ORIGINAL ARTICLE

Prevention of post-dural puncture headache: a randomized controlled trial

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Keywords:
headache, lumbar puncture, post-dural puncture headache, randomized controlled trial

Received 4 October 2019
Accepted 9 January 2020

European Journal of Neurology 2020, **27:** 871–877

doi:10.1111/ene.14158

Background and purpose: We investigated 952 subjects undergoing diagnostic lumbar puncture (LP) to study the effects of needle size, needle design and stylet reinsertion on the risk of post-dural puncture headache (PDPH).

Methods: This randomized double-blind study was performed at Umeå University Hospital in Sweden during 2013–2018. Subjects were randomly assigned one of three needles [22 gauge (G) atraumatic, 25G atraumatic and 25G cutting] and stylet reinsertion before needle withdrawal or not. The main outcome measure was PDPH assessed by standardized telephone interview(s) 5 days after the LP, repeated until headache cessation. We used logistic regression to calculate odds ratios (ORs) with 95% confidence intervals (CI) for PDPH.

Results: The mean (SD) age was 51.1 (16.7) years and 53.6% were females. The smaller bore (25G) atraumatic needle incurred a lower risk of headache compared with the larger bore (22G) atraumatic needle [22.0% (69/314) vs. 30.2% (98/324); OR, 0.65; 95% CI, 0.45–0.93] and compared with the cutting needle [32.8% (103/314); OR, 0.58; 95% CI, 0.40–0.82]. Reinserting the stylet before needle withdrawal did not reduce the risk of headache.

Conclusions: These data suggest that a 25G atraumatic needle is superior to a larger atraumatic needle, and to a same-sized cutting needle, in preventing PDPH after diagnostic LP. In contrast to one earlier report, this study did not find that stylet reinsertion was effective in preventing PDPH. This study provides class I evidence that a small atraumatic needle decreases the risk of PDPH and that stylet reinsertion does not influence PDPH risk.

Introduction

Post-dural puncture headache (PDPH) [post-lumbar puncture (LP) headache] is common and several methods to lower the risk of this complication were suggested in the American Academy of Neurology guidelines from 2000 and 2005 [1,2]. These include using small-bore needles, atraumatic (non-cutting/pencil-point) needles and, when using atraumatic needles, reinserting the stylet before needle withdrawal. Two large meta-analyses later confirmed that atraumatic needles are effective in preventing PDPH [3,4] but only one study shows that stylet reinsertion in atraumatic needles is associated with a lower risk of headache after diagnostic LP [5,6]. A study on cutting needles in spinal anesthesia showed no protective effect from stylet reinsertion [7]. Questionnaire studies suggest that the compliance to the American Academy of Neurology guidelines is poor [8,9]. The objectives of the current study were to investigate the effects of needle size, needle design and stylet reinsertion on the risk of PDPH.

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Methods

Setting and study participants

This was a randomized double-blind study including subjects undergoing diagnostic LP during their neurological work-up at Umeå University Hospital, Sweden, between 28 May 2013 and 19 June 2018 when the study was fully recruited. Subjects unable to provide informed consent or participate in the follow-up (i.e. aphasic subjects or subjects with cognitive deficits) and subjects denying participation were excluded.

Interventions

The LPs were performed by physicians of differing experience and by medical students under supervision using sterile equipment with the patient lying in the right lateral decubitus position. The position was changed to sitting if deemed necessary by the treating physician. Local anesthesia was optional. The bevel of the cutting needle was always inserted parallel to the dural fibers. Needles could be switched without model or size limitations at the physician's discretion in case of needle failure, i.e. not obtaining cerebrospinal fluid (CSF). In the case of needle switch, the allocated stylet reinsertion option was retained; puncture site switch was allowed. A small plastic tube was used as a siphon device to increase CSF draw speed. Trained study staff obtained informed consent and collected all procedural data during the LP. The participants were not informed about needle and stylet

