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Implementation of Low-Intensity Thrombolysis Monitoring Care in Routine Practice: Process Evaluation of the Optimal Post rtPA-IV Monitoring in Acute Ischemic Stroke Study in the USA

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Abstract
Introduction: The ongoing OPTIMISTmain study, an international, multicenter, stepped-wedge cluster randomized trial, aims to determine effectiveness and safety of low-intensity versus standard monitoring in thrombolysis-treated patients with mild-to-moderate acute ischemic stroke (AIS). An embedded process evaluation explored integration and impact of the intervention on care processes at participating US sites. ***Methods:*** A mixed-methods approach with quantitative and qualitative data was collected between September 2021 and November 2022. Implementer surveys were undertaken at pre- and post-intervention phases to understand the perceptions of low-intensity monitoring strategy. A sample of stroke care nurses were invited to participate in semi-structured interviews at an early stage of post-intervention. Qualitative data were analyzed deductively using the normalization process theory; quantitative data were tabulated. ***Results:*** Interviews with 21 nurses at 8 hospitals have shown low-intensity monitoring was well accepted as there were less time constraints and reduced workload for each patient. There were initial safety concerns over missing deteriorating patients and difficulties in changing established routines. Proper training, education, and communication, and changing the habits and culture of care, were key elements to successfully adopting the new monitoring care into routine practice. Similar results were found in the post-intervention survey (42 nurses from 13 hospitals). Nurses reported time being freed up to provide patient education (56%), daily living care (50%), early mobilization (26%), mood/cognition assessment (44%), and other aspects (i.e., communication, family support). ***Conclusions:*** Low-intensity monitoring for patients with mild-to-moderate AIS, facilitated by appropriate education and organizational support, appears feasible and acceptable at US hospitals.

Introduction

Intravenous thrombolysis (IVT) using recombinant tissue plasminogen activator (rtPA) or alteplase, and more recently with tenecteplase, is an effective reperfusion treatment for acute ischemic stroke (AIS) [1], but treated patients are at risk of neurological deterioration and the most serious complication symptomatic intracranial hemorrhage (sICH). Guidelines therefore recommend close monitoring of vital signs with a neurological function assessment every 15 min for the first 2 h, every 30 min for the next 6 h, and then every hour until 24 h [2, 3], in an intensive care unit or other high dependency setting (i.e., a unit where patients can be cared more extensively than on a normal ward but less than in intensive care unit). The standard monitoring guideline was developed by the National Institute of Neurological Disorders and Stroke (NINDS) rt-PA Stroke Study Group [4] and subsequently utilized for decades due to safety concerns over sICH risks. However, the incidence of sICH is low (2.5%) in AIS patients with mild to moderate neurological deficits (i.e., National Institute of Health Stroke Scale [NIHSS] scores <10) [5], and most sICH occurs within 12 h after IVT [6]. A single-center, open-label, single-arm, Optimal Post rtPA-IV Monitoring in Ischemic Stroke Trial (OPTIMIST, NCT02039375) suggests clinically stable AIS patients with mild-to-moderate deficits do not need intensive post-IVT care [7].

OPTIMISTmain (NCT03734640) is an international, multicenter, stepped-wedge cluster randomized trial to determine effectiveness and safety of less-intensive versus standard high-intensity monitoring in thrombolysis-treated patients with mild-to-moderate AIS at 120 hospitals in both middle-high income (Mexico, Malaysia, China, Vietnam) and high-income (USA, Australia, UK, Chile) countries [8]. Eligible patients are adults (age ≥18 years) who receive IVT for AIS according to guideline criteria, have mild-to-moderate neurological impairment (NIHSS <10), and are clinically stable at 2 h post-IVT infusion, who can be managed in an appropriate monitoring ward. Patients are allocated to either low-intensity monitoring (intervention) or standard monitoring (control) according to the guideline recommendations [2]. The low-intensity monitoring involves vital signs (heart rate and blood pressure) and neurological function (Glasgow Coma Scale [GCS] and/or NIHSS, whatever is the most appropriate according to local protocols) every 15 min for 2 h, every 2 h for the following 8 h, and then every 4 h until the first 24 h, post-IVT.

