

Rationale, Patient Characteristics and First Interim Insights from NeofiLos – A Data Collection to Evaluate Utility and Added Value of Serum NfL in MS

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KEY FINDINGS & CONCLUSIONS

This is the 1st physician reported data on implementation of sNfL in routine medical care setting highlighting the importance and added benefit of sNfL as additional assessment in MS patient management.

A broad range of patients was included in this project (with regards to age, time since first diagnosis of MS and DMT status) indicating the need for disease activity measurement throughout the entire patient journey.

Results show that sNfL measurements will mainly be used to

- determine disease activity (complementing clinical and MRI assessments)
- monitor therapy effectiveness

Although none of the participating physicians had experience with sNfL testing before start of this project, the majority indicated that they would act on or be alerted by elevated sNfL level.

INTRODUCTION

- Neuroaxonal damage results in release of neurofilaments such as neurofilament light chain (NfL) into cerebrospinal fluid (CSF) and blood with elevated NfL potentially indicating disease activity in RMS patients.^{1,2,3}
- Elevated NfL levels may reveal subclinical disease activity before lesions on MRI or clinical symptoms appear.⁴
- Measuring serum NfL (sNfL) levels may help to reflect ongoing disease activity, uncover “subclinical” disease and be of prognostic value for future disease activity, with the potential to contribute to allowing for optimized individual treatment decision making.

OBJECTIVE

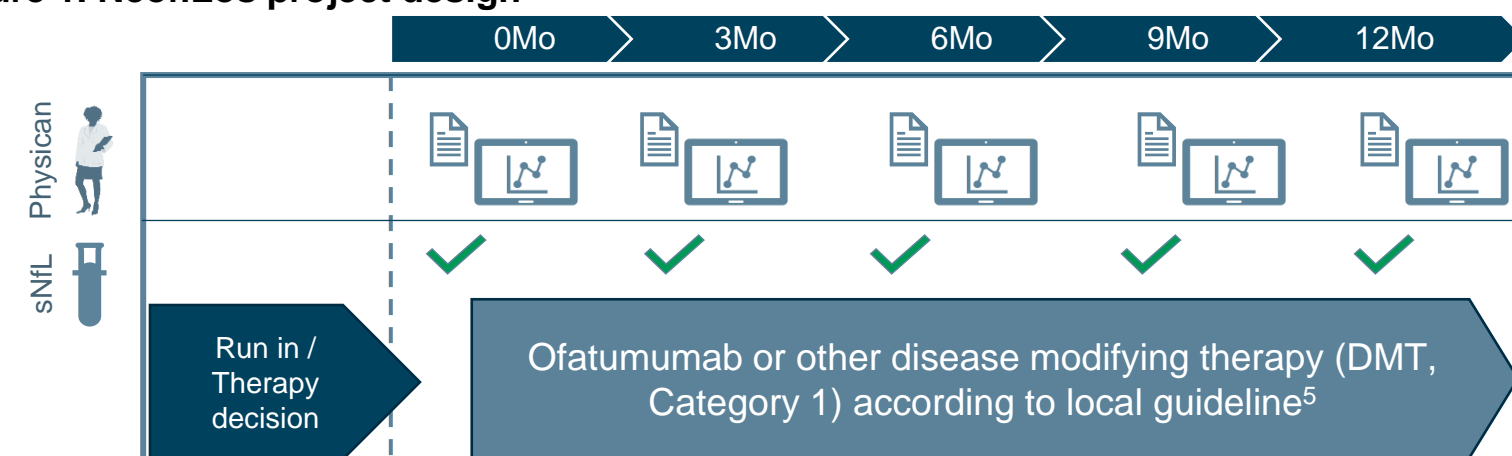
- NeofiLos enables office-based physicians to access sNfL testing aiming to assess utility of sNfL measurements in clinical routine

RESULTS

Project overview

- NeofiLos is a data collection program conducted at multiple established neurology specialist centers to assess the benefit and added value of sNfL from a physician’s perspective in RMS patients scheduled for ofatumumab or another approved disease modifying therapy (DMT, category 1 according to DGN Sk2 guideline⁵) as routine medical treatment (Figure 1).
- Participating physicians will be given the opportunity to gain initial experience with sNfL measurements (up to five measurements per patient within one year) and to test the possible application and integration of sNfL measurement into everyday practice.

