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REVIEW ARTICLE

Inclusion of People With Aphasia in Stroke Trials: A Systematic Search and Review

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Abstract

Background: Although people with aphasia (PwA) represent 30% of stroke survivors, they are frequently excluded from stroke research, or their inclusion is unclear. Such practice significantly limits the generalizability of stroke research, increases the need to duplicate research in aphasia-specific populations, and raises important ethical and human rights issues.

Objective: To detail the extent and nature of inclusion of PwA in contemporary stroke randomized controlled trials (RCTs).

Methods: We conducted a systematic search to identify completed stroke RCTs and RCT protocols published in 2019. Web of Science was searched using terms "stroke" and "randomized controlled trial". These articles were reviewed by extracting rates of PwA inclusion/exclusion, whether "aphasia" or related terms were referred to in the article or supplemental files, eligibility criteria, consent procedures, adaptations made to support the inclusion of PwA, and attrition rates of PwA. Data were summarized, and descriptive statistics applied when appropriate.

Results: 271 studies comprising 215 completed RCTs and 56 protocols were included. 36.2% of included studies referred to aphasia/dysphasia. Of completed RCTs, only 6.5% explicitly included PwA, 4.7% explicitly excluded PwA, and inclusion was unclear in the remaining 88.8%. Among RCT protocols, 28.6% of studies intended inclusion, 10.7% intended excluding PwA, and in 60.7%, inclusion was unclear. In 45.8% of included studies, sub-groups of PwA were excluded, either explicitly (ie, particular types/severities of aphasia, eg, global aphasia) or implicitly, by way of ambiguous eligibility criteria which could potentially relate to a sub-group of PwA. Little rationale for exclusion was provided. 71.2% of completed RCTs did not report any adaptations that could support the inclusion of PwA, and minimal information was provided about consent procedures. Where it could be determined, attrition of PwA averaged 10% (range 0%-20%).

Conclusion: This paper details the extent of inclusion of PwA in stroke research and highlights opportunities for improvement.

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Introduction

Aphasia is a common acquired language impairment affecting 1 or more language modalities (spoken language, language comprehension, reading, and/or writing),[1] creating a significant communication disability. Affecting approximately one-third of stroke survivors,[2] aphasia can negatively impact an individual's functioning, activities, relationships, rights, wellbeing, participation, and quality of life.[3] Compared with stroke survivors without aphasia, people with aphasia experience poorer outcomes (eg, longer lengths of hospital stay, increased use of rehabilitation services), greater long-term effects (eg, poorer quality of life, greater social isolation, higher incidence of depression), and higher health care costs,[4-8] with greater impacts also experienced by caregivers.[9]

Despite these poor outcomes, and the large proportion of stroke survivors living with aphasia, systematic reviews in distinct topic areas such as post-stroke mental health,[10-12] sexuality,[13] and patient experience research[14] have found that people with aphasia are excluded from stroke research; and while some researchers intentionally exclude people with aphasia, many more do not adequately describe their eligibility criteria and research participants, leaving readers uncertain about the inclusion of people with aphasia.

Stroke researchers may find it challenging to include people with aphasia in their research, given the communication barriers created by the high language demands of many research processes.[15] However, when appropriate adaptations and accommodations are made, it is possible for people with aphasia to meaningfully participate in research. Such adaptations include the use of aphasia-friendly written materials[16] and supported communication techniques.[17]

Excluding people with aphasia from stroke research means that the results may not be applicable to those with aphasia,[18] and research is not representative of the stroke population at large. This increases the need to duplicate research efforts within aphasia-specific populations. These exclusionary practices also raise significant ethical and human rights implications—as well as resulting in an inequitable evidence base for stroke care,[15] they deny people with aphasia the opportunity to participate in research[14,19] and reap the reported benefits from this participation.[20,21] Finally, excluding people with aphasia reduces the pool of potential study participants[15] and prevents stroke researchers from developing the skills required to include people with aphasia in future research. A comprehensive overview of these issues and the implications of exclusion within stroke research can be found in a companion paper by Shiggins et al.[15]

In this paper, we review the state of inclusion of people with aphasia in stroke clinical trials from 1 year, 2019. This paper builds on preliminary evidence suggesting some exclusion of people with aphasia from stroke research, by investigating and describing the extent and specific nature of this problem across topics, disciplines, and the continuum of care. Further, it details the ways in which some stroke researchers support the inclusion of people with aphasia through various adaptations and accommodations to the research process, and the attrition rates of people with aphasia in stroke research.

In relation to stroke trials, the specific aims were to investigate and describe (1) whether "aphasia" or related terms were referred to in stroke trial articles or supplemental files; (2) the rate of inclusion/exclusion of people with aphasia; (3) the eligibility criteria used by stroke researchers relating to people with aphasia; (4) consent procedures; (5) whether completed randomized controlled trials (RCTs) reported making accommodations and/or adaptations to any stage of the research process to support the inclusion of people with aphasia, and (6) the attrition rate of people with aphasia.

