

Delaying Intracranial Progression in NSCLC Brain Metastases: Clinical and Patient-Centered Value

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Background

- Brain metastases in NSCLC carry a heavy clinical, humanistic, and economic burden.
- Trials of brain-directed therapies often use intracranial progression (ICP) as a clinical endpoint.
- OS and PFS may not capture the full value of delaying ICP.
- The non-survival value of delaying ICP has not been systematically characterized.

Methods

- Design.** Issues panel with 19 experts, 8 from the United States, 4 from France, 4 from Japan, and 3 from Germany, including radiation oncologists, medical oncologists, and neurosurgeons.
- Pre-meeting inputs.** Targeted literature review and structured questionnaire, completed by all 19 panelists, 31 March 2026.
- Panel meeting.** Three-hour moderated virtual discussion, 7 April 2026, 17 attending, using nominal group technique.
- Domains.** Clinical, humanistic, and economic.
- Analysis.** Transcript review and thematic synthesis, informing ongoing Delphi statement development.

Results

Clinical domain

- ICP delay was clinically meaningful even without an OS benefit.
- Neurological function was the top-ranked endpoint at 58 percent, versus 26 percent for OS (**Figure 1**).
- Leading benefits of a 10.6-month delay were preserved neurological function (84 percent) and cognition (63 percent) (**Figure 2**).
- ICP is measured inconsistently across centers, and brain metastasis velocity is applied intuitively.
- Progression in eloquent regions carries greater clinical weight and drives therapy and imaging escalation.