In addition to determining the effectiveness of less-intensive monitoring, it is important to understand what is required to produce replicable outcomes in the context of daily practice. Process evaluations (PEs) of recent complex interventions in stroke management have highlighted significant system barriers that contribute to suboptimal implementation and variation in the observed effect of interventions [9, 10]. PEs can examine the perspectives of nurses on the intervention, explain discrepancies between expected and observed outcomes, provide a deeper

understanding of how contextual determinants (e.g., workforce, health infrastructure) influences outcomes, and provide insights to aid implementation [11, 12].

The OPTIMISTmain trial was initiated as a start-up (vanguard) phase at 20 US sites in 2021 to inform feasibility of the intervention being embedded in routine practice before a broader roll out across non-US sites as additional grant funding became available. A PE alongside the trial aims to better understand of adoption and integration of low-intensity monitoring into routine practice and how it impacts on patient care and to inform ongoing implementation.

Methods

Theoretical Framework

Normalization process theory (NPT) was used to develop the interview guide to evaluate adoption and integration of the low-intensity monitoring into routine healthcare practice in the OPTIMISTmain trial [13]. Adoption is defined as the intention, initial decision, or action to try or employ an innovation or evidence-based practice, and integration is defined as the incorporation of a practice within a service setting and its subsystems [14]. Components of NPT to evaluate include coherence (meaning and sense-making by participants); cognitive participation (commitment and engagement); collective action (the work participants do to make trial function); and reflexive monitoring (participants reflect on or appraise the trial) [13]. NPT provides a deeper appreciation of implementation as a dynamic process, to identify and explain the fundamental mechanisms that promote or impede implementation, and how a complex intervention can be embedded into everyday practice [13, 15].

Sample, Participants, and Settings

Purposive sampling was used to select representative sites for semi-structured interviews [16]. Based upon prespecified criteria to achieve representativeness, interviews were stratified by geographical location, hospital type, department (e.g., acute stroke unit, high dependent unit, neurological department), and rate of recruitment (actual enrollment number divided by expected weekly enrollment) using routine monitoring chart and data entry quality assessed for operation report (online suppl. Table S1; for all online suppl. material, see https://doi.org/10.1159/000538136). Twelve sites were invited to participate during the early intervention phase, and at least 3 intervention implementers (e.g., nurse managers, bedside nurses) at each sampled site were invited to obtain information from the perspective of different roles. All the participating sites received training on the OPTIMISTmain protocol provided by the central coordinating center and ongoing remote monitoring. The nominated "local champion" from the designated research team at each site was responsible for promoting the study at the hospital; he/she was required to provide refresher training for staff on the intervention at regular intervals. An anonymous survey was collected online to understand the concepts and integration of low-intensity monitoring in the pre- and post-transfer phases from usual care (control) to implementation (intervention) in the 20 participating sites. The survey participants included overseeing nursing managers and bedside nurses who delivered the low-intensity monitoring.

Data Sources and Collection

Both quantitative and qualitative data were collected (Fig. 1). Pre- and post-intervention implementer survey was collected between September 1, 2021, and November 21, 2022. Semi-structured interviews were conducted by two trained researchers (MM and AP) between October 27, 2021, and August 12, 2022, with audio recordings collected and transcribed for analysis. Interview guide questions were informed by the NPT components. During the process of conducting the interviews, questions were iteratively modified to allow the exploration of emergent themes identified by the research team. All interviews were conducted online via telephone due to restricted health services access during the COVID-19 pandemic. Other trial data sources, including monthly reports on recruitment speed and a hospital organization questionnaire, were used to capture contexts of sampled hospitals, particularly the impact of COVID-19 at the intervention phase.

Ethical Approval and Participant Consent

Ethical approvals were obtained at each participating site. An information sheet and consent form were provided to each participant prior to an interview, when verbal consent was obtained. All the interviews were audio-recorded and transcribed and de-identifiable data were analyzed.

Data Analysis and Reporting

Quantitative data were analyzed using descriptive statistics and reported in numbers (N) and percentages (%). Qualitative data were analyzed independently by 2 researchers (MO and FG) trained in qualitative methods to ensure credibility of the findings. An initial thematic codebook was developed inductively and deductively from the first three sites (five interviews) to examine the key variations of context, intervention acceptability, adoption, fidelity, and implementation and integration into routine care at each site. Themes emerging from the qualitative data were discussed and refined by the PE team at regular intervals to ensure the data were of high quality. Thematic saturation was achieved after 21 interviews (from 8 sites), with no new codes being created and agreement reached. Preliminary findings were discussed with the research team regarding analysis using the NPT components and interpretation about the implications of findings. Nvivo 11.0 was used to manage the qualitative data [17]. Standards for reporting qualitative research (SROQ) checklist was used for reporting of the analysis (online suppl. Material 1) [18] and implementation outcomes were aligned to the "six practical recommendations for improved implementation outcomes reporting" (online suppl. Material 2) [19]. Joint display technique, a helpful approach to visualize data integration to enhance insights into the findings in mixed-method research [20, 21], was used to display integrated findings through a merging of percentages obtained from the quality survey and themes from qualitative data.