List of abbreviations:

RCT **randomized controlled trial**

Methods

A systematic search and review[22] of stroke RCTs was conducted. This method was chosen as it "combines the strengths of a critical review with a comprehensive search process".[22(p102)] It is suitable for broad questions, allows for included literature to be critiqued, and leads to recommendations for practice.[22] This review did not appraise article quality, as the focus was on methods rather than results. This aligns with a systematic search and review methodology.[22]

Searching the literature

We searched "Web of Science", a comprehensive website that provides access to multiple academic databases across various disciplines, using search terms "stroke" and "randomized controlled trial" (linked by "AND"). We limited the search to publications written in English and including adults over 18 years.

An initial search of studies published over a 10-year period (January 2009-December 2019) was conducted in February 2020 to investigate inclusion practices across a range of years. However, given the resulting high yield (n=19,033), and the goal of providing a detailed in-depth snapshot of the state of inclusion in contemporary trials, we refined the review period to a single year (2019).

We decided to include both completed RCTs and RCT protocols in this review, as completed trials may have been conceptualized and/or completed many years prior to publication, whereas RCT protocols would capture studies currently being conducted. Where applicable, we adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[23] (see supplemental file 1, available online only at http://www.archives-pmr.org/).

Screening the literature

Retrieved articles (January 2009-December 2019; n=19,033) were transferred to Endnote, duplicates removed, and those published in 2019 (n=1900) identified. Title, abstract and full-text level screening was completed by the lead author (C.S.) according to the predefined eligibility criteria (table 1). When C.S. was uncertain about the eligibility of an article this was discussed with 2 co-authors (B.R. and M.R.) to reach a final decision. In 8 instances, the corresponding author of an article was emailed for clarification regarding eligibility; 4 of these authors responded. When clarification was not obtained the article was excluded.

Table 1 Eligibility criteria

Inclusion	Exclusion
Target area is stroke	Not stroke
Must include participants—empirical research	Not empirical research, for example, big data or epidemiology studies, review papers (systematic, narrative, or meta-analysis, including systematic reviews of RCTs), guidelines, methods papers
Study design—RCT (including pilot, feasibility studies, and quasi RCTs & protocols) Double or single-blinded RCTs	Not an RCT
Primary data from an RCT, rather than sub analysis, that is, not secondary analysis or post hoc analysis	Sub analysis of RCT data, for example, secondary analysis or post hoc analysis
Adults 18+ years	Younger than 18 years
Peer-reviewed article	Not peer-reviewed publications, for example, opinion pieces, magazine articles, blogs; not conference abstracts
Published in English	Published in any language other than English
Published in 2019	Not published in 2019
Human studies	Animal studies
Interventions focused on stroke survivors or stroke survivors and close other(s)	An intervention that is focused on family members or close other(s) only

Data extraction

The following data were extracted from each of the included studies: (1) authors, (2) lead country of research, (3) intervening discipline (the discipline/s of the person(s) that administered the target intervention), (4) time post-stroke at point of intervention (according to the Bernhardt et al,[24] classifications), (5) intervention target (eg, upper limb function, depression), (6) specific design of RCT (as stated in the article), (7) research aim (as stated in the article), (8) whether the term "aphasia" or related terms (eg, "dysphasia", "communication") were referred to in the article or supplemental files, (9) whether people with aphasia were included in, or excluded from, the study, (10) the eligibility criteria used by stroke researchers relating to people with aphasia, (11) the consent procedure, and (12) any adaptations or accommodations made to any stage of the research process that could support the inclusion of people with aphasia. When adaptations or accommodations were made, it was noted where in the research process these adaptation(s) occurred using the National Health and Medical Research Council (NHMRC)[25] 7 elements of the research process (Element 1—Research Scope, Aims, Themes, Questions and Methods; Element 2—Recruitment; Element 3—Consent; Element 4—Collection, Use and Management of Data and Information; Element 5—Communication of Research Findings or Results to Participants; Element 6—Dissemination of Research Outputs and Outcomes; and Element 7—After the Project). The number of elements adapted per study was also noted. When people with aphasia were included in the study and the number of people with aphasia included stated, we extracted the number of participants with aphasia randomized and the number that left the study so that an attrition rate could be calculated.

Determining inclusion and exclusion

Completed RCTs were categorized as including people with aphasia if the number of people with aphasia included in a study was explicitly stated in the article. Data were then extracted to identify the percentage of people with aphasia included in the study in relation to the total sample size. RCT protocols were categorized as including people with aphasia if this intention was reported in the study eligibility criteria. Both completed RCTs and RCT protocols were deemed to have excluded people with aphasia if the eligibility criteria stated that all people with aphasia were / would be excluded (ie, total exclusion). Studies that did not fulfil criteria for either including or excluding people with aphasia were labeled "unclear".

