

Recommendations for Implementing the INTERACT3 Care Bundle for Intracerebral Hemorrhage in Latin America: Results of a Delphi Method

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Keywords

Implementation science · Intracerebral hemorrhage · Care bundle · Stroke · Latin America

Abstract

Introduction: The third Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial (INTERACT3) showed that the implementation of a care bundle improves outcomes after acute intracerebral hemorrhage (ICH). We aimed to establish consensus-based recommendations for the broader integration of the care bundle across Latin American countries (LAC). **Methods:** A 3-phase Delphi study allowed a panel of 32

healthcare workers from 14 LAC to sequentially rank statements relevant to 7 domains (training, resources/infrastructure, patient education, blood pressure, temperature, glycemic control, and anticoagulation reversal). The pre-defined consensus threshold was 75%. **Results:** A total of 43 statements reached consensus by the third round, with 12 new statements emerging through rounds. The highest-ranked statements in each domain emphasized critical aspects, but successful implementation requires appropriate resourcing. Key priorities were con-

Names of the LATAM INTERACT3 Consensus Statement Panel are listed in the supplementary material (for all online suppl. material, see <https://doi.org/10.1159/000540038>).

tinuous training of all healthcare workers in ICH management, establishing protocols aligned with available resources, and collaborative interdisciplinary care supported by institutional networks. Statements related to anticoagulation reversal had the highest priority.

Conclusions: Consensus statements are provided to facilitate integration of the INTERACT3 care bundle to reduce disparities in ICH outcomes in LAC.

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Introduction

Intracerebral hemorrhage (ICH) is less frequent but has a higher loss of productive life than ischemic stroke [1, 2]. The third Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial (INTERACT3) used an international stepped-wedge cluster-randomized design to show that the re-configuration of hospital services to implement a care bundle involving early intensive blood pressure (BP) lowering (systolic BP <140 mm Hg), glycemic control (6.1–7.8 mmol/L and 7.8–10.0 mmol/L without and with diabetes mellitus, respectively), treatment of pyrexia (temperature level $\leq 37.5^{\circ}\text{C}$), and reversal of anticoagulation (international normalized ratio [INR] <1.5) improves outcomes from acute ICH [3].

Latin American countries (LAC) have a high burden of stroke [4] and unique challenges in implementing evidence-based strategies, fragmented healthcare systems, social disparities, and diversity in culture and health literacy [5, 6]. Although the INTERACT3 process evaluation captured some implementation barriers, we wished to consolidate such information by generating strategies specific to LAC. Herein, we report our efforts to establish recommendations to implementing the INTERACT3 care bundle in LAC.

Methods

We performed a 3-phase online Delphi study, following the Recommendations for the Conducting and Reporting of Delphi Studies (CREDES), as outlined in detail in the online supplementary material [7]. In brief, the first draft followed a comprehensive review of the INTERACT3 process evaluation among participating sites in LAC (unpublished data) to produce 43 statements categorized into 7 domains which outline the four primary interventions plus domains frequently mentioned in the process evaluation: (i) training and education; (ii) human resources and infrastructure; (iii) early intensive BP control; (iv) strict glucose control; (v) body temperature control;

(vi) rapid reversal of anticoagulation; and (vii) education for patients and family members. Participants for our study were recruited from 14 LAC according to the following criteria: healthcare professionals with ≥ 5 -years postgraduation, ≥ 1 -year work experience in a public health facility; and active involvement in the care of ICH patients. People working in a facility without computerized tomography or an emergency area were excluded.

In the first round, panelists rated each statement according to their level of agreement on a 4-point Likert scale (strongly agree [SA], agree, disagree, and strongly disagree); an open-box section allowed for comments. Pre-defined consensus threshold was set at 75% agreement (SA or agree) to retain a statement [8, 9]; statements below this threshold were modified according to feedback.