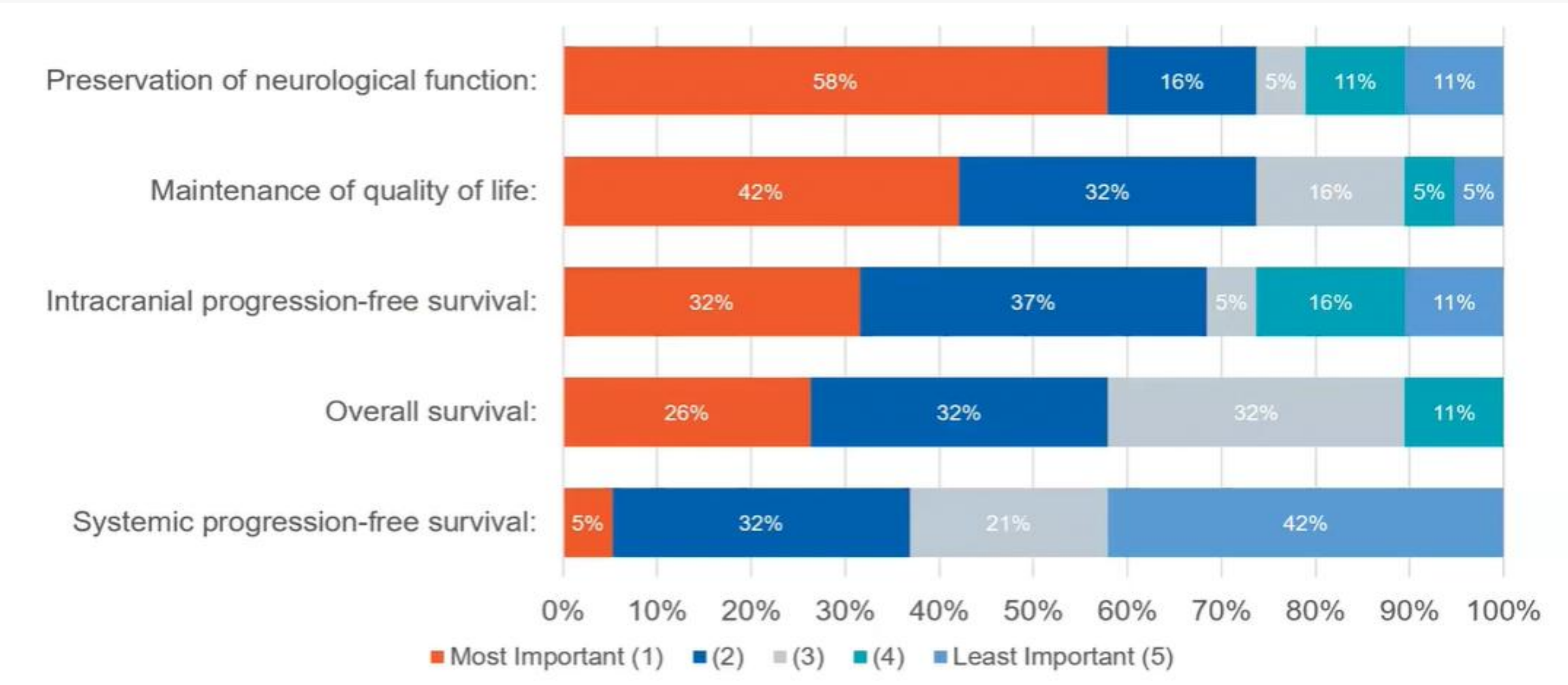


Figure 1. Ranking of endpoints in clinical practice, NSCLC with brain metastases. n = 19

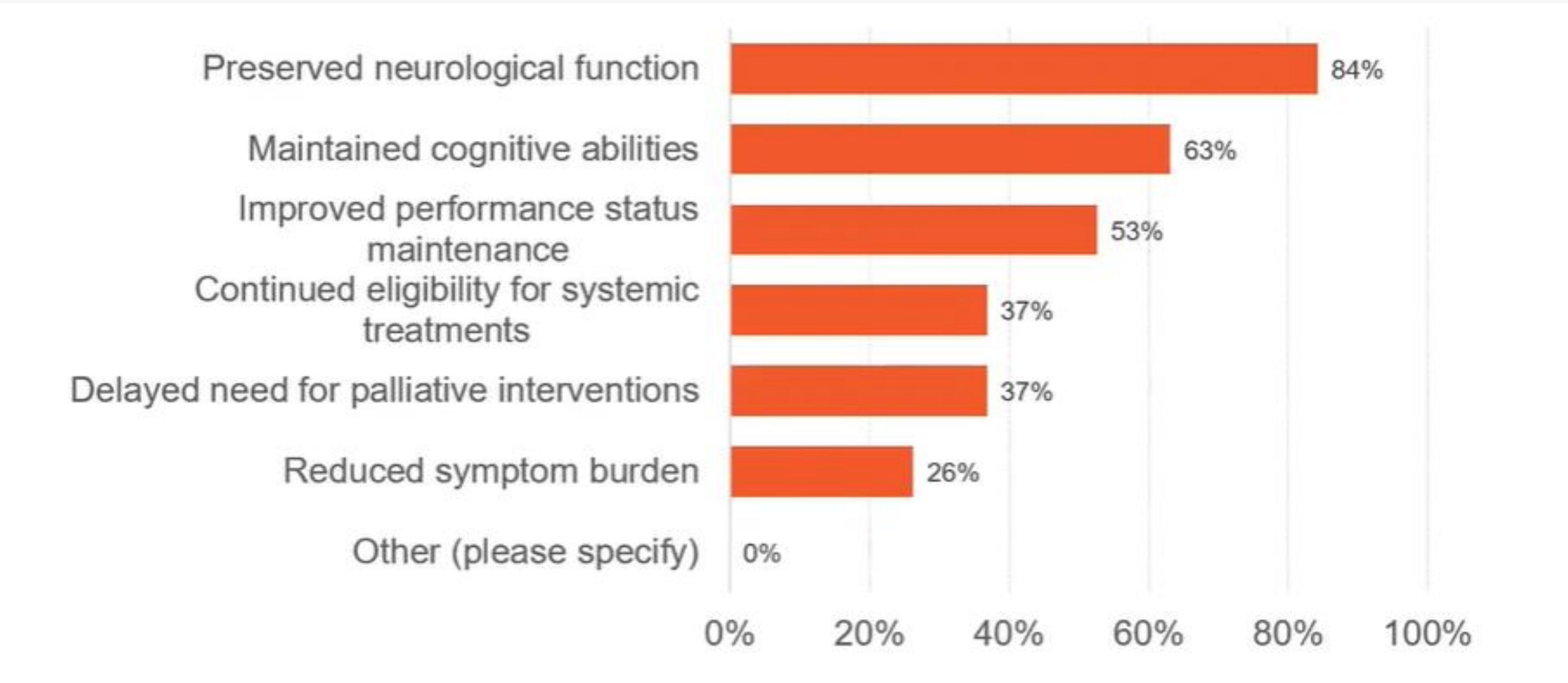


Figure 2. Clinical benefits of a 10.6-month ICP delay, percentage placing each in the top three. n = 19.