It was also noted when studies explicitly excluded a sub-group of people with aphasia (ie, people with a particular type or severity of aphasia such as global or severe aphasia), or when a lack of clarity in a study's eligibility criteria could relate to a sub-group of people with aphasia (eg, "those who have difficulty understanding instructions"). For the purpose of this article, the latter were termed "ambiguous statements", and when either of these cases occurred, we termed this "partial exclusion". When provided, the rationale, methods, and assessments used to determine exclusion or partial exclusion were noted.

Rigor

Additional steps were taken to enhance the stringency of the data extraction process. To ensure that all relevant references to aphasia, related terms and/or the consent procedure were identified, all articles were searched for the terms "aphasia", "dysphasia", "language", "communication", "speech", "cognition", and "consent". This was completed manually and then cross-checked using the electronic "find" (Ctrl + F) function. When available, supplemental materials were also searched. Data extraction was completed by the first author (C.S.), and a second reviewer (F.D.) independently extracted 10% of articles. C.S. and F.D. met to cross-check the data extraction, and any inconsistencies were discussed with a third reviewer (B.R.). For data relating to partial exclusion and eligibility criteria, extraction and cross-checking was completed for all included articles (100%) by both C.S. and B.R.

Data analysis and synthesis

Data were managed in Microsoft Excel software. A descriptive summary of the included studies was collated, and descriptive statistics (counts, percentages) were conducted where appropriate. Percentages were rounded to 1 decimal place. Completed RCTs

and RCT protocols were analyzed separately. As per Hui et al,[26] attrition rates of people with aphasia were calculated for each trial by dividing the number of participants who left the study at the primary endpoint by the total number of participants at randomization and multiplying by 100 to obtain a percentage (%). A narrative synthesis of these results is provided.

Results

Study characteristics

A total of 274 articles consisting of 218 completed RCTs and 56 RCT protocols were included. Five of these publications[27-31] reported data from 2 completed studies. Therefore, these 5 publications were counted as 2 studies, making the final number of included studies 271: 215 completed RCTs and 56 RCT protocols. See the PRISMA flowchart for further details (fig 1).

Supplemental files 2 and 3 (available online only at http://www.archives-pmr.org/) provide a complete reference list of the included studies and supplemental files 4 and 5 (available online only at http://www.archives-pmr.org/) present the study characteristics (completed RCTs and RCT protocols, respectively). There were 37 lead countries across the dataset, representing 5 continents. South Korea, China, and the United Kingdom were the countries with the largest number of studies included in the review. Intervening disciplines included alternative therapies (eg, acupuncture and Chinese medicine, n=12), medicine and pharmacy (n=68), mixed (more than 1 intervening discipline, n=65), nursing (n=6), occupational therapy (OT, n=22), physiotherapy (PT, n=81), psychology (n=2), speech and language therapy (SLT, n=10), and "unclear", when the intervening discipline(s) could not be determined, (n=5). These studies were conducted across the continuum of stroke care, including hyper-acute (n=28), hyper-acute/acute (n=6), acute (n=21), acute/sub-acute (n=38), sub-acute (n=49), sub-acute/chronic (n=14), chronic (n=90), acute to chronic (n=14), and unclear (n=11).

To what extent was aphasia referred to in stroke trials published in 2019?

Of the 271 included RCTs and RCT protocols, 98 studies (36.2%; comprising 73 completed RCTs and 25 RCT protocols), used the term "aphasia" or "dysphasia" in the article or supplementary files. In 122 studies (45%; 98 RCTs and 24 protocols), there was no mention of aphasia. In the remaining 51 articles (18.8%; 44 RCTs and 7 protocols) aphasia was not referred to directly but reference was made to speech, language, communication, or cognition, or an ambiguous statement that could relate to people with aphasia was used in the eligibility criteria. Examples of these ambiguous statements included "inability to complete the scale evaluation due to communication or cognitive difficulties",[32(p657)] "difficulty in understanding or executing commands",[33(p487)] and "able to communicate properly".[34(p1043)]

To what extent were people with aphasia included in stroke trials in 2019?

Supplemental files 6 and 7 (available online only at http://www.archives-pmr.org/) outline the extent of inclusion and exclusion of people with aphasia across completed RCTs and RCT protocols, respectively.

