2$ were more likely to receive FDP injections ($\chi^2=6.12$; $p=0.013$); a trend was observed in participants with wrist $MAS \geq 2$ to more frequently receive FCU injections ($\chi^2=3.69$; $p=0.055$); and finally participants with elbow $MAS \geq 2$ were more likely to receive biceps brachii injections ($\chi^2=8.70$; $p=0.003$). The frequency of injection into others muscles (FDS, FCR, B, BR) did not differ between participants in the higher and lower MAS groups ($\chi^2=0.03-2.47$; $p>0.05$).

Injection dose in the elbow and wrist flexors was not correlated with MAS scores at the elbow and wrist ($\rho=0.08$, $p=0.35$; $\rho=0.02$, $p=0.86$, respectively). Finger flexor dose showed a weak positive association with finger MAS scores ($\rho=0.22$; $p=0.003$).

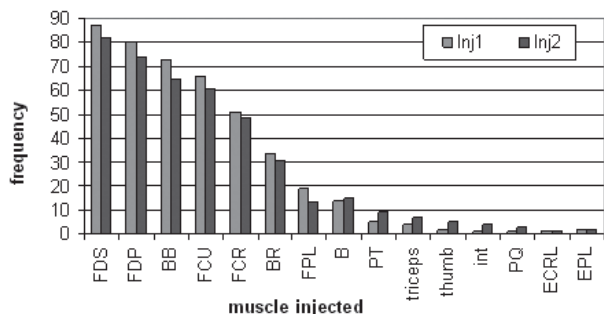


Fig. 1. Frequency of muscle selection at Injection 1 and Injection 2 ($n=90$). FDS: flexor digitorum superficialis; FDP: flexor digitorum profundus; BB: biceps brachii; FCU: flexor carpi ulnaris; FCR: flexor carpi radialis; BR: brachioradialis; FPL: flexor pollicis longus; B: brachialis; PT: pronator teres; int: intrinsic hand muscles; PQ: pronator quadratus; ECRL: extensor carpi radialis longus; EPL: extensor pollicis longus.

Table I. Muscle selection (%) at each site with χ^2 values highlighting significant differences between sites for all muscles

	Site 1 <i>n</i> =36	Site 2 <i>n</i> =22	Site 3 <i>n</i> =26	Site 4 <i>n</i> =48	Site 5 <i>n</i> =30	Site 6 <i>n</i> =18	χ^2
BB	94	77	100	52	87	56	36.66*
B	0	14	89	0	10	0	121.22*
BR	3	14	69	35	87	0	77.94*
FCU	97	86	89	50	37	89	50.32*
FCR	97	86	89	6	37	50	96.99*
FDP	97	77	96	94	50	94	42.00*
FDS	97	100	100	96	97	61	38.25*
FPL	17	23	4	6	54	6	36.00*

* $p<0.001$.

BB: biceps brachii; B: brachialis; BR: brachioradialis; FCU: flexor carpi ulnaris; FCR: flexor carpi radialis; FDP: flexor digitorum profundus; FDS: flexor digitorum superficialis; FPL: flexor pollicis longus.

The second research hypothesis proposed a relationship between injection strategy and patient-identified goals. More than three-quarters of the participants in this study specified one or more goals related to hand function ($n=72/90$). However, having a hand goal did not increase the frequency of receiving injections into the wrist flexors (FCU, FCR), finger and thumb flexors (FDP, FDS, FPL), or the intrinsic muscles of the hand ($\chi^2=0.01-1.29$; $p>0.10340.05$). When injection dosage at the wrist and hand were compared between participants with active ($n=50$) or passive goals ($n=22$), the hypothesized relationship was not evident. The median wrist dose for participants with passive and active function goals was equal (300 units; $z=-0.39$, $p=0.70$). Median hand dose for participants with passive (375) and active (400) hand goals was similar ($z=-0.40$, $p>0.05$).