In the second round (R2), new and modified statements that achieved consensus were removed and included in round 3 (R3) where panelists provided their percentage agreement and relevant citations. R3 followed a similar dynamic process using a ranking on a 9-point Likert scale, from 1 “most important” to 9 “least important.” Panelists could indicate the statements they considered could be removed with 75% exclusion agreement so that the final report included all statements with a substantial level of importance.

Results

The panel comprised 32 participants (mean age 37.1 ± 5.8 years) from 14 LAC (Fig. 1) who were predominantly neurologists (87.5%) with a mean 9.7 ± 3.7 years of experience (Table 1). In the first round, 11 of the 43 statements achieved consensus so they were not modified and did not pass to R2. The 32 statements that failed to achieve consensus, and another 8 new statements, were included in R2, where 32 of 40 statements achieved consensus and 4 new statements emerged. Thus, the final round involved 12 statements in which all achieved consensus and none were excluded in the final report. In R3, the panelists ranked all 55 statements across the rounds (Fig. 2), with key aspects of each domain highlighted below. Figure 3 contains the top half recommendations in each domain, full details of the consensus-based statements and supporting quotes are outlined in the online supplementary material.

Training and Education

Statements concerning national initiatives were the highest ranked and achieved substantial consensus; for example, the need to create a “stroke code” protocol for the early treatment of ICH patients (SA 93.8%; ranking 1.34 ± 1.45). Education to the public was to emphasize the importance of symptom recognition and need to promptly call emergency services (SA 84.4%; ranking 1.46 ± 1.31).