Figure 1. NeofiLos project design



- 72 sites participated until data cut-off (17-JAN-2024).
- 622 (99.5%) of 625 enrolled patients were included in this interim analysis. Three patients (0.5%) were excluded from the analysis set as they met not all eligibility criteria for the program
- The primary endpoint of this project is the assessment of usability and benefits of sNfL values for physicians via questionnaires.
- Up to 419 (67.0%) of the possible 622 questionnaires were answered until data cut-off.

Patient demographics and Therapy status at program inclusion

- Patient demographics of the analyzed population are depicted in Table 1.
- The analyzed population was shifted towards female patients (70.1% female compared to 29.9% male patients). The mean age was 43±11.5 years.
- On average patients measured 171.6±8.7 cm with a mean weight of 77.0±17.7 kg resulting in an average Body-Mass-Index (BMI) of 26.1±5.3 kg/m².

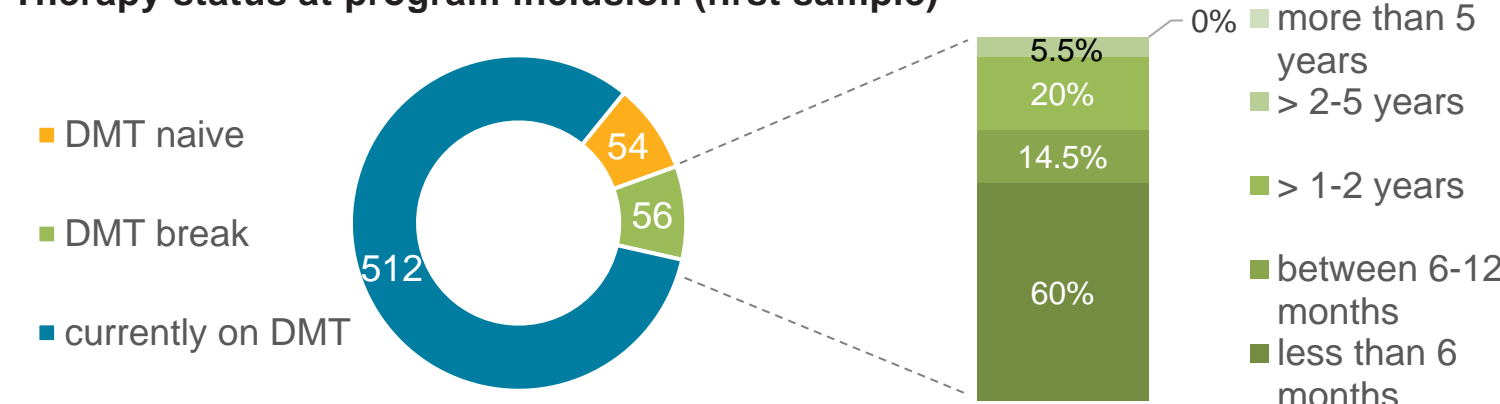
Table 1. Patient Demographics

Patient demographics at the timepoint of program inclusion	Total (N=622)
Sex, n(%)	
Male	185 (29.9)
Female	434 (70.1)
Age [years]	43 (11.5)
Height [cm]	171.6 (8.7)
Weight [kg]	77 (17.7)
BMI [kg /m ²]	26.1 (5.3)

If not otherwise specified, data are presented as mean (±SD)

- 512 of 622 patients (=82.3%) received a therapy at timepoint of program inclusion (first blood draw) while 110 (17.7%) received no therapy. 54 (49.1%) of patients who did not receive therapy were therapy-naïve and 56 (50.9%) patients did receive a therapy in the past but were currently on a break. (Figure 2)

Figure 2. Therapy status at program inclusion (first sample)