Outcome data

The primary outcome was any PDPH according to the international classification of headache disorders 3 (ICHD-3) as assessed by telephone interview 5 days after the LP. If day 5 occurred during a holiday or weekend the telephone interview was postponed until the nearest following weekday. The subjects were equipped with a headache diary and instructed to document their headache upon dismissal. A nurse not involved in the LP procedure, thus unaware of randomization allocation, performed the telephone interview. If the participant still had headache at follow-up, the procedure was repeated after another 5 days until headache cessation. During the interview, the headache was graded as: (i) mild, not needing intervention, (ii) intermediate, i.e. exceeding the previous grade but not meeting the criteria for severe headache, and (iii) severe, preventing daily activities such as studies, work, etc. Secondary outcomes included severe PDPH, headache duration, analgesia consumption, sick leave, back pain, radiating leg pain, needle switch and interactions between needle size and stylet allocation, needle design and stylet allocation, and needle and age. Procedural variables included the number of LP attempts, whether or not the first CSF was blood-tinged, CSF opening pressure (not in sitting position), CSF volume drawn, procedure duration and reason for LP. A retrospective search in the administrative systems for all blood-patches performed at the neurology clinic during the study was conducted in October 2018.

Randomization, sample size and statistical analyses

The randomization was performed using a custom-made computer program that randomized the participants to one of the three needles and to stylet reinsertion or not (six categories) in blocks of 12, stratified by three previously recognized predictors of PDPH: sex, body mass index (BMI) (<25 vs. ≥ 25) and age (<50 vs. ≥ 50 years) to ensure an even distribution of these variables. The desired sample size ($n = 900$) was decided based upon previously reported data, choosing an alpha of 0.05 and a power of 80% using chi-squared tests to detect a difference between the atraumatic and cutting needle of the same size (12.2% vs. 24.4%) [10] ($n = 157$ per group), to detect a difference between the 25 gauge (G) and 22G needles (12% vs. 20%) [1] ($n = 329$ per group) and to detect a difference for stylet reinsertion (5% vs. 16%) [5] ($n = 121$ per group). After a pre-defined outcome-blinded interim analysis at $n = 600$ participants, we detected a 7% loss of participants due to protocol non-adherence or loss to follow-up. We therefore decided to extend to 1000 randomized participants. Baseline data are presented in descriptive tables. Outcomes are presented as ratios and the protective effects of each factor (needle size, needle design, stylet reinsertion) were estimated using separate univariate logistic regression models for each outcome. The intention-to-treat cohort was used in the primary analyses. In the per-protocol (PP) analyses, we also adjusted the logistic regression models for sex, BMI (continuous) and age (continuous) as the distribution of these predictors of PDPH might have been skewed due to selection bias. Interactions were assessed in multivariable logistic regression models with interaction terms that were the product of the variables of interest. $P < 0.05$ was considered statistically significant. IBM SPSS Statistics (version 24, IBM Corp., Armonk, NY, USA) was used to perform the statistical analyses.

The study was approved by the regional ethical review board in Umeå, Sweden (2013/151-31). All study subjects provided oral and written informed

consent to participate. The study was retrospectively registered at ClinicalTrials.gov (NCT03960749), where the full study protocol including the statistical analysis plan can be accessed in English.

Results

The flow chart for the 1000 randomized study participants is shown in Fig. 1. The needle was switched in 87/314 (atraumatic 25G), 61/324 (atraumatic 22G) and 71/314 (cutting 25G) subjects due to procedural difficulties, most commonly to a larger bore cutting needle (189/219 of subjects). Due to the large number of needle switches, the PP cohort was also investigated and displayed almost identical results (Appendix S1).

Baseline data

Baseline characteristics were well balanced over the different needles (Table 1). The mean age of participants was 51 years and the majority were females. Approximately one-third reported frequently occurring headaches before LP.

Outcome data

Needle size

Participants undergoing LP with the thinner (25G) atraumatic needle had a lower risk of PDPH compared with those undergoing LP with the 22G atraumatic needle [22.0% (69/314) vs. 30.2% (98/324); odds ratio (OR), 0.65; 95% confidence interval (CI), 0.45–0.93] (Fig. 2).

Needle design

Participants undergoing LP with the 25G atraumatic needle had a lower risk of PDPH compared with those undergoing LP with the same size cutting needle [22.0% (69/314) vs. 32.8% (103/314); OR, 0.58; 95% CI, 0.40–0.82] (Fig. 2).