Inclusion of people with aphasia across completed RCTs

Fourteen of the 215 completed RCTs (6.5%) explicitly included people with aphasia in their studies.[35-48] In 8 of these studies, aphasia was the primary focus and, therefore, all included participants were people with aphasia.[35,38,39,41,43,45–47] Among the remaining 6 studies, 6 to 46% of the included participants at randomization were people with aphasia. These 6 studies focused on an oral health program (dysphagia and nutrition; n=6 people with aphasia included, [6% of total sample]),[36] medication (fluoxetine; n=906, [29%]),[42] psychological well-being (n=26, [46%]),[44] models of care and follow-up (n=203, [10%]),[48] balance training (n=10, [16%]),[37] and caregiver mediated physiotherapy (n=14, [25%]).[40] Four of the 14 studies that included people with aphasia excluded a sub-group of people with aphasia, either explicitly (severe receptive aphasia[44] and severe global aphasia[47]) or included an ambiguous eligibility statement that could be applied to a sub-group of people with aphasia (ie, participants had to be "able to understand instructions",[37] "able to understand instructions" with a Mini Mental State Examination Score >18[40]). Therefore, only 10 of 215 completed RCTs (4.7%) employed eligibility criteria allowing the inclusion of people with aphasia of any severity or type. In terms of exclusion, 10 of the 215 completed RCTs (4.7%) explicitly excluded all people with aphasia.[49-58] It was unclear whether people with aphasia were included or not in the remaining 191 studies (88.8%).

Inclusion of people with aphasia across RCT protocols

Sixteen of the 56 RCT protocols (28.6%) reported an intention to include people with aphasia in their studies.[59-74] Aphasia, specifically aphasia therapy, was the stated focus of 3 of these protocols.[61,68,71] The remaining 13 studies focused on hyper-acute medicine,[59,67,72] sub-acute medicine,[74] primary care,[65] the effectiveness of a virtual multi-disciplinary team stroke care clinic,[60] upper limb function,[62,73] secondary stroke prevention,[63,66] acupuncture,[64] a rehabilitation transition program,[70] and home-based virtual reality training.[69] Five of the 16 studies intended to exclude certain sub-groups of people with aphasia —namely, severe aphasia,[60,73] moderate to severe aphasia,[70] or above/below specific cut-off scores on outcome or assessment measures.[66,74] Therefore, 11 of the 56 included protocols (19.6%) intended to include people with all types and severities of aphasia. The authors of 6 of the 56 RCT protocols (10.7%),[75-80] planned to exclude all people with aphasia from their studies. It was unclear whether the remaining 34 protocols (60.7%) intended to include people with aphasia or not.

To what extent were people with aphasia excluded (totally or partially) from stroke trials, and what were the "criteria" used to determine exclusion?

The extent of total exclusion across completed RCTs and RCT protocols is outlined in the section above. Supplemental files 8 and 9 (available online only at http://www.archives-pmr.org/) outline the extent of partial exclusion, eligibility criteria, and the criteria (rationale, methods and/or assessments) used to determine total and partial exclusion for completed RCT and RCT protocols, respectively.

Criteria for total exclusion

The criteria (rationale, methods, and/or assessments) for total exclusion of people with aphasia from stroke trials were not consistently