Results

The characteristics of the 8 hospitals which participated in the interviews are shown in online supplementary Table S1. The recruitment speed of these

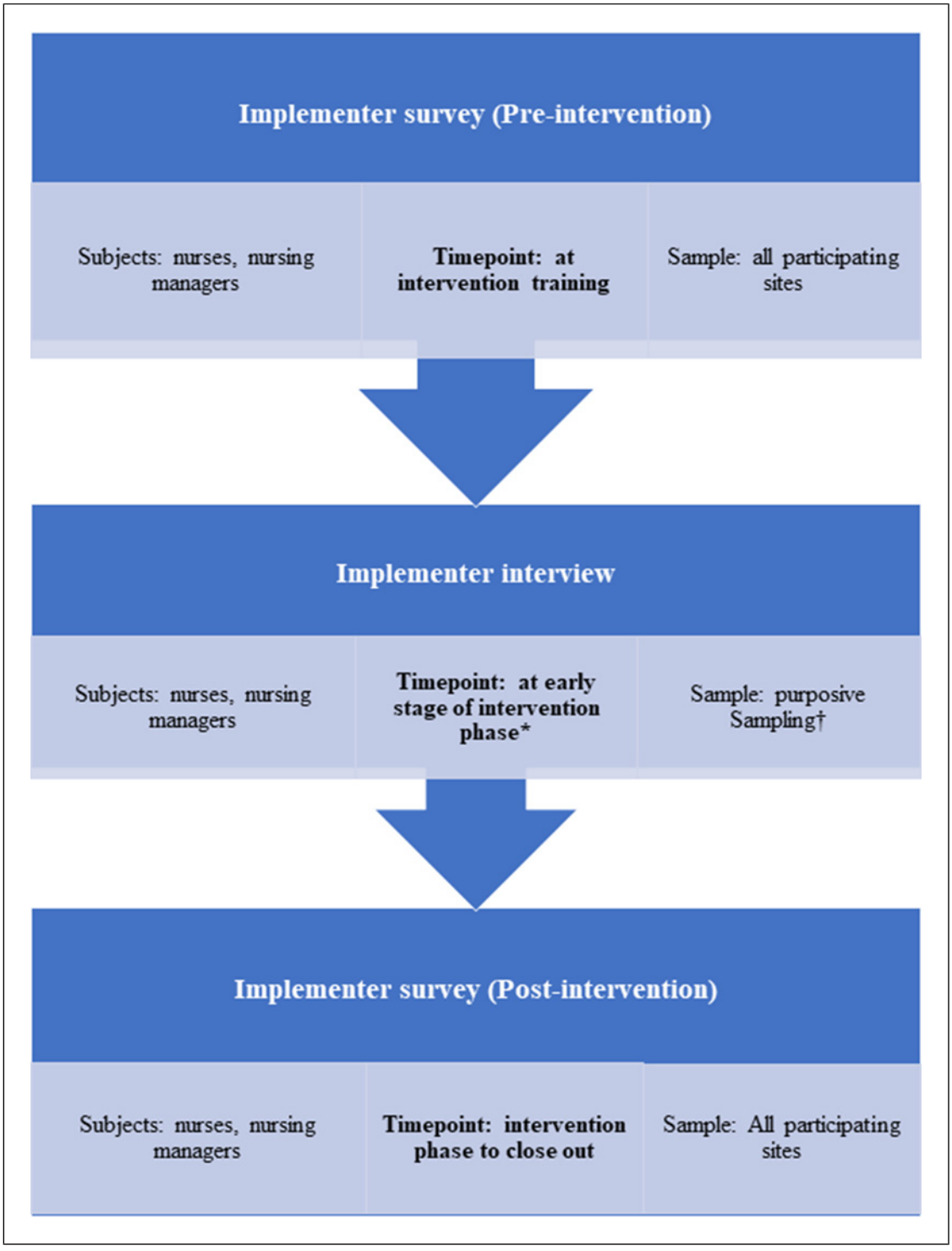

Fig. 1. Diagram of data collection for the PE at US sites. *At the time point of 5–10 patients enrolled in the intervention phase (2–3 patients if the total number of patients is small at the site). †Purposive sampling criteria include country, region, department (ASU vs. high dependency unit), recruitment speed.