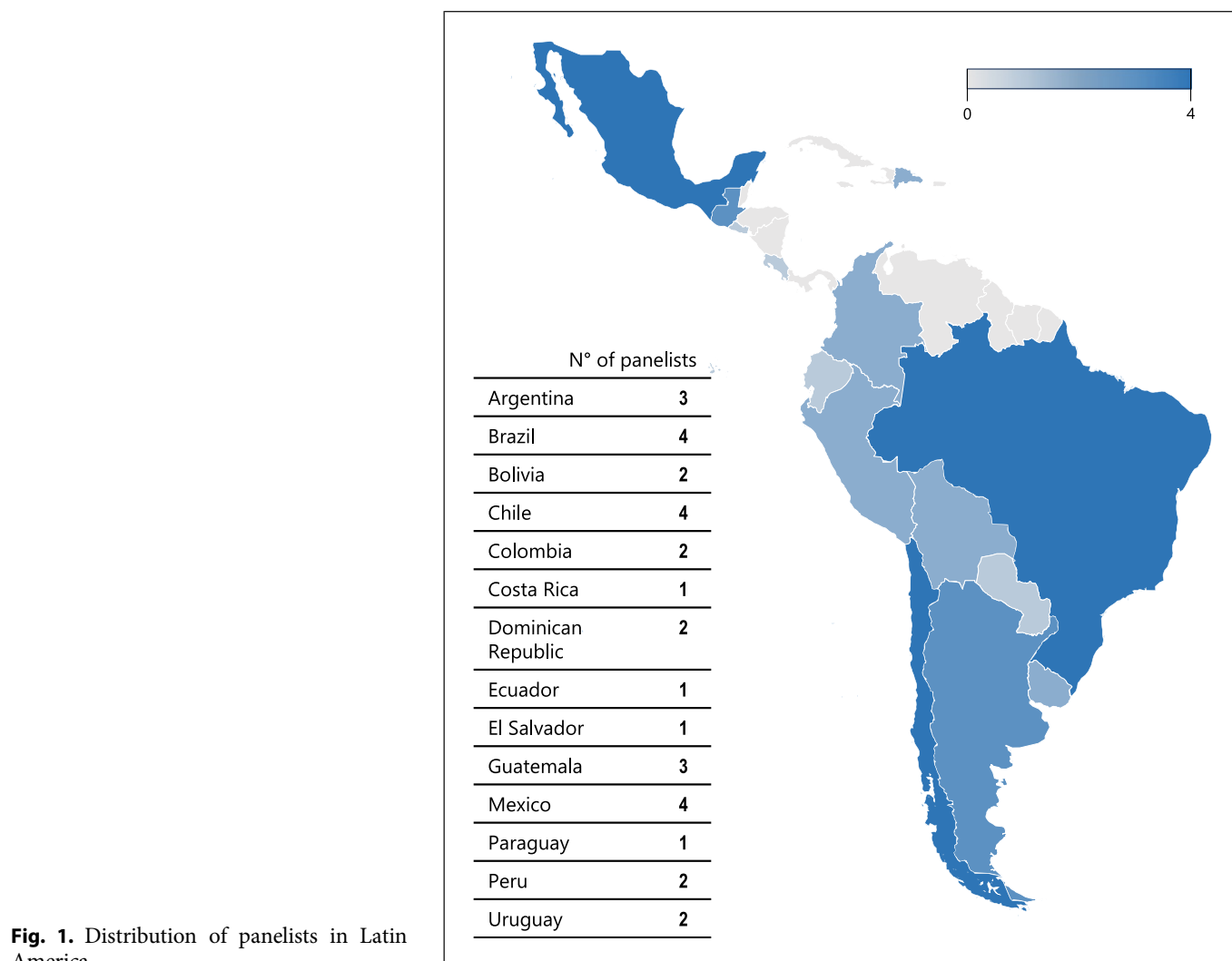


Fig. 1. Distribution of panelists in Latin America.

Human Resources and Infrastructure

The key concern was the provision of training to healthcare workers (SA 90.6%; ranking 1.09 ± 0.29) and need for cohesion between different discipline units. Assurance over the allocation of minimum resources in countries (SA 81.3%; ranking 1.43 ± 0.84) was given a high priority. Importance was also given to statements highlighting a collaborative approach and communication pathways to ensure prompt notification of imaging results (SA 68.8%; ranking 1.71 ± 1.05) and continuity of management between units (SA 68.8%; ranking 1.75 ± 1.27).

Early Intensive BP Control

Adherence to the INTERACT3 monitoring protocol was a high priority but also had a high level of disagreement (combined disagreement 15.7%, ranking 1.28 ± 0.58). Although panelists agreed on the frequency

of BP measurements used in INTERACT3, they also indicated that monitoring should be based on the requirements of individual patients. They also wished to emphasize that a minimum level of resources should be readily available (e.g., intravenous antihypertensive drugs) (SA 81.3%; ranking 1.31 ± 0.64) as this was considered a key barrier to effective implementation. Given challenges over resource allocation, initiatives to align protocols with local resources was encouraged (SA 87.5%; ranking 1.37 ± 0.55).

Strict Glucose Control

As insulin pumps are generally reserved for patients with very poor levels of glucose control in LAC, the panelists expressed concern over their availability and highlighted the need for training in glycemic management with low agreement (SA 59.4%; ranking 1.5 ± 0.80). Panelists agreed

Table 1. Baseline panelists characteristics

Participants (n = 32)	
Sociodemographic	
Male	21 (65.6)
Age, years mean±SD	37.1±5.8
Income of country ^a	
Lowermiddle-income	2 (6.25)
Uppermiddle-income	24 (75)
High-income	6 (18.75)
Profession	
Physiotherapist	1 (3.13)
Medical doctor	31 (96.88)
General practitioner	1 (3.13)
Specialist	
Neurology	28 (87.50)
Internal medicine	1 (3.13)
Urgenciology	1 (3.13)
Experience	
Years in profession, mean±SD	9.71±3.70
Years in ICH patient care, mean±SD	7.62±2.76
Years in the public health system, mean±SD	8.12±4.05
INTERACT3 investigator	6 (18.75)
Panelist hospital	
Location	
Urban	30 (93.75)
Semi-urban	2 (6.25)
Rural	0 (0)
Health sector	
Private	6 (18.75)
Public	25 (78.13)
Other	1 (2.70)
Computerized tomography available	32 (100)
Service units	
Emergency department	32 (100)
Neurosurgery	27 (84.38)
Intensive care unit	32 (100)
Stroke unit	16 (50.00)
Laboratory facilities	31 (96.88)
Stroke protocol	26 (81.25)
Inclusion of ICH treatment	17 (65.38)