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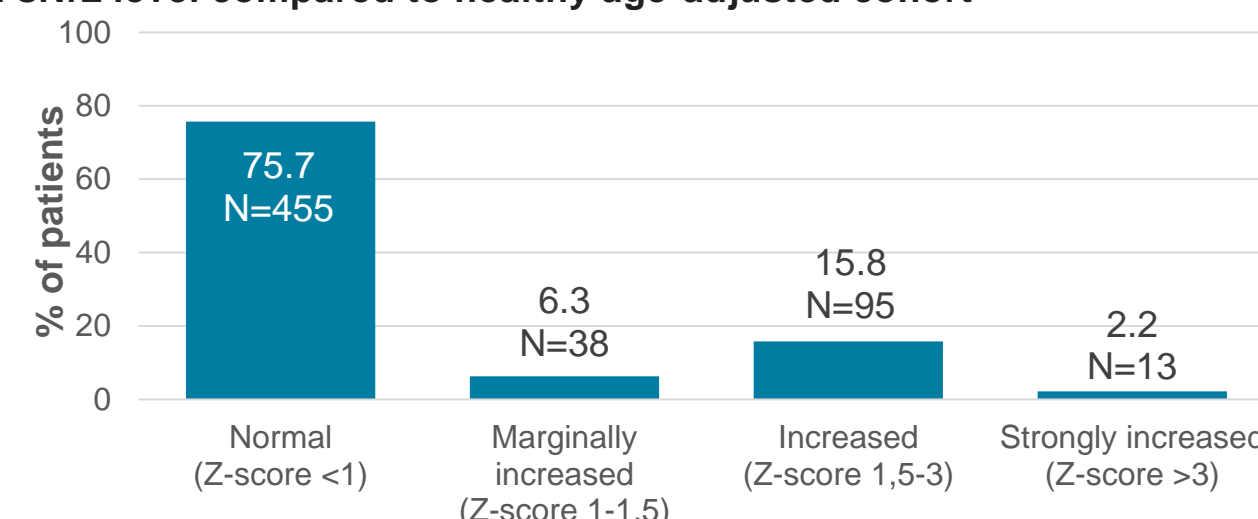
METHODS

- Project design: NeofiLos is a program conducted at 80 sites in Germany, expected to enroll 500 RMS-patients receiving Ofatumumab or other first line disease modifying therapies (DMT) (Figure 1)
- This project was reviewed by an independent ethics committee and notified as a project to the responsible higher federal authority, the National Association of Statutory Health Insurance Funds, the Association of Private Health Insurance Funds and the National Association of Statutory Health Insurance Physicians in accordance with statutory regulations.
- Assessments
 - sNfL is measured from routine blood draws at program inclusion followed by quarterly intervals up to 5x per patient
 - sNfL is documented in electronic data collection form, visualized using scientific context implementing patient demographics and reported to treating neurologists/ physicians

Aggregated sNfL values

- At the time point of interim analysis, 455 (75.7%) of 622 patients showed at timepoint of program inclusion an sNfL level comparable to a healthy, age-adjusted cohort (Z-score <1 times) despite having RMS.
- 38 (6.3%) of patients showed marginally increased sNfL level (Z-score 1-1.5 times) and 95 (15.8%) showed increased sNfL level (Z-score 1.5-3 times) while 13 (2.2%) showed a strongly increased sNfL level (Z-score >3 times) (Figure 4).

Figure 4. sNfL level compared to healthy age-adjusted cohort



sNfL as an easily accessible biomarker regarding disease activity

- Comparing answers „before start of therapy“ (mean=5±1.4; median=5) and „during therapy“ (mean=5.5±1.1; median=5.9), neurologists considered sNfL measurements as more valuable during therapy and monitoring/ follow up of MS disease than at therapy start (Figure 4).
- Overall, participating neurologists would appreciate an easily accessible biomarker for measuring disease activity in their daily clinical routine (Figure 5).

Figure 4: Perception of sNfL as a biomarker regarding MS disease activity assessment