While few associations existed between muscle selection, injected dose, MAS or patient-identified goals, examination of the final hypothesis revealed several significant between-site differences. χ^2 analysis identified statistically different injection frequency by site for all examined muscles: BB, B, BR, FCU, FCR, FDP, FDS, and FPL (Table I). Differences between sites for injection of triceps, pronator quadratus (PQ), pronator teres (PT), thumb, intrinsic hand muscles, extensor carpi radialis longus and extensor pollicis longus could not be calculated due to low injection frequency.

Differences between sites for selection of elbow muscles are highlighted in Fig. 2 as an example of between-site differences. In selecting muscles to reduce elbow flexor spasticity,

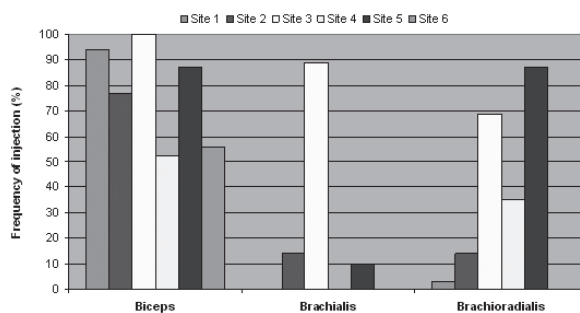


Fig. 2. Between-site differences in the frequency of elbow flexor injections.

Table II. Injection dose to each muscle group by site. Dose median (IQR) expressed in Dysport units

	Site 1	Site 2	Site 3	Site 4	Site 5	Site 6	Kruskal–Wallis
Elbow flexors	300 (50)	350 (100)	500 (0)	250 (200)	450 (50)	250 (150)	62.89*
Wrist flexors	300 (0)	300 (0)	200 (0)	225 (150)	300 (163)	250 (250)	47.72*
Finger flexors	400 (50)	300 (200)	300 (0)	550 (100)	250 (113)	375 (238)	75.61*

*Significant difference between sites for all muscle groups $p < 0.001$

Table III. Between-site variations in muscle spasticity measured by the Modified Ashworth Scale (MAS) at the fingers, wrist and elbow

	Site 1 Median (IQR)	Site 2 Median (IQR)	Site 3 Median (IQR)	Site 4 Median (IQR)	Site 5 Median (IQR)	Site 6 Median (IQR)	Kruskal–Wallis
MAS Elbow	2 (1.3)	2 (0.8)	2 (1.5)	1.5 (0.5)	2 (0.5)	2.5 (1)	12.62; $p = 0.027$
MAS Wrist	2 (1.5)	2 (1.5)	2 (1)	2 (1)	2 (0.5)	3 (1)	22.16; $p < 0.001$
MAS Fingers	2 (1)	2 (1.5)	3 (1)	3 (1)	2 (1)	3 (1)	8.83; $p = 0.12$

Site 6 targeted BB only, whereas Sites 3 and 5 chose to inject all 3 elbow flexors: BB, B, and BR. When considering wrist flexors, Sites 1–3 injected over 85% of participants in FCU and FCR, while Site 5 injected one-third of participants in these muscles, and Site 4 preferentially injected FCU 8 times more frequently than FCR. Differences in finger muscle selection were also evident. For example, Sites 1–4 tended to concomitantly inject FDP and FDS, whereas Site 5 preferentially injected FDS and Site 6 favoured FDP. Site 5 injected FPL in half their participants, while Sites 3, 4 and 6 injected FPL in less than 10% of cases.

Between-site differences for injected dose were also evident for the 3 flexor muscle groups (elbow flexors, wrist flexors, finger flexors) (Table II). Non-parametric ANOVA results highlighted significant between-site differences. For example, Sites 3 and 5 injected 100–200 units more at the elbow than the other sites, whereas Site 4 injected around 150–200 units more into finger flexors than other sites. By reviewing the pattern of injected dose across the different sites, the ratio of dose injected for elbow to wrist/hand flexor muscles (i.e. proximal:distal muscle groups) revealed multiple strategies; two sites injected in a 1:1 ratio (sites 3 and 5), two sites in a 1:2 ratio (sites 1 and 2) and the remaining two in a ratio of 1:3 or greater (sites 4 and 6).