Data are n (%) or mean ± SD. ^aIncome of countries based on the World Bank classification system: high-income includes Chile and Brazil; upper middle-income includes Argentina, Brazil, Colombia, Costa Rica, Dominican Republic, Ecuador, El Salvador, Guatemala, Mexico, Paraguay, and Peru; lower middle-income includes Bolivia. ICH, intracerebral hemorrhage; INTERACT3, third Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial.

that specific protocols (SA 87.5%, ranking 1.68 ± 0.89) and communication with endocrinologists and pharmacists (SA 40.6%, ranking 1.75 ± 0.76) need to be established for complex patients.

Body Temperature Control

Emphasis was placed on the training of healthcare workers (SA 75%; ranking 1.53 ± 1.13) and the monitoring of patients (SA 59.4%; ranking 1.75 ± 0.84).

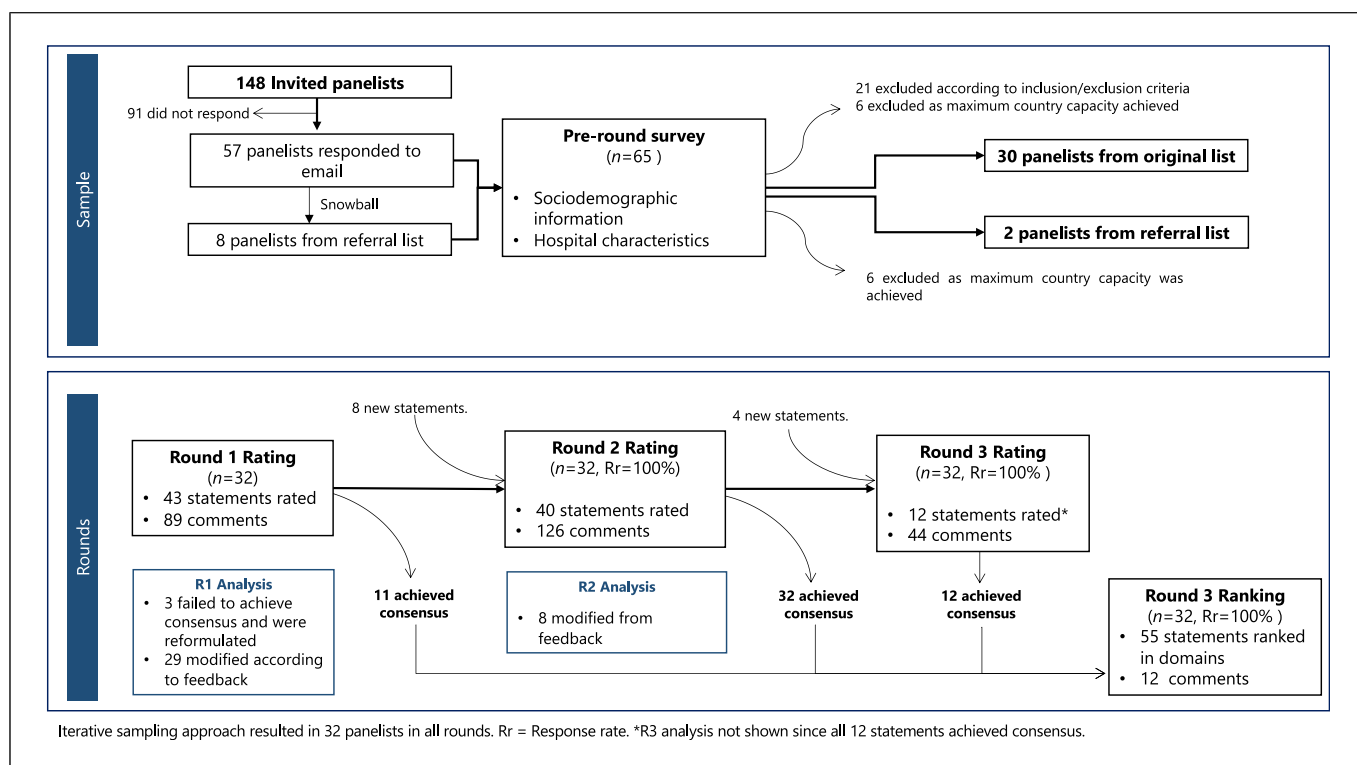


Fig. 2. Flowchart of sampling and Delphi rounds.