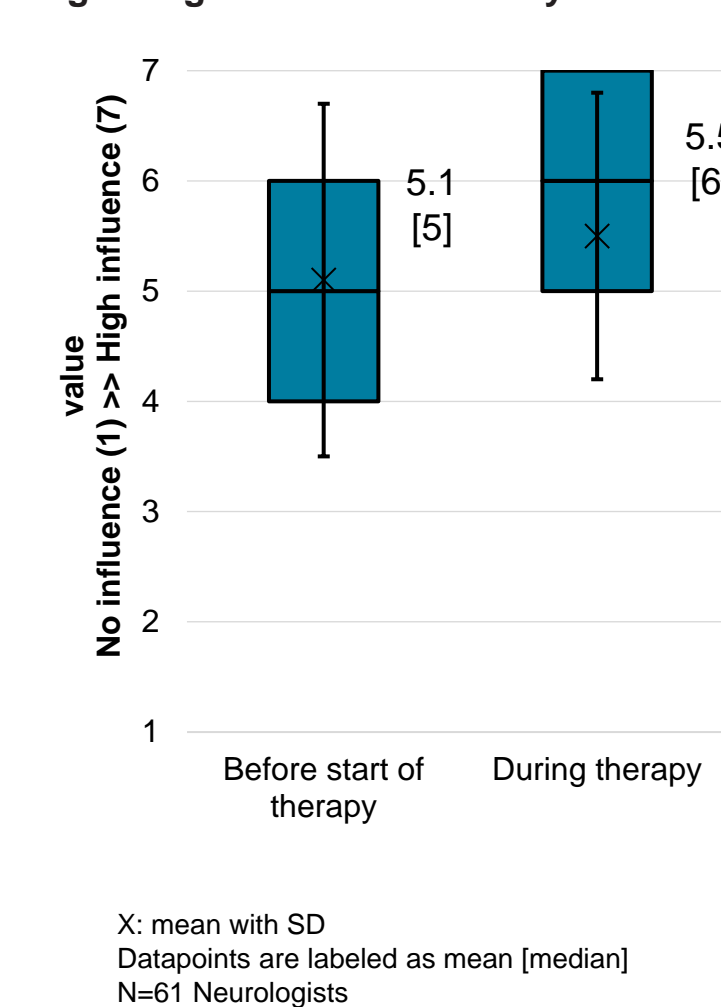
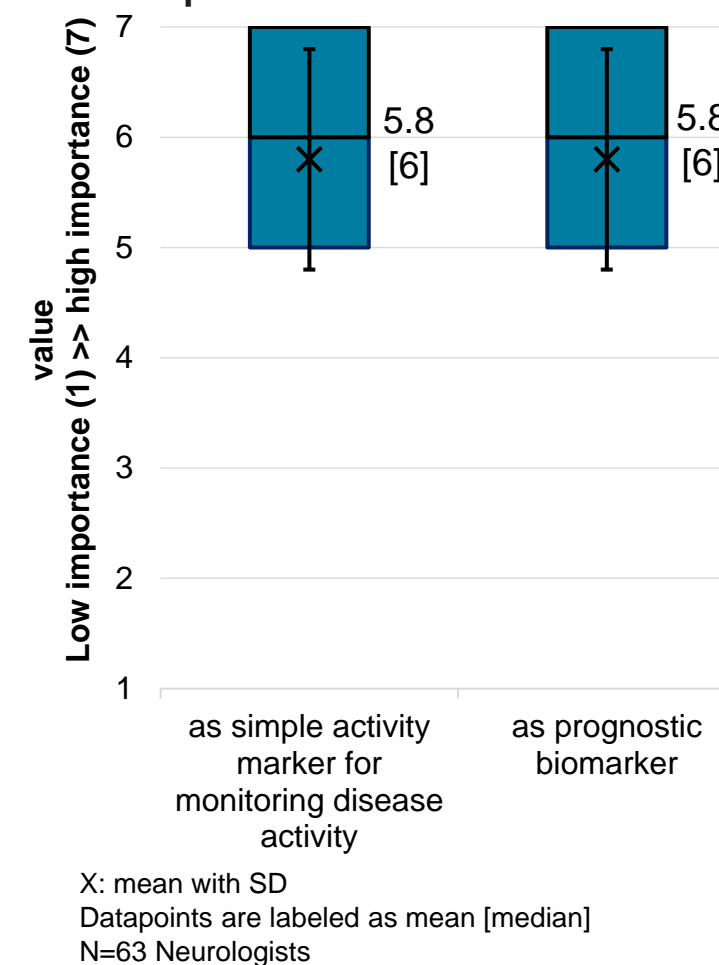


Figure 5: importance of an easily accessible biomarker for measuring disease activity for clinical practice



- Most neurologists would consider sNfL values in their decision to switch or modify the current MS therapy (79.7%) while 20.3% base their decision solely on other factors (Table 1).
- 56.5% of all neurologists think that sNfL levels can be used as a first hint for the need of treatment optimization. 6.8% of neurologists would base this decision on single sNfL levels and 16.4% of neurologists on a trend of increasing sNfL levels.
- 92.9% of neurologists expect that sNfL levels can be used to assess if a patient is stable on or responding to therapy (Table 2).

Disclosures

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- treating neurologists/physicians answer digital questionnaires regarding usability and benefits of sNfL measurements in everyday treatment per patient
- Mean values were calculated as mean of all evaluations for patients treated by the same neurologist.
- This first interim analysis includes 622 patients (at timepoint of program inclusion) for which up to 419 questionnaires were completed.
- Results of this interim analysis descriptively depict patient demographics including median age, gender and body-mass-index of the patient collective, as well as diagnosis and therapy decisions made by treating neurologists of those patients at the timepoint of program inclusion.
- Z-Score analysis was used to compare sNfL levels of the project population against a healthy, age-adjusted cohort.