Between-site MAS scores were examined as a potential confounding variable that may have contributed to these dosage differences. Table III presents median and inter-quartile range of MAS scores for each of the 3 functional muscle groups (finger flexors, wrist flexors, elbow flexors). Statistically significant differences between sites were present at the

wrist and the elbow, but were not evident for finger flexors. While observed differences in MAS score achieved statistical significance, MAS varied by < 1 point, suggesting that the difference may not have been clinically significant.

While the total dosage and the dosage distribution into muscle groups (i.e. elbow, wrist and finger flexors) did not significantly differ from Inj1 to Inj2, the opposite was found at an individual participant and individual muscle level (see Table IV).

As can be seen, 2 sites (1 and 3) changed dosage regime in approximately half of the participants, averaging redistribution of ≤ 150 units when changes were made. The remaining sites changed dose in $\geq 80\%$ of participants, highlighting significant between-site differences in the frequency of individual dose changes ($\chi^2 = 19.8$; $p = 0.001$). There was large inter-site variability in how dose was redistributed at Inj2 compared with Inj1. Almost one-quarter (23%) of subjects had 400 units or more redistributed to different muscles or in different doses from Inj1 to Inj2, with 9% having changes of $> 50\%$ of the available dose between Inj1 and Inj2. The overall dose tended to be redistributed rather than reduced, as the full 1000u allocation per participant was used in almost all cases on both injection occasions.

Finally, in light of the between-site differences in muscle selection and dosage practices, the next logical step in this analysis was a comparison of outcomes achieved by participants injected with BoNT-A at each site. Reduction in muscle spasticity, measured by MAS change at the elbow, wrist and hand, did not significantly differ between sites ($\chi^2 = 2.90$; 4.16;

Table IV. Frequency of individual dose changes from Inj1 to Inj2 with mean dose redistribution for each site

Site	Participants with dose redistribution	Mean dose redistributed (u)
1	44% ($n = 8/18$)	130
2	82% ($n = 9/11$)	280
3	54% ($n = 7/13$)	150
4	92% ($n = 22/24$)	240
5	93% ($n = 14/15$)	260
6	89% ($n = 8/9$)	365

Table V. Median goal attainment scale (GAS) scores with inter-quartile range (IQR) recorded at each site from start to end of study

Site	GAS median (IQR)		
	Week 0	Week 20	Change
1	30.8 (11.1)	36.3 (11.2)	5.5
2	22.9 (12.7)	31.7 (18.3)	8.8
3	29.1 (5.3)	32.4 (7.3)	3.3
4	22.6 (1.5)	27.2 (11.3)	4.6
5	36.3 (10.6)	40.9 (14.3)	4.6
6	26.1 (8.3)	33.2 (11.3)	7.1

2.68: $p > 0.05$ for all). Furthermore, while all sites achieved improvements in median GAS scores, the level of goal attainment did not significantly differ between sites (Kruskal–Wallis $\chi^2 = 1.41$, $p = 0.92$). Median GAS scores recorded at each site from start to end of the study are presented in Table V.

DISCUSSION

This secondary analysis sought to examine the clinical reasoning underlying BoNT-A injections in the management of UL post-stroke spasticity. The primary hypotheses, that injection protocols would be related to MAS score and patient goals, were largely incorrect. Instead the principal difference determining muscle selection and the injected dose was study site, suggesting individual injector preference. Redistribution of injected dose between Inj1 and Inj2 occurred in 50% of subjects at 2 sites compared with >80% in the remaining 4. Combining these inter-site variations revealed that no 2 sites used similar approaches to their injection protocols. These findings suggest that the individual injectors had markedly different views of how to achieve maximal effect from their intervention. These beliefs were not clearly related to patient-identified hand goals or to the degree of UL spasticity measured by the MAS; however, different injector practices did not appear to influence MAS or GAS gains in this study, as similar outcomes were achieved at all sites.