Rapid Reversal of Anticoagulation

High priorities were given to the availability and affordability of modern new oral anticoagulation reversal agents (SA 81.3%; ranking 1.21 ± 0.49) and for 24/7 availability of INR measurement as part of a collaborative network work approach (SA 81.3%; ranking 1.21 ± 0.49).

Education for Patients and Family Members

Use of plain language to educate patients and families (and/or caregivers) was a priority (SA 90.6%; ranking 1.37 ± 0.75) covering the need for frequent monitoring (SA 78.1%; ranking 1.62 ± 0.75) and to avoid projecting unrealistic expectations.

Discussion

Our study provides perspectives on areas to be addressed for successful integration of the INTERACT3 care bundle in LAC hospitals, with high priority given to BP control, anticoagulation reversal, resourcing, and education and training. A common perspective was that a minimum level of resources should be made available to allow effective integration of the care bundle. The pan-

elists expressed concern over the shortage of antihypertensive drugs and modern approach to anticoagulation reversal, which were deemed critical barriers to effective ICH management. Consistent with previous studies [10], the most frequently mentioned barriers were the poor availability of glucometers, thermometers, and BP monitors, although these were ranked as a lower priority of need.

The generation of a “stroke code” emerged as critical aspect. While the implementation of reperfusion therapy for acute ischemic stroke has been a global focus in recent decades, no such urgency has been uniformly applied to patients with ICH. While 90% of the panelists reported having a local “stroke code” protocol at their hospital, only two-thirds had this integrated with a pathway for ICH management. This was the practice gap that needs to be addressed, given the evidence that is emerging over the effectiveness of treatments for ICH being dependent on the time from symptom onset. The passive approach of clinicians to patients with ICH is further reflected in many having a low threshold to withdraw active care [11]. Thus, training on the benefits of the care bundle was considered a means of addressing premature use of do-not-resuscitate orders and clinician misjudgment over

Top Half recommendations in each domain for the implementation of the INTERACT3 care bundle in Latin America.

Training and Education in Intracerebral Hemorrhage

- Countries should establish "stroke code" protocols that include early treatment for patients with intracerebral hemorrhage.
- General public education about intracerebral hemorrhage should include a focus on the importance of recognizing symptoms and promptly seeking emergency services.
- When conducting training on the INTERACT3 care bundle, health institutions should provide it to all healthcare workers who are involved in the management of patients with intracerebral hemorrhage, including healthcare workers who are not part of the neurological area.
- To achieve effective healthcare professional education, it is essential that it is carried out systematically, resulting in highly trained personnel in the management of intracerebral hemorrhage and stroke in general. Ideally, this education should include official certifications or other formal courses.

Early intensive blood pressure control

- To maintain the blood pressure (BP) target, its monitoring should consider at a minimum:
 - Monitor every 15 minutes during the first hour.
 - Monitor every hour for the following four hours.
 - Monitor every 4 hours for up to 24 hours.
 - Monitor every 12 hours for 7 days or until hospital discharge.
- Early and intensive blood pressure control is not achievable with the exclusive use of oral antihypertensive drugs, so intravenous antihypertensive drugs should be prioritized in resource planning.
- Locally, there should be treatment regimens with options for intravenous antihypertensive medications for the acute phase, prioritized based on evidence and adapted to the available local resources, including transitioning to oral antihypertensive medications when appropriate.
- To maintain the blood pressure target, it is relevant that blood pressure control be carried out strictly and frequently, depending on the requirements of each patient and considering invasive monitoring when necessary and available.