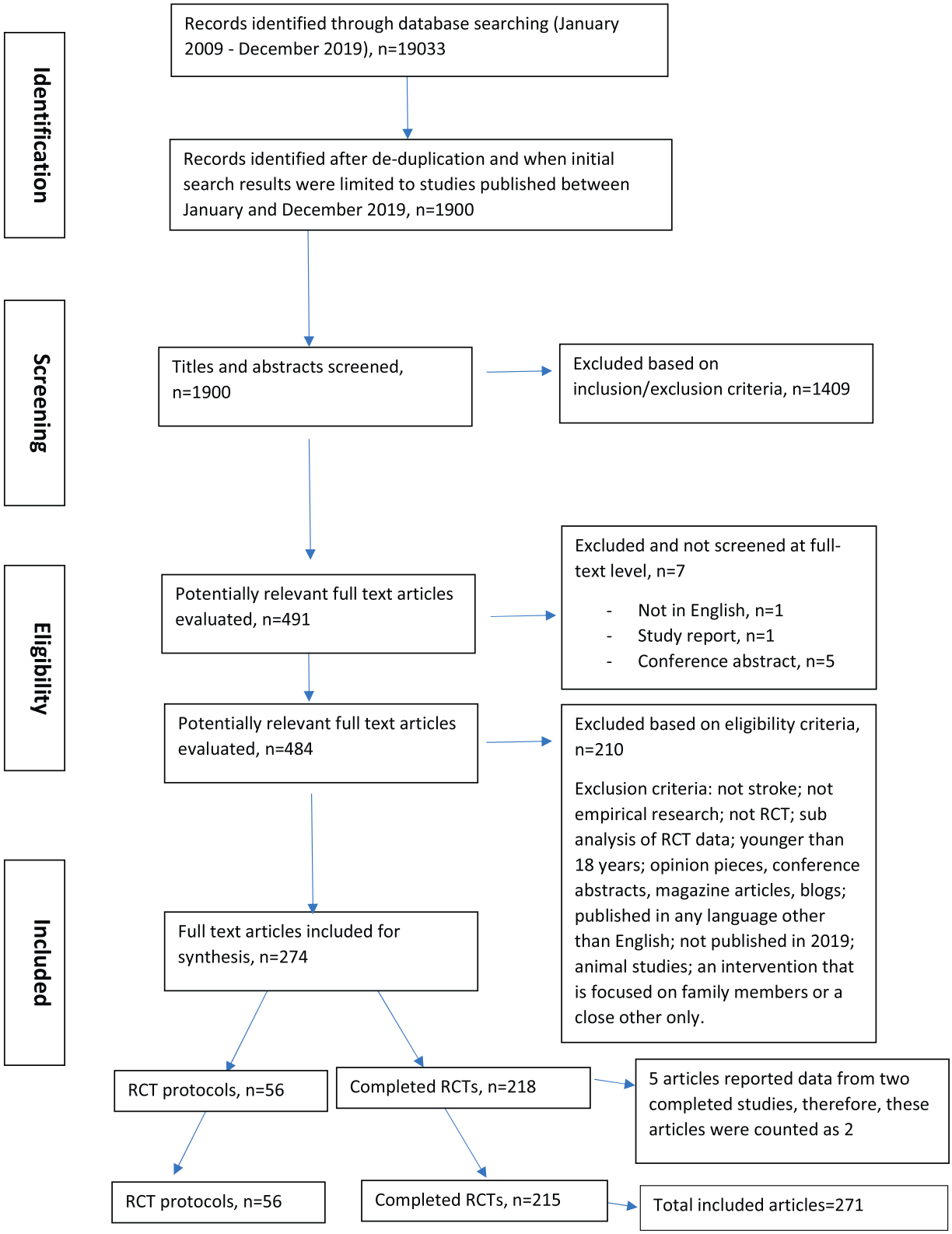

Fig 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses process of identifying, screening, and assessing eligibility for inclusion of studies.

provided. Ten completed RCTs explicitly excluded all people with aphasia; however, only 2 of these provided a rationale for doing so. These rationales included: "educability (lack of consciousness, aphasia, and memory, hearing disorders)"[51(p1346)] and "aphasia that impeded communication".[55(p517)] Six RCT protocols intended to exclude all people with aphasia, and 2 of these provided a rationale for exclusion: "incapable of understanding the instructions given by therapists",[75(p3)] and that aphasia makes it difficult to understand

Table 2 Sub-groups of people with aphasia explicitly excluded from completed RCTs and RCT protocols

Sub-groups of Aphasia	Completed RCTs (n=45)	RCT Protocols (n=6)
Severe aphasia	20	3
Moderate to severe aphasia	2	1
Specific combinations of aphasia (eg, severe receptive aphasia)	7	0
Total/Global/"Comprehensive aphasia"	6	0
Specific level of command that a person with aphasia needed to be able to understand (eg, 1-step command)	4	1
Receptive aphasia	4	0
Sub-group of aphasia determined through specific cut-offs on outcome measures (eg, Score <8 on the Sheffield Screening test for Acquired language Disorders)	2	1

instructions, describe their condition, and for safety reasons due to the "specific nature of the device and training program".[80(p4)]

Extent of partial exclusion

Of the 271 studies included in the review, 124 studies (45.8%; 107 completed RCTs and 17 protocols) stated explicitly that a sub-group of people with aphasia (eg, global aphasia) would be excluded or used eligibility criteria that were ambiguous and could apply to a sub-group of people with aphasia (eg, people "who can follow directions"[81(p266)]). Fifty-one of these 124 studies (41.1%; 45 completed RCTs and 6 protocols) explicitly excluded a sub-group of aphasia, with people with severe aphasia being excluded most frequently (all excluded sub-groups and frequencies are outlined in table 2). Seventy-three of the 124 studies (58.9%; 62 RCTs and 11 protocols) used eligibility criteria that were ambiguous and could be applied to exclude some people with aphasia.

Criteria for partial exclusion

Forty-three of the 124 studies that partially excluded people with aphasia (34.7%; 40 RCTs and 3 protocols) provided a rationale for doing so. The rationales varied across included studies and are outlined in table 3. Difficulties communicating with the therapist/intervention provider, following and understanding study instructions, and engaging and participating in the intervention were cited as the primary reasons for exclusion.

What assessments/methods underpinned the partial exclusion of people with aphasia in stroke trials?

Only 45 of the 124 studies that partially excluded people with aphasia (36.3%; 37completed RCTs and 8 protocols) outlined how the severity, type, or impact (eg, ability to follow directions) of aphasia was assessed or determined. Where this information was provided, cognitive assessments were the primary method used. The full range of assessments and methods used is outlined in table 4.

In many studies, cognitive status appeared to be conflated with language abilities, with the term "cognitive abilities" used when "language or communication abilities" may potentially have been more appropriate (eg, "cognition level enough to follow simple instructions and understand the content and purpose of the study".[82(p214)] Eighty-eight of the 124 studies that partially excluded people with aphasia (71%; 76 completed RCTs and 12 protocols) mentioned cognition in their eligibility criteria. We noted this as we acknowledge that these criteria may be applied to people with aphasia.