Table 1. Perception of sNfL as a biomarker regarding therapy modification

Would you optimize MS treatment based on the sNfL level? n (%)	Total (N=410)
Yes	28 (6.8)
Yes, based on increasing sNfL levels over time	67 (16.4)
It gives me a first hint	231 (56.5)
No	83 (20.3)

Table 2. Perception of sNfL as a biomarker to assess therapy response

sNfL as a biomarker to assess treatment response, n (%)	Total (N=409)
Would sNfL help to assess if a patient is stable / responding to therapy?	
Yes	380 (92.9)
No	29 (7.1)

Future benefits, implementation and usage of routine sNfL testing

- Neurologists would use sNfL testing in daily clinical routine for multiple reasons (Figure 6). Most neurologists (90.7%) would use sNfL to complement traditional clinical measures in order to detect disease activity, followed by its use as an additional prognostic factor.
- Neurologists would measure sNfL levels at various timepoints in the patient journey (Figure 7) with a frequency of around two to four times per year (Figure 9).
- To implement sNfL testing into daily clinical routine, most neurologists would like to have more evidence of benefits and a recommendation from clinical guidelines (each 66.3%) or from professional society and MS competence network (59.7%) as well as more own experience with sNfL testing (54.8%) (Figure 8).
- If a licensed sNfL test was available and a certain sNfL level was exceeded, 75.6% of neurologists would immediately act on this result and advise further disease activity assessments like MRI (Figure 10).