Education to patients and family members

- Education to patients and/or their families (and/or caregivers) about the benefits of the care package should be in plain language.
- Education of patients and/or their families (and/or caregivers) about the benefits of the INTERACT3 bundle of care should include a focus on the benefits on the prognosis, avoiding providing unrealistic expectations.

Human Resources and Infrastructure

- To start the care bundle proposed in INTERACT3 early and intensively, the healthcare workers in charge of the care of intracerebral hemorrhage patients from the different services where the patient may be admitted should be trained.
- Countries should ensure the allocation of the minimum necessary resources to provide the required care for patients with intracerebral hemorrhage, supported by level I (1) evidence available, as presented in the INTERACT3 study.
- Imaging team protocols should be established to promptly notify the treating teams of a new case of intracerebral hemorrhage once imaging exams have been conducted.

Body temperature control

- Training to healthcare workers on the INTERACT3 bundle of care, should focus on emphasizing the body temperature target (less than 37.5°C).
- To maintain the body temperature target, it is relevant that temperature control is carried out frequently, depending on the requirements of each patient.
- The management of body temperature should be carried out according to established local protocols that are in line with the available resources, including both physical and pharmacological measures.
- For the serial control of body temperature, there should be a sufficient number of thermometers for patients with intracerebral hemorrhage.

Strict glucose control

- Training should always include practical sessions on glycemic management in patients with intracerebral hemorrhage to be effective and prevent complications and serious effects like hypoglycemia.
- To maintain the glycemic level target, it is relevant that the control be carried out frequently, depending on the requirements of each patient.
- In the management of patients with difficult glucose level control (e.g., Type 1 diabetics, steroids users, patients with concomitant infections, etc.), it should be considered to establish specific protocols for these groups.
- In cases where it is feasible, healthcare workers should have expedited communication channels with endocrinologists and pharmacists to address doubts regarding the management of glycemic levels in complex patients.
- It is important to create meetings to review clinical cases of patients with intracerebral hemorrhage and difficult glycemic control to improve their care and facilitate feedback in the team.
- For the serial control of glycemia, there should be a sufficient number of glucometers to meet the demand of the hospital service for patients with intracerebral hemorrhage.
- Trainings should always include a section that emphasizes strict glycemic control, also incorporating the management of stress-induced hyperglycemia.

Rapid reversal of anticoagulation

- Countries should ensure the availability of treatments for anticoagulation reversal and their expedited use in acute cases.
- When not available locally, healthcare institutions should establish support networks with other health centers to have laboratories available for 24-hour INR measurement.
- It is important to provide training for the management of patients with intracerebral hemorrhage related to the use of anticoagulants, including the use of reversal agents, INR monitoring frequency, and the resumption of anticoagulation.

Fig. 3. Top half recommendations in each domain for the implementation of the INTERACT3 care bundle in Latin America.

prognosis [12]. Hence, inclusion of a CODE-ICH pathway and training all personnel on the INTERACT3 care bundle were considered pivotal first steps in re-shaping perspectives on ICH management.

Our findings further highlight the need for a collaborative approach in stroke care by the recommendation of creating communication channels between professionals and through networks between healthcare institutions. This would foster safe and effective glycemic control and anticoagulation reversal when there is limited availability of treatments and knowledge in those areas. Panelists were reluctant to promote the use of insulin pumps, which is consistent with barriers found in fever, hyperglycemia, and swallowing dysfunction in the Quality in Acute Stroke Care (QASC) study [13], where two-thirds of participating clinicians found a key barrier post-implementation of the intervention. Similarly, process evaluation undertaken in the Chinese INTERACT3 participants found that blood glucose control was the most complex intervention to implement; in addition, facilitators included collaboration and consultations with the endocrine department, aligning with our findings [14]. During the rounds, the use of subcutaneous insulin was often mentioned, but it did not reach a high ranking,

which emphasizes the need for training and protocols in the region. Notably, the lack of protocols and training is found as a common barrier across various settings including both high-income [15] and low-to-middle-income countries [16].