Table 1. Core constructs of NPT and codes identified

NPT components	Themes
Coherence (i.e., meaning and sense-making by participant)	• Accepted by nurses with recognition of benefits to patients • No safety concerns because knowing patients is at lower bleeding risk • Easier to deliver due to reduced workload and less time constraint • Fear to miss safety issues with reduced frequency of monitoring at beginning
Cognitive participation (i.e., commitment and engagement by participant)	• Cost-efficient and improved the flexibility in work assignment • Push back or negative feedback from floated nurses impede the participation • Lack of neurologist team to assess the eligible patients
Collective action (i.e., work done to make the intervention happen)	• Additional training or guidance are necessary at crossover to change workflow • Develop tracking documents, paperwork template, and labelling to remind low-intensive care, champion sites to share experience and worksheet • Staffing shortage, nursing travelers, and new staffs lack of communication and delayed process affected the delivery of low-intense monitoring
Reflexive monitoring (i.e., participants reflect on the intervention)	• Difficult to change habit/behavior to adjust the low-intense care in the beginning • Sufficient staffing resources, adapt changes in the hospital, and stroke responses system to scale up • Solid less-intense care protocol in guideline recommendations

NPT, normalization process theory.

hospitals varied from 0 to 7 participants per month, and the nurse-to-patient ratios ranged from 1:2 to 1:6 in the units. There were 5/8 of the hospitals with a moderate impact of COVID-19 on the delivery of their stroke service in the intervention phase; two of them had a change of nurse-to-patient ratio with more patients assigned. Regarding the implementer survey, there were a total of 60 responses (18 pre-intervention and 42 post-intervention). These participants had a mean 6.4 years of nursing experience in stroke, and most were study coordinators or ward managers in comprehensives stroke care or neurocritical care units at hospitals (online suppl. Material 3).

Table 1 summarizes adoption and integration of the less-intensity monitoring as analyzed by NPT components and elaborated upon below. The core themes and corresponding quotes analyzed by NPT are listed in online supplementary Table S2.

Coherence and Cognitive Participation

The low-intensity monitoring was well accepted by the nurses who recognized the benefits of less disruption to a patient's sleep and ease of its delivery compared to usual standard monitoring. The low-intensity monitoring reduced their workload, improved flexibility in their work assignment, and motivated their continual engagement in the trial. While nurses acknowledged their initial fear of missing an important safety issue in patients, this was only at the beginning of implementation of low-intense monitoring. They subsequently reported reduced concerns over sICH as they observed that eligible patients remained stable. Results of the survey conducted after staff had transferred to the intervention phase indicated a high degree of agreement that low-intensity monitoring could become a normal routine at the hospital (median 9 [IQR: 8–10]; online suppl. Material 3). Most of the respondents agreed, both before (83%) and after (81%) transfer to intervention (online suppl. Fig. S1). This was particularly relevant for bedside nurses who delivered the intervention; they were more likely to strongly agree that less-intense monitoring care is worthwhile (44.4% vs. 29.2%) and that it can be easily integrated into existing work patterns (55.6% vs. 29.2%), as compared to the responses of overseeing/managing nurses (online suppl. Fig. S2).

Collective Action and Reflexive Monitoring

Nursing staff shortage (due to strikes and the COVID pandemic), staff turnover, and the need for "travel nurses" (registered nurses who work in short-term

Table 2. Recommendations and actions to improve implementation of low-intensity monitoring in workflow

Levels	Recommendations/suggestions	Actions
Individual	• Constant training to enhance understanding and familiarity of the low-intensity monitoring • Improve knowledge to respond and identify patients with risk of neurological deterioration • Effective communication between staff (e.g., eligibility assessors, i.e., neurologists) and care implementer (i.e., bedside nurses) to facilitate implementation • Proper handover of patients labelled in the low-intensity group to ensure continuity of the monitoring care	Project team to the following: - Provide additional training of the low-intensity monitoring before crossover - Provide template of adjusted charts or documents that enhance the delivery and record of low-intensity monitoring
Organizational	• Ensure staffing resources to assess eligible patients and deliver low-intensity monitoring • Establish stroke responses code to patients at risk of neurological deterioration • Adapt screening to identify eligible patients in the workflow • Adjust documents/charts to guide delivery of low-intensity monitoring	Site investigators to the following: - Develop labelling material/signal to distinguish eligible patients for low-intensity monitoring - Constant training on the study rationale and low-intensity monitoring strategy - Establish protocol/responses to patients at risk of neurological deterioration - Ensure sufficient workforce and staffing resources