Figure 6: Usage of sNfL in daily clinical routine

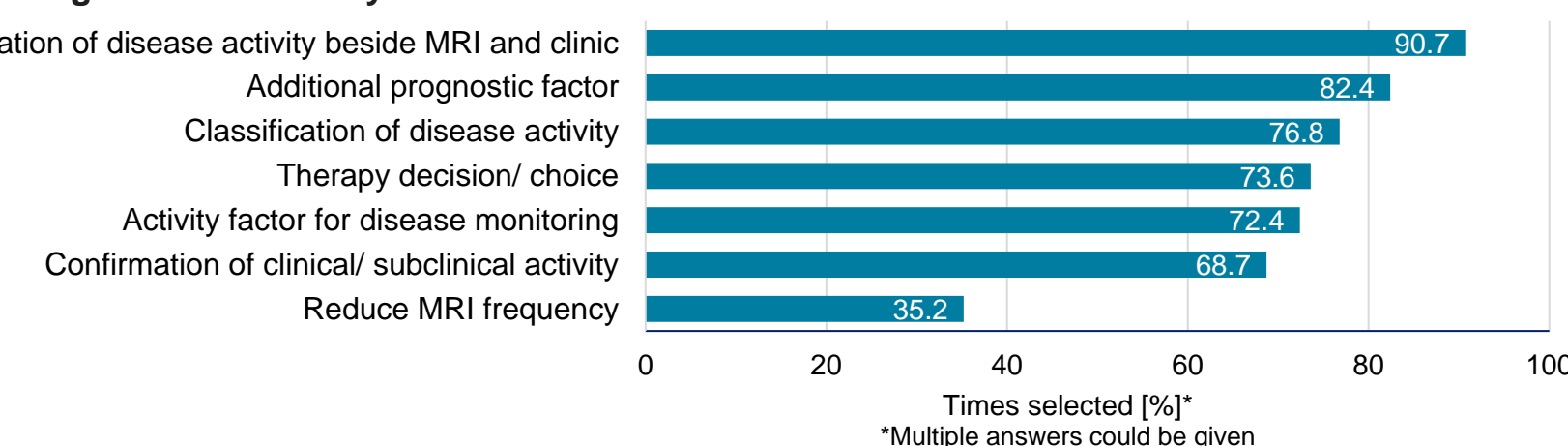


Figure 7: Timepoint of sNfL testing

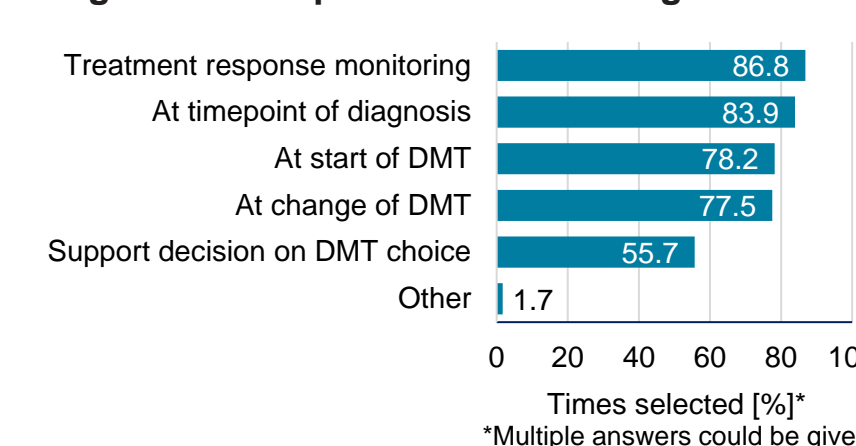


Figure 8: Conditions for implementation in daily routine

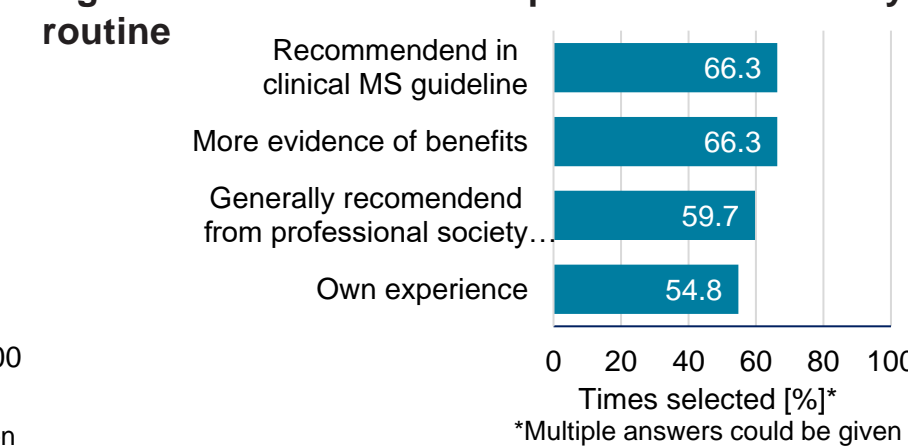


Figure 9: Frequency of sNfL testing

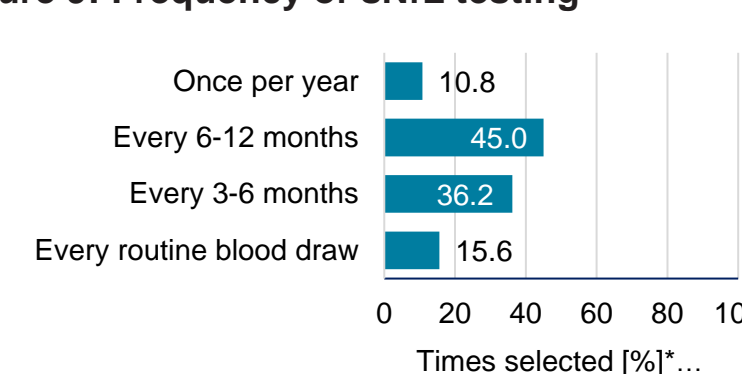
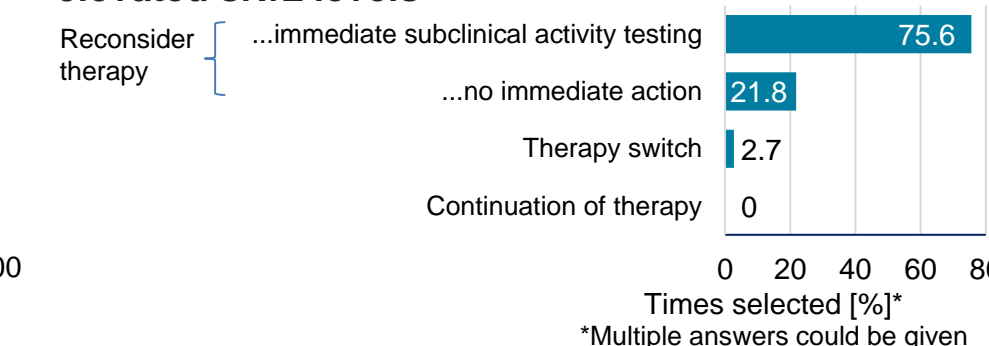


Figure 10: Consequences in daily routine after elevated sNfL levels



References

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