Given the relative low use of warfarin anticoagulation in LAC [17], and thus limited exposure to anticoagulation reversal, adequate supply of relevant agents on their own is unlikely to influence implementation of the care bundle. A study conducted in rural and community departments in the USA shows that the elevated cost and lack of knowledge about the utility and concerns about short shelf life were the main factors associated with the availability of anticoagulation reversal agents [18]. Our findings show that continuous training on drug reconstitution, organizational support, and ensuring 24/7 availability on INR measures through collaborative networks were important components of successful integration. Other studies have emphasized these aspects as key steps in reducing door-to-needle time for anticoagulation reversal [19] and are arguably even more relevant in the era of reversal agents for direct oral anticoagulants.

Our study has several strengths. The Delphi technique recommendations were formulated from the perspective

of a range of clinician stakeholders from different healthcare settings and cultural contexts. Their commitment to completing responses to all the rounds enhances the reliability of results. However, there are limitations that are worth mentioning. Despite our efforts to construct a multidisciplinary panel, it was mainly comprised of neurologists, and there was no lived-experience perspective from patients or family and community engagement. Although the panelists were experienced and able to provide holistic views, these may not necessarily reflect those of junior or different background staff who work on the frontline or in the day-to-day management of patients with ICH, such as nurses, nurse technicians, and other disciplines. Nevertheless, the process evaluation conducted prior to this study, upon which we based the first round, included other healthcare professionals as well as patients and caregivers. Furthermore, prescriptions for BP control, glycemia, temperature, and anticoagulation reversal medications must be provided by a physician, making their contribution to the topic relevant to us. Finally, Latin America is a region composed by mainly uppermiddle-income and high-income countries, with only 5 countries categorized as lower middle-income; as this study was undertaken in LAC, the views may not represent lower middle-income regions or those of healthcare systems elsewhere.

In summary, the INTERACT3 care bundle has the potential to reduce the burden of ICH in LAC, alleviate the strain on diverse and complex health systems, and improve the health and well-being of those affected. Our study provides a priority list of key recommendations for the effective integration of time- and target-based protocols into systems of care in the region. These findings can be used to devise context-specific strategies toward effective implementation of the INTERACT3 care bundle and thus facilitate the incorporation of ICH into stroke care codes for patients in the region.

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Statement of Ethics

The study was approved by the Scientific Ethics Committee of Clínica Alemana-Universidad del Desarrollo (No. 2023-68). All panelists provide an online written informed consent before participation in the study.

Conflict of Interest Statement

C.S.A. reports receiving research grants from the National Health and Medical Research Council (NHMRC) of Australia, the Medical Research Council (MRC) and Medical Research Foundation (MRF) of the UK, and Takeda and Penumbra. He is the Editor-in-Chief of *Cerebrovascular Diseases*. P.M.-V. reports receiving research grants from ANID Fondecyt Regular 1221837, Pfizer, and Boehringer Ingelheim. B.C. reports research grants from Fondecyt Regular 1201461. A.O. reports a research grant from Merck. V.C.-N. reports a research grant from AstraZeneca and was a speaker for Boehringer and Sanofi. The other authors declare no conflict of interest.

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Author Contributions

P.M.-V., C.S.A., B.C., M.I.A., and A.O. contributed to the concept and rationale for the study. M.O., C.S.A., V.C.-N., A.A., P.M.-V., F.G., F.B., and M.I.A. contributed to the development and design of all three surveys. V.C.-N. and A.A. performed language refinement in neural Spanish and C.S.A. and M.O. in English. All the authors made substantial contribution to the methodology. F.B. was responsible for provision of software. M.I.A., F.G., and P.M.-V. performed formal analysis and data curation. M.I.A. wrote the first draft of the manuscript with input from F.B., F.G., and P.M.-V. All the authors reviewed and approved the final manuscript.

Data Availability Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author P.M.V. upon reasonable request.

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