Stylet reinsertion

Reinserting the stylet before needle withdrawal resulted in a non-significant reduction in the risk of PDPH [26.3% (125/475) vs. 30.4% (145/477); OR, 0.82; 95% CI, 0.62–1.1]. Limiting the analysis to atraumatic needles attenuated this difference [25.5% (81/318) vs. 26.9% (86/320); OR, 0.93; 95% CI, 0.65–1.3]. In contrast, the cutting needle displayed a stronger association [28.0% (44/157) vs. 37.6% (59/157); OR, 0.65; 95% CI, 0.40–1.04]. However, the formal interaction model, a logistic regression model limited to the two 25G needles, including the terms 'needle design', 'stylet' and the cross-product between these two, did not show an interaction between stylet reinsertion and needle design ($P = 0.85$) (OR, 0.93; 95% CI, 0.45–1.9) for the interaction term. When assessing the effect of stylet reinsertion over needle size in atraumatic needles an inverse effect was suggested for the smaller needle compared with the

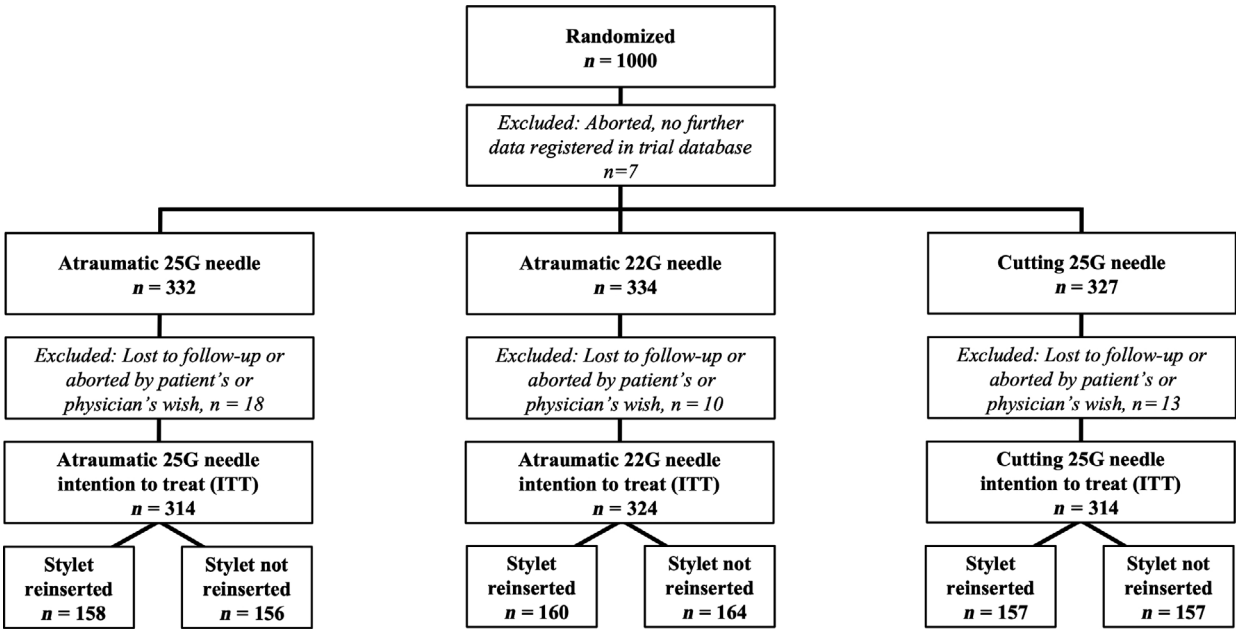


Figure 1 This flow chart of study participants shows the sequential exclusion of participants by needle arm allocation. Of the 1000 randomized participants, 952 underwent lumbar puncture and were analyzed in the intention-to-treat (ITT) cohort. G, gauge.

Table 1 Baseline characteristics: intention-to-treat cohort (n = 952)

	Atraumatic 25G (n = 314)	Atraumatic 22G (n = 324)	Cutting 25G (n = 314)
Female	167 (53.2)	175 (54.0)	168 (53.5)
Age (years)	51.6 ± 16.9	50.3 ± 16.3	51.4 ± 16.9
BMI	26.2 ± 4.8	25.9 ± 4.7	26.3 ± 5.0
Admitted	91 (29.0)	92 (28.4)	85 (27.1)
Primary operator			
Student	72 (22.9)	75 (23.1)	76 (24.2)
Physician in training	109 (34.7)	113 (34.9)	106 (33.8)
Specialist	133 (42.4)	136 (42.0)	132 (42.0)
Headache at the time of LP	13 (4.1)	16 (4.9)	18 (5.7)
Local anesthesia	304 (99.7)	319 (99.4)	241 (79.5)
Right lateral decubitus position	247 (79.7)	262 (82.6)	254 (82.7)
Volume CSF withdrawn (mL)	17 ± 3	17 ± 4	17 ± 4
Days until follow-up	6 (5–7)	6 (5–7)	6 (5–7)
Do you have frequent headaches? – yes	108 (34.4)	117 (36.1)	107 (34.1)
Coffee intake since LP (cups/day)	2.9 ± 1.9	3.0 ± 2.0	3.2 ± 2.0