positions at hospitals) introduced inconsistency in delivery of the low-intensity monitoring care in hospitals. Other barriers to implementation mainly related to staff resourcing in neurology specialists, such as the lack of a designated neurologist team to assess and identify eligible patients for trial recruitment. Nurses reflected that it was initially difficult to change their processes, especially at the initial crossover phase, but not through the whole process. Table 2 summarizes the recommendations and actions to optimize implementation, including in-place tracking and flow sheets from the trial office, having champion sites share their experience, and that additional training helped them transition smoothly to low-intensity monitoring. Regarding generalizability, sufficient staffing, appropriate stroke responses system with 24/7 coverage, and a well-defined low-intensity monitoring protocol in a guideline would facilitate wider implementation. From the survey, the number of respondents who agreed that the new monitoring schedule should be widely used across the country increased post-implementation (72.2–78.6%, online suppl. Fig. S1).

Flow-On Activities from Low-Intensity Monitoring

Nurses reported flow-on activities of care provided due to the spare time that was saved by low-intensity monitoring (online suppl. Fig. S3). The reduced frequency of monitoring compensated for staffing shortages and freed up bedside nurses to cover other units/wards and other aspects of patient care: better patient education (reported in 64.3%), followed by care of continence and other daily activities (52.4%), patient mood or cognition care/assessment (47.6%), and assistance with early rehabilitation (28.6%). Improved input into other activities included family support, as well as more frequent assessment and engagement with patients. There was only one respondent who reported no spare time for other aspects of care due to a change in the nurse-to-patient ratio (1:2 to 1:3). There were 88.1% of the participants at the post-intervention phase who agreed the low-intensity monitoring affects the nature of work (online suppl. Material 2), and the aspects to be affected were mainly in workflow in patient care (84.2%) and work assignment and collaboration with colleagues (70.3%). However, the nurses who delivered the intervention were less likely to agree that communication with patients had been affected by low-intensity monitoring, compared to responses from the overseeing/managing nurses (33.3% vs. 63.6%; online suppl. Material 4).

Discussion

This PE of US hospital staff indicates that low-intensity monitoring strategy for post-thrombolysis patients with mild-to-moderate AIS is feasible and well accepted in clinical practice. Nurses perceived it to be easier to undertake compared with standard monitoring as less time was required for both action and documentation, and it allowed them to better engage in activities such as early

mobilization and education, and the needs of all patients. Key elements to wider adaption of this new monitoring care in routine practice include appropriate training, education, and communication to successfully change behaviors and systems at an early phase of implementation.

Nurses reported difficulties in changing habits and incorporating new processes in their routine care, albeit this was mainly in the early phase of transferring to the intervention. Behavioral change is a crucial barrier to translating evidence into practice due to limited understanding of evidence-based care, time constraints, and lack of support from colleagues or leaders [22, 23]. A theory-led systematic review suggests that successful behavior change requires normative and relational restructuring as that people can work together to implement an intervention and legitimate new practice norms through experience [24]. Thus, staff should fully understand the rationale for low-intensity monitoring, and have organizational support for ongoing learning and adaptation, which corresponds nicely with NPT domains.

We found several contextual factors at the organizational level, such as the presence of new staff during shifts and "travel nurses, that impeded effective implementation due to unfamiliarity with the low-intensity monitoring protocol. The COVD-19 pandemic impacted on health systems in unprecedented ways, causing shortage of staffing, supplies, and space. In the USA, many hospitals reported critical staffing shortages during 2020–2021 [25], leading to redeployment of allied healthcare workers into other practice settings and greater use of "travel nurses" compared to previous years [26]. A particular concern over the use of "travel nurses" during the pandemic was the negative impact on the morale of incumbent staff nurses due to differing payment structures and the requirement for extra work in training them in systems and technology, which contributed to feelings of overwork and under-appreciation [27]. Organizational support for nurses to implement practice change should therefore not just be to improve the workforce but also to foster the health and wellbeing of staff.