At first review, the lack of association between muscle selection and injection dose, level of spasticity in targeted muscle groups, and participants' hand goals is difficult to explain. Although the MAS is a commonly used method for assessing UL spasticity (22), it has received considerable criticism (23–25), and in fact, may not be sensitive to the clinical reasoning processes guiding injection practices. The lack of association between patient goals and muscle selection is of greater concern, as this finding suggests that injection procedures may not have been client-centred, that goals may not be consistently communicated between multi-disciplinary team members or that physicians have widely varying beliefs on how to achieve these goals. Furthermore, our hypothesis that injection dosage for participants with active function goals would be more conservative than injection dosage for participants with passive function goals was not supported. In contrast to previous findings (22), injection dose was almost identical irrespective of the intended level of function indicated by the client goal. Recommendations that treatment decisions be based on individual evaluation and the goals of treatment (18) may be more consistently implemented in a multi-disciplinary collaborative approach to goal setting.

The parent study of this secondary analysis showed significant positive treatment effects for the active group compared with the placebo group in terms of MAS and GAS scores (5). Additional analysis of the data indicated that there was a strong correlation between reduction in spasticity, GAS score and perceived global benefit (17). However, the results from this study pose the question of whether the positive findings from the primary study may have been enhanced if the injector strategies had been more consistent.

This *post-hoc* analysis allows us to examine inside the “black box” of rehabilitation. It seems probable that the differences in injector beliefs, and hence injection protocols, are the result of limitations in the state of the science of spasticity management. In clinical usage, the term “spasticity” remains an umbrella term that takes into account a range of positive features of the upper motor neurone syndrome (26). The state of the science would benefit from a specific nomenclature for spasticity subtypes, followed by differentiation of the efficacy of various forms of intervention. Based on our current understanding, there is no way of determining what UL BoNT-A injection strategy or strategies are likely to maximize treatment efficacy.

Further research is required to assist clinicians to develop an “algorithm of best practice” to follow based on specific spasticity subtypes. In addition, the majority of past studies have placed an emphasis on outcome measures that are not directly meaningful to the patient or carer. Although treatment goals are being set prior to BoNT-A injection, outcomes continue to be measured almost exclusively at the impairment level, with very few clinicians using functional outcome scales (22). As such, patient-centred goals may be used to demonstrate whether a reduction in muscle spasticity translates into functional gains, thereby suggesting that patient-centred goals become the key determinant of the injection strategy. There remains a need to develop sensitive and functionally relevant measures of spasticity to better understand how to target muscles according to their contributions to and degree of spasticity and desired outcomes.

As a secondary analysis of previously collected data, some limitations need to be considered when interpreting the findings of the above study. With respect to factors potentially influencing physician injection decisions, such as knowledge of MAS and client-goals, the degree of multi-disciplinary or client-physician communication at each study site was not reported, and cannot be assumed to be similar. Goal-setting practices varied between sites, some using the previously recommended SMART (specific, measureable, achievable, realistic and timed) goal technique (18), while other sites reported non-specific goals (e.g. “To be able to open fingers”). These goals could not be clearly classified as active or passive. Future research involving GAS as an outcome measure for spasticity interventions would benefit from a precise protocol for goal setting. Furthermore, with respect to the functional outcomes achieved following BoNT-A injections, physical and occupational therapy follow-up was not mandated in the primary study protocol, therefore factors other than injection strategy may have influenced functional change and goal attainment. Small sample numbers at each site (site $n = 9–18$) prevented multi-factorial analysis between sites. A more complete analysis of these issues will require recruitment of a much larger sample.

This secondary analysis examined the “black box” of rehabilitation, revealing that injector beliefs, rather than patient characteristics, were the dominant feature driving BoNT-A injection strategy for post-stroke UL spasticity. The study suggests that the impact of enhanced inter-disciplinary communication and clearer treatment goal differentiation needs to be examined in larger multicentre cohort analyses. These findings highlight the need for further basic scientific research

to maximize the outcomes from spasticity interventions, and in particular following BoNT-A injections.

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