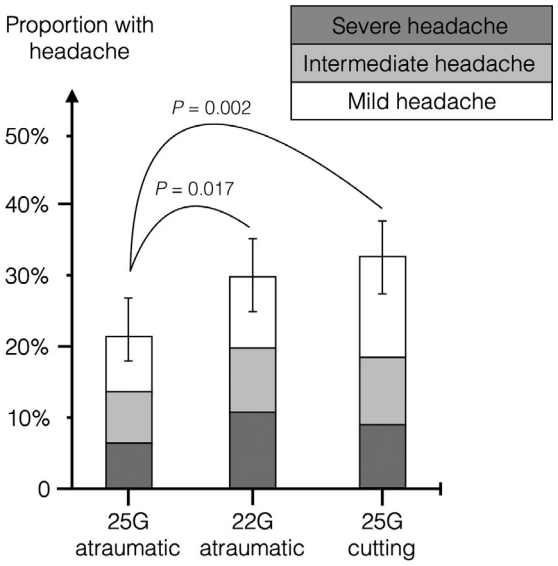
Missing data: body mass index (BMI), n = 3; local anesthesia, n = 23; position, n = 18; cerebrospinal fluid (CSF) volume, n = 30; days until follow-up, n = 9; coffee consumption, n = 9. G, gauge; LP, lumbar puncture. Data are given as n (%), mean ± SD and median (interquartile range).

larger one. For the 25G needle, a lower risk of PDPH with stylet reinsertion was suggested [17.7% (28/158) vs. 26.3% (41/156); OR, 0.60; 95% CI, 0.35–1.04] and for the 22G needle a higher risk of PDPH with stylet reinsertion was suggested (33.1% (53/160) vs. 27.4% (45/163); OR, 1.3; 95% CI, 0.81–2.1]. The interaction model, a logistic regression model limited to the two atraumatic needles, including the terms 'needle size', 'stylet' and the cross-product between these two, suggested that there was an interaction between needle size and stylet reinsertion regarding the outcome PDPH for atraumatic needles (P = 0.035) (OR, 0.46; 95% CI, 0.22–0.95) for the interaction term.

Secondary outcomes

As shown in Fig. 1, more participants randomized to the 25G atraumatic needle switched needle compared with the other two needle groups. Despite this, the PP analyses, including the adjusted models, mirrored the intention-to-treat results regarding the effects of needle size, needle design and stylet reinsertion on the risk of PDPH, as well as the findings regarding interactions between needle size and stylet reinsertion, and needle design and stylet reinsertion, on the risk of PDPH (Appendix S1).

Compared with the 25G atraumatic needle, the risk of needle switch was lower with the 22G atraumatic needle (OR, 0.62; 95% CI, 0.43–0.91) but not with the 25G cutting needle (OR, 0.75; 95% CI, 0.52–1.09). Furthermore, the risk of needle switch increased with increasing age (OR, 1.17; 95% CI, 1.06–1.29 for each 10-year increase) and with increasing BMI (OR, 1.55; 95% CI, 1.33–1.81 for each 5 BMI points increase). The larger bore (22G) atraumatic needle performed differently compared with the smaller needles, displaying a notably shorter procedure duration (mean 20 min vs. 26 and 29 min for the two 25G needles, respectively). This was explained by higher CSF flow speed through the larger needle (Table 2). The effect of needle allocation and the overall risk of PDPH differed over age strata. The youngest participants had the highest risk of PDPH but the least distinct needle effect. Conversely, the older participants had a lower base risk of PDPH but a clearer needle effect (Fig. 3). No formal interactions between needle and age were found in the interaction model for the intention-to-treat cohort, a logistic regression model including the terms 'needle' and 'age' (continuous, by 10-year increase) and the cross-product between these two, P = 0.25, OR, 1.1; 95% CI, 0.91–1.4 for the interaction term for needle size vs. age, and P = 0.10, OR, 1.2; 95% CI, 0.96–1.5 for the interaction term for needle design vs. age. However, in the per-protocol analyses, interactions (modelled as above) were found, P = 0.04, OR, 1.4; 95% CI, 1.0–1.9 for the interaction term for needle size vs. age and P = 0.03, OR, 1.4; 95% CI, 1.0–1.9 for the interaction term for needle design vs. age. One participant in the 25G atraumatic needle category, none in the 22G atraumatic needle category and three in the 25G cutting needle category were treated with epidural blood-patch for their PDPH. No serious adverse events were detected during study follow-up.