What adaptations and accommodations were used to support the inclusion of people with aphasia in completed stroke trials?

One hundred and fifty-three of the 215 completed RCTs (71.2%) did not report any adaptations or accommodations to support inclusion across any of the NHMRC elements of the research process.[25] Adaptations or accommodations were reported in 62 studies (28.8%) with adaptations most commonly being made for element 3 "Consent" (51 studies), and element 4 "Collection, Use and Management of Data and Information" (22 studies). No adaptions or accommodations were reported for elements 5-7 in any studies. Frequency of adaptions across all elements of the research process are displayed in figure 2.

In 8 studies, authors made adaptations to 2 elements of the research process.[47,83-89] Four studies reported adaptations to 3 elements[43,44,90,91] and 1 study reported adaptations to 4 elements.[38] No studies reported adaptions to all elements. The types of adaptations and accommodations used to support inclusion are detailed below. Supplemental file 10 (available online only at http://www.archives-pmr.org/) outlines the adaptations and accommodations used to support the inclusion of people with aphasia in completed stroke RCTs.

Table 3 Rationales provided for partial exclusion

Rationale Provided	Completed RCTs (n=40)	RCT Protocols (n=3)
Difficulties communicating with the therapist/intervention provider, understanding/following instructions	21	0
Difficulties with treatment, participation, engagement, implementation, adherence, or "unsuitable for treatment"	8	1
Difficulties with outcome measurement	3	0
Difficulties with consent	2	0
Risk/safety	2	2
Combination of 2 or more of reasons above	4	0

Table 4 Assessments or methods used to determine partial exclusion of people with aphasia

Assessment/Methods Used	Completed RCTs (n=37)	RCT Protocols (n=8)
Cognitive assessment (eg, the MMSE)	12	1
Stroke impairment or severity assessments (eg, the National Institutes of Health Stroke Scale)	8	1
Opinion/judgment/evaluation of a clinician or investigator	7	3
Specific level of command that a person with aphasia needed to be able to understand (eg, 1-step command)	5	1
Language/aphasia specific assessments (eg, Mississippi Aphasia Screening Test)	4	1
Participant self-report	1	0
Combination of the above assessments/methods	0	1

Abbreviations: MMSE, Mini Mental State Examination.

Consent procedures

Minimal information was provided about the consent procedures used across the completed RCTs. One hundred and sixty-five of the 215 completed RCTs (76.7%) stated that consent was obtained through a "signed consent form". This was denoted using the terms "informed written consent", "written/signed consent", and "written/signed informed consent". Forty completed studies (18.6%) stated that consent was obtained from participants but did not report how this consent was obtained or documented (eg, "participants consented", "provided informed consent", "agreed to participate", and "be willing to participate"). One study was approved on a "two physician best interest consent principle, and deferred consent was obtained from each participant when they became competent".[92(p740)] There was no mention of 'consent' or how consent was obtained from participants in 9 completed studies (4.2%).

Adaptations to the consent procedure

Fifty-nine of the 215 completed RCTs (27.4%) provided additional information on the consent procedure or made an adaptation to their consent procedure that could support inclusion. Proxy consent was the adaptation most frequently used, being reported by 30 studies. A further 20 studies provided additional information about how the consent procedure was conducted and the specific adaptations that were made. For example, they outlined the steps that were taken to explain the participant information sheet, who provided the explanation or where this occurred. Six studies used a combination of adaptations to the consent procedure (ie, using alternative means for obtaining consent [for example, proxy consent] and making an adaptation to their consent procedure [for example, using aphasia-friendly materials]).[38,48,85,93–95] A consultee was appointed in 2 of these studies—when a person lacked capacity to consent[85]; and "where it was not possible to obtain informed consent from the patient due to communication and/or cognitive difficulties".[94(p1920)] As outlined in the Mental Capacity Act (England and Wales),[96] a consultee is a person who is able to advise on a person's likely wishes and desires regarding participation in research when they have been deemed to lack capacity. In 1 study,[38] a declaration of belief or proxy consent was used, and the consent support tool was also employed to identify the level of support needed for each person with aphasia. In 3 studies,[86,97,98] it was unclear whether proxy consent was being used, whether caregivers were giving their consent in addition to the participant, or whether they were signing the consent form on the potential participant's behalf. Three of the 215 studies stated that they provided aphasia-friendly information sheets and consent forms[43,85] or study materials,[94] and in 1 of these studies a neuropsychologist met with potential participants to discuss the information and answer any questions.[43]