Objectives

- To assess the clinical and humanistic value of delaying ICP in patients with brain metastases from NSCLC, focusing on impacts on cognition, independence, and functional outcomes beyond survival.

Results

Humanistic domain

- Care is palliative in intent, with function preservation as the primary goal.
- Cognition was the QoL domain most affected at 95 percent, then independence at 79 percent (**Figure 3**).
- Scan-related anxiety was among the most significant humanistic burdens.
- ICP-related seizures trigger legally mandated driving bans in France, Germany, and Japan, heavily impacting independence.
- Cognition, functional status, psychological burden, and caregiver impact are rarely measured in routine practice.

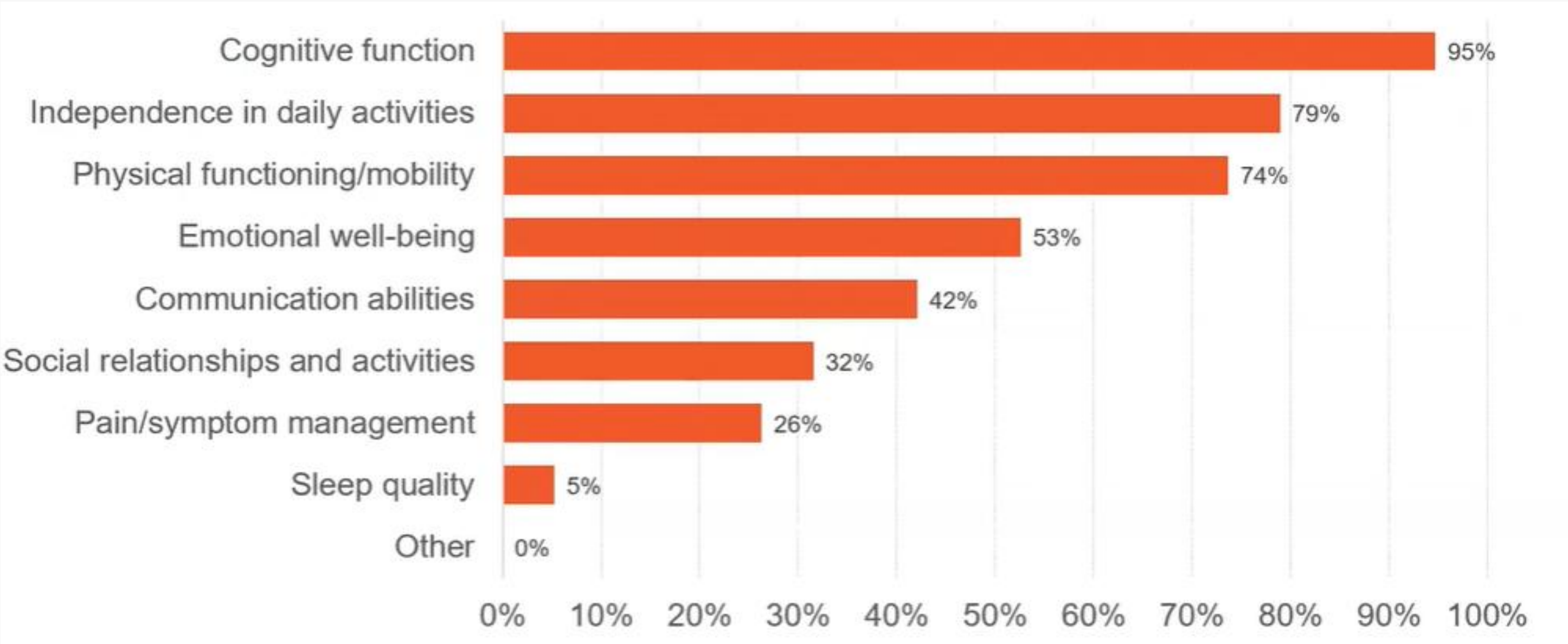


Figure 3. QoL domains most affected by ICP, up to four selections. n = 19.