No. of subjects with post lumbar puncture headache	69/314	98/324	103/314	
Odds ratio (OR) and 95% confidence interval (CI) for any headache	0.65 (0.45–0.93)	Reference	–	(size)
Odds ratio (OR) and 95% confidence interval (CI) for any headache	0.58 (0.40–0.82)	–	Reference	(design)

Figure 2 Proportion of subjects within each needle arm reporting post-dural puncture headache (PDPH). The PDPH was graded as mild (not needing intervention), intermediate (exceeding the previous grade but not meeting the criteria for severe headache) and severe (preventing daily activities such as studies, work, etc.). Bars denote proportions with headache and whiskers denote 95% confidence intervals (CI) for any headache. *P*-values refer to chi-squared comparisons of proportions with any headache between the needles. Crude odds ratios (ORs) with 95% CI for PDPH by needle size [comparison between 25 gauge (G) atraumatic needle vs. 22G atraumatic needle] and needle design (25G atraumatic needle vs. 25G cutting needle) were derived using logistic regression.

Discussion

This randomized double-blind study on diagnostic LPs demonstrated a lower risk of PDPH with a 25G atraumatic needle compared with a larger atraumatic as well as compared with a same sized cutting needle. This suggests, together with previously published data, that small-bore atraumatic needles should be chosen over larger and/or cutting ones when performing diagnostic LP [1–4].

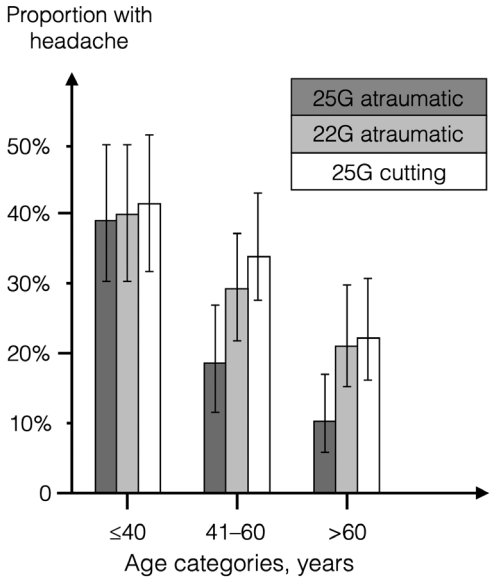
Current American Academy of Neurology LP recommendations suggest that the stylet should be reinserted before needle withdrawal when using atraumatic needles despite the fact that only one study has examined this [5,6]. The study was first published in 1997 [5] and LPs were performed in the sitting position with a 21G needle. The study showed a 5.0% vs. 16.3% risk of PDPH with versus without stylet reinsertion. In contrast, there were no statistically significant effects on the risk of PDPH by stylet reinsertion detected in our study. The interaction model suggested that needle size may be of importance for the effect of stylet reinsertion, a post-hoc finding for which it is difficult to provide a physiological rationale. One earlier study on stylet reinsertion in cutting needles in spinal anesthesia was negative but, to our knowledge, no previous studies have investigated cutting needles in diagnostic LPs. We thus suggest that the stylet should not be reinserted before needle withdrawal in diagnostic LPs given the uncertainty regarding the effect on the risk of PDPH and the possible risk of complications (nerve filament transection and infection) [1].

The current study suggests that the overall risk of PDPH was lower among older participants, which concurs with our clinical experience. Notably, the effects of needle size and design differed over age strata and the most pronounced effect was seen among the oldest participants. This has not been previously addressed and argues that small-bore atraumatic needles for diagnostic LPs should be used even when the *a-priori* risk of PDPH is estimated to be low. The finding of virtually no effect of needle choice in individuals below the age of 40 years is intriguing

Table 2 Secondary outcomes: intention-to-treat cohort (n = 952)