Adaptations to elements of the research process beyond consent

Twenty-seven of the 215 completed studies (12.6%) included adaptations to the research trial that could support the inclusion of people with aphasia. These adaptations included tailoring the intervention or research process to the needs of individual participants, producing written documents in accessible formats, using supported communication techniques,[17] including visual supports and prompts (eg, photographs or displaying topics or questions on a PowerPoint slide), using technology, providing instructions and information in multiple modalities (eg, using both written materials and training videos), sending information in advance of meetings or sessions, conducting communications and data collection through various mediums (eg, email, face-to-face or telephone and digital and hardcopy versions of materials), making environmental adaptations (eg, removing distractions), and working with significant others or clinicians. The appropriateness and accessibility of outcome measures for people with aphasia were considered in 5 studies.[38,42,88,90,99] One study[99] used the Visual Analog Self-Esteem Scale[100] as an outcome measure because it was developed for people with aphasia, and another[38] adapted the EuroQol-5 Dimension[101] to be aphasia friendly.

What was the attrition rate of people with aphasia from completed stroke trials?

Fourteen studies explicitly included people with aphasia. In the 8 studies where all participants were people with aphasia,[35,38,39,41,43,45–47] sample sizes at randomization ranged from 17 to 278. The attrition rate prior to the primary endpoint in these studies ranged from 0% to 20% with an average attrition rate of 10%. In the remaining 6 studies, where stroke participants included those with and without aphasia,[36,37,40,42,44,48] it was not possible to ascertain the rates of attrition for individuals with aphasia as information about the number of participants with aphasia was only provided at the point of randomization.

Discussion

This review builds on previous systematic reviews in distinct topic areas[10-14] and highlights patterns of exclusion for people with aphasia across a diverse range of stroke research. Across the stroke RCT literature, inclusion rates of people with aphasia are low, and documentation of both intended and actual inclusion is poor, resulting in a lack of clarity regarding inclusion practices. This review also provides insights into the nature of these problems.

The findings of this review contrast sharply with the fact that aphasia affects 30% of stroke survivors,[2] results in worse outcomes than those experienced by stroke survivors without

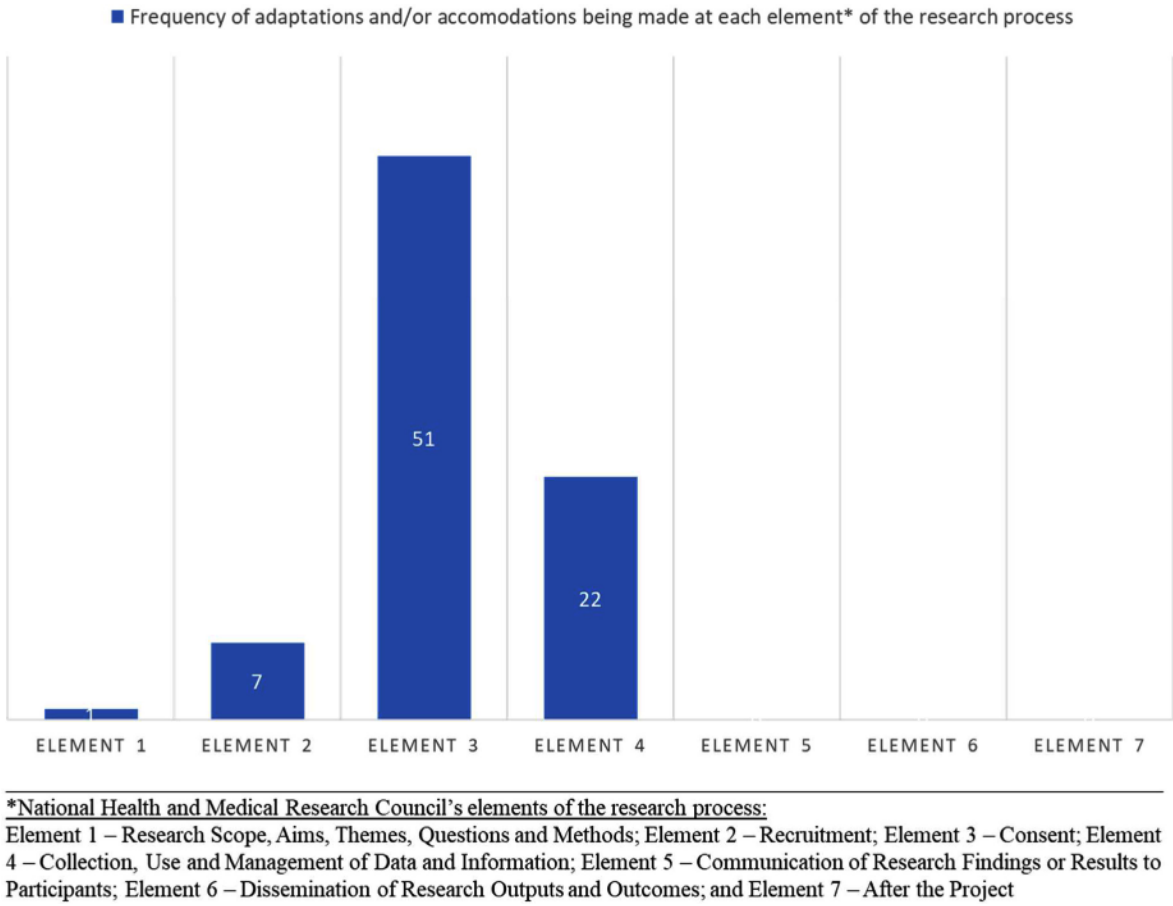

Fig 2 Frequency of adaptations made to the elements of the research process.