Current standard post-IVT care involves high frequent monitoring, which interrupts the sleep/rest of patients in the first 24 h. Sleep is important for recovery from stroke, as in other critical illnesses. Studies have shown that short sleep cycles, waking early, and the perception of poorer sleep quality are all associated with worse recovery, while uninterrupted sleep improves cognition and mood [28, 29]. In our study, nurses reported the low-intensity monitoring resulted in their patients being more rested and cooperative. However, as these findings were only of nursing observations, more insights at the patient level are required to provide a more rigorous assessment of the impact of low-intensity monitoring on sleep and its impact on recovery, which are secondary outcomes in this ongoing trial.

Reflections and Implications

Conduct of this trial is now at the close out stage in the USA, but several sites have indicated that they wish to continue low-intensity monitoring as a standard of care. We have identified common obstacles related to the organization of care processes, resources, and leadership that need to be addressed to ensure successful implementation of this new process of care. This will guide widespread adoption of low-intensity monitoring into clinical practice if this approach shows effectiveness and safety from the main trial results.

We recommend that nurses conduct NIHSS assessments together when handing over patients, so there is seamless transfer of care for patients at perceived high risk of sICH. Use of a modified NIHSS card may facilitate observations and assessments [30]. Moreover, as our study involves hospitals in multiple countries, ongoing implementation requires significant ongoing efforts to address local contextual and cultural issues in the health system [31]. The issues and corrective actions identified in this study have been critical in facilitating successful roll out of the trial across other countries where periodic and constant training has been required. Actions taken to reduce the misdiagnosis of eligible patients for thrombolysis treatment, which ranges from 14.0% to 22% [32], could also improve the uptake of the low-intensity monitoring.

Strengths and Limitations

This study used a mixed-methods approach to explore implementation of a new care strategy in the vanguard phase of a major clinical trial. Identifying and addressing challenges at an early stage strengthened our ability to efficiently implement low-intensity monitoring in the main phase as well as enabling post-trial scale up of the intervention at a national level. We acknowledge limitations from the anonymous approach to survey collection, and that before and after comparisons were undertaken on different participants, and that more responses were obtained from managing or overseeing nurses, particularly at pre-intervention. Despite our efforts at purposive sampling, most of the participating

hospitals were urban and included staff with capacity and interest in clinical research. As the sample was not perfectly balanced for level of hospitals, we may have missed insights from regional and semi-urban locations, which we will endeavor to obtain in subsequent PE interviews alongside the main trial.

In summary, post-IVT low-intensity monitoring for AIS is feasible and acceptable to US healthcare professionals. Compared to the standard high-intensity monitoring care, it is perceived to be easier to deliver and beneficial to patients and services. To ensure successful implementation and address obstacles, a comprehensive approach is required to address barriers at professional setting, clinical teamwork, resources, leadership, and organizational level.

Statement of Ethics

This study protocol was reviewed and approved by Sydney Local Health District (Royal Prince Alfred Hospital) Ethics Review Board (Approval Reference Number X20-0014). This full list of participating site and Ethics Committees can be found at https://karger.com/ced/article/doi/10.1159/000534706/868453/The-main-Optimal-Post-rTpa-Iv-Monitoring-in. A variable, mixed written informed consent process is used, according to local/national rules and regulations: (1) cluster guardian consent or appropriate approval (e.g., signed by the General Manager or Chief Executive of the hospital) for patients to receive the low-intensity monitoring to be implemented for eligible patients in the stroke unit, intensive care unit, or neurology/neurosurgery wards and (2) use of individual standard consent for the collection of data through in-person assessment and data extraction from medical records during the hospital stay and routine follow-up. Written informed consent was obtained for participation in this study.

Conflict of Interest Statement

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Author Contributions

H.L. and M.O. designed the process evaluation of the OPTIMISTmain trial. M.O. wrote the first draft of the manuscript, with input from F.G., H.L., and C.S.A. M.M. and A.P. contributed to the data collection with support from B.J., P.K., D.V.S., M.I., and V.C.U. M.O. and F.G. analyzed the data. S.J., X.W., B.J., D.V.S., P.K., R.F., P.M.V., D.D., T.R., R.I.L., and C.D. provided comments on study design and the first draft of the manuscript. A.M., M.I., F.U.G., A.C.D., A.E., L.S., Y.S., and W.A.W.Z. were responsible for trial data collection and quality control procedures. All authors reviewed and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its supplementary material files. Further inquiries can be directed to the corresponding author.

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