	Atraumatic 25G (n = 314)	Atraumatic 22G (n = 324)	Cutting 25G (n = 314)	P-value
No. of attempts[a]	1 (1–2)	1 (1–2)	1 (1–2)	0.180
Opening pressure (cm H_2O)[b]	15.9 ± 5.1	17.3 ± 4.1	16.8 ± 5.0	0.010
Blood-tinged CSF	19 (6.3)	32 (10.2)	58 (19.2)	<0.001
Duration of procedure (s)[b]	1756 ± 588	1203 ± 657	1539 ± 655	<0.001
Duration until CSF contact (s)[b]	708 ± 478	704 ± 569	726 ± 611	0.874
Duration of CSF draw (s)[b]	954 ± 437	451 ± 263	751 ± 352	<0.001
Severe headache, grade 3	20 (6.4)	35 (10.8)	28 (8.9)	0.138
Number of headache days[a]	3 (2–4)	3.5 (2–5)	3 (2–5)	0.410
Any back pain, grades 1–3	166 (52.9)	165 (50.9)	151 (48.1)	0.484
Any leg pain, grades 1–3	31 (9.9)	28 (8.6)	32 (10.2)	0.780
Any pain killers	113 (36.2)	151 (46.6)	135 (43.3)	0.026
Any sick leave	18 (5.7)	28 (8.6)	18 (5.7)	0.236

All proportions were compared using the chi-squared test. G, gauge. Data are given as median (interquartile range), mean ± SD and n (%). Missing data: number of attempts, n = 8; opening pressure, n = 302; blood-tinged cerebrospinal fluid (CSF), n = 33; duration, n = 1; painkiller use, n = 4. [a]Independent samples Kruskal–Wallis test. [b]One-way ANOVA.



No. of subjects	277	354	321	
No. of subjects with headache	35/91	22/116	12/107	(25G atraumatic)
	38/94	37/126	23/104	(22G atraumatic)
	39/92	39/112	25/110	(25G cutting)

Figure 3 Proportions and numbers of participants with post-dural puncture headache (PDPH) by needle allocation and age. Bars denote proportions with any PDPH and whiskers denote 95% confidence intervals. The risk of headache increased with increasing age (P for trend < 0.001). The visual impression suggests a more pronounced effect from needle allocation among the elderly, although tests for interaction were negative in the intention-to-treat cohort. G, gauge.

and deserves further study. The current study detected a higher PDPH occurrence compared with some [5,11] but not all [12–14] earlier reports, which may be attributed to the fact that we did not exclude participants who had headache before the LP and that we did not select participants for older age.

This study has limitations. The LPs in the study were performed by physicians of varying experience as well as by medical students under supervision. This may have introduced variability in the technical performance of the LPs, including a higher risk of needle switch due to procedural difficulties. However, this also

reflects the real-life clinical workflow and may thus increase external validity. It furthermore suggests that even those with limited LP experience should primarily aim to perform their LPs with atraumatic needles. Another limitation is that the PDPH follow-up assessments were not performed daily after the LP, but on day five, which may contribute to PDPH incidence underestimation. The headache diary that the participants took home after the procedure was used in an effort to overcome the possibly lower sensitivity in detecting early headache with this follow-up strategy.

In conclusion, this randomized controlled study has shown that the risk of PDPH can be decreased by using a small-bore atraumatic needle compared with a larger and/or cutting one. It has also shown that reinserting the stylet before needle withdrawal does not influence the risk of PDPH in a consistent manner. These results should be incorporated in future recommendations regarding diagnostic LPs. Further studies on possible ways to reduce the risk of PDPH in younger individuals are warranted.

Acknowledgements

This study would not have been possible without the kind and competent assistance of all of the personnel and the management at the Neurology Department, Umeå University Hospital. We would specifically like to extend our gratitude to Carina Gillewård and Mari Bäckström for inviting participants and collecting procedural data, and to Lena Lund for performing the follow-up telephone calls. This study was funded by a research grant from the Department of Clinical Science, Neurosciences at Umeå University.

Disclosure of conflicts of interest

J.S. has received material research support from SYNAPSYS and Interacoustics, and institutional consultancy fees from Mabion S.A. M.V. reports research grants and speaker's honorarium from BiogenIdec AB and Neuro Sweden, travel grants from Novartis, BiogenIdec AB and Baxter Medical AB, a writing honorarium from Pharma Industry and BestPractice Multiple Sclerosis, and material research support from UmanDiagnostics AB. G.G., P.S. and A.S. declare no financial or other conflicts of interest.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Supplementary results data, per-protocol cohort (n = 733).

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