aphasia,[4-8] and is often chronic. The lack of explicit reference to aphasia in eligibility criteria, methods, or results in stroke research is problematic. There is a pressing need for greater inclusion of people with aphasia across stroke research. While this population requires additional support to enable their inclusion, 6 studies, spanning a range of medical and rehabilitation interventions beyond the discipline of speech pathology, demonstrated that people with aphasia can be successfully included in RCTs. It is also noteworthy that in the 8 studies that successfully included people with aphasia, the average rate of attrition was only 10%— similar to attrition rates found in other stroke RCT research (2%-7%).[102]

RCT protocols showed higher intended levels of inclusion (28.6%) than those seen in completed RCTs. This may indicate growing awareness, confidence, and skills among stroke researchers regarding the inclusion of people with aphasia. However, it may also indicate that while researchers intend to include people with aphasia in their studies, they face barriers to inclusion when the trial begins, leading to lower actual inclusion rates in practice. Taking an optimistic view, we could also hypothesize that the higher rates of planned inclusion seen in protocols reflect the opportunities in protocol publications for researchers to outline their methods in more detail than they can in the final publication of research findings; meaning that inclusion rates may be higher than reported. When publication word-counts limit the description of the trial population, supplementary files could provide additional or more specific information.

This review highlights the need for clear documentation and reporting processes regarding the inclusion of people with aphasia in stroke research. For example, some studies in this review implied the inclusion of people with aphasia but did not explicitly report it.[85,88,89,91,94,99,103-105] These studies reported broad inclusion criteria that could encompass people with aphasia (eg, individuals with cognitive and communication difficulties) and reported that they adapted their research processes to support the inclusion of those with aphasia (eg, by using aphasia-friendly materials). In 1 case, a participant with aphasia was mentioned for the first time in an appendix of the article.[103] However, as these authors did not report the number of people with aphasia that were included in the study, they did not meet our criteria to be counted as including people with aphasia. Unclear reporting practices of this nature make it difficult for readers to interpret stroke research and assess whether interventions were successfully trialed with people with aphasia, leading to uncertainty around the generalizability of stroke research findings to this population. Explicitly reporting data for participants with aphasia can reduce research waste, as it reduces the need for the duplication of research efforts specifically for this population and can enable sub-group analysis within larger studies. Given the pervasive lack of clarity regarding inclusion across stroke trials, reporting guidance specific to the inclusion of people with aphasia is needed.

Most stroke trials in this review lacked justification for the exclusion (whether total or partial) of people with aphasia. When provided, exclusion criteria and rationales often conflated aphasia with other conditions such as cognitive difficulties, and/or were open to interpretation. The primary reasons for exclusion across the literature in this review reveal a perception that people with

aphasia cannot meaningfully participate in research, whether because of difficulties communicating with the therapist/intervention provider, understanding and following study instructions, and/or engaging in interventions. However, there are many evidence-based accommodations that can be used to support people with aphasia to understand and participate in interventions and research successfully for example, supported communication techniques.[17] Further research is needed to understand stroke researchers' reasons for excluding people with aphasia, so that support and training tailored to stoke researchers' needs can be developed and more aphasia-inclusive research practices introduced.

This review also identified that aphasia was frequently assessed inadequately and inappropriately. Only 36.3% of the studies that excluded people with a particular sub-type or severity of aphasia stated how this was assessed or determined. The assessments/methods most frequently used to assess language were cognitive assessments, followed by researcher or investigator perception or opinion. Neither of these approaches are suitable, validated, or comprehensive methods of assessing aphasia. While they are informative, cognitive assessments do not differentially diagnose language from other cognitive impairments, and often rely heavily on language skills (eg, auditory comprehension and naming abilities),[106] which can lead to an overestimation of cognitive deficits in people with aphasia.[107] Without the use of standardized aphasia assessments, the process of recruitment and screening individuals with aphasia appeared to be left to subjective judgment—a concerning finding given that awareness of aphasia is low, even among healthcare professionals.[108] A lack of experience and skill in communicating with people with aphasia may further perpetuate these issues,[109] disadvantaging people with aphasia and affecting recruitment across sites. There is clearly a need for increased guidance and reporting