Economic domain

- Delayed need for radiation interventions (84 percent) and fewer hospitalizations (47 percent) led utilization effects (**Figure 4**).
- Only 5 percent expected minimal impact on resource utilization.
- Survival-anchored metrics undervalue ICP delay, since brain-directed trials rarely show an OS benefit.

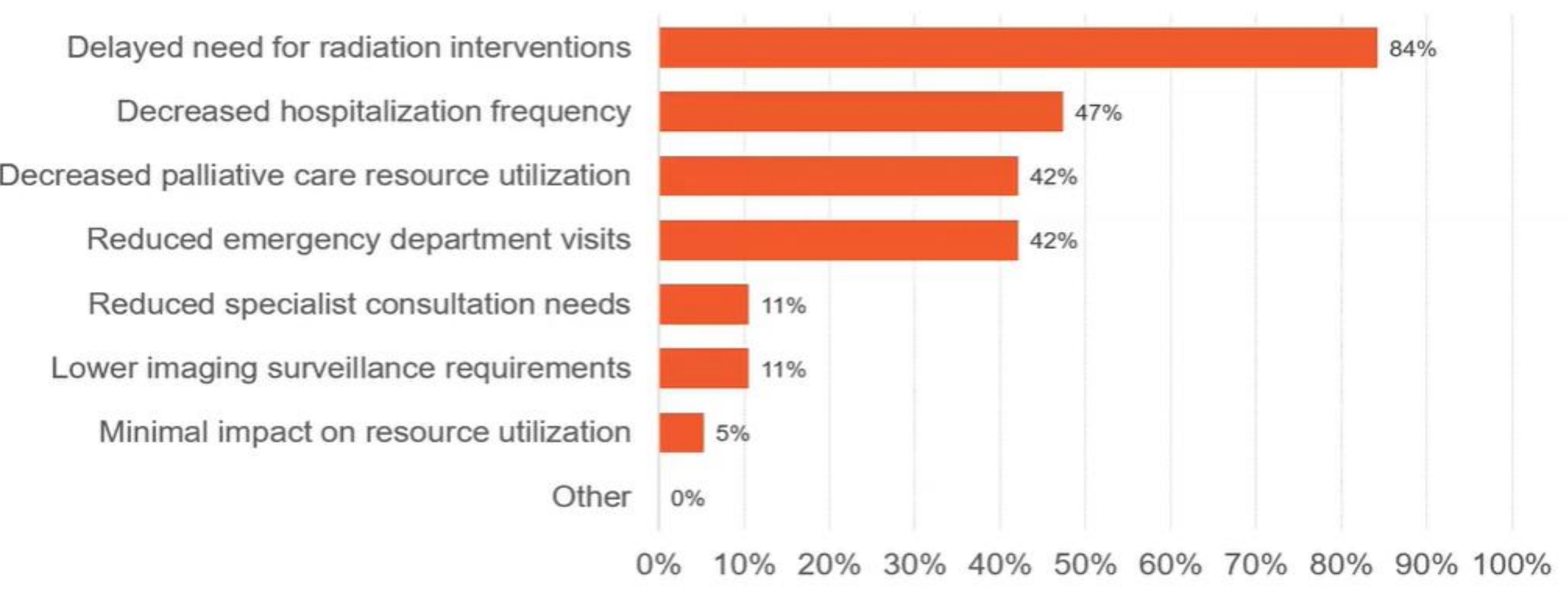


Figure 4. Impact of delaying ICP on healthcare resource utilization, up to four selections. n = 19.

Limitations

- Qualitative consensus study, not designed for statistical inference.
- Panel of 19, weighted toward radiation oncology and four countries, so each respondent represents about 5 percentage points.
- Findings reflect stated rather than observed practice.

Conclusion

- Delaying ICP preserves function, independence, and cognition, independent of survival benefit.
- The outcomes experts value most are the least measured, a measurement gap rather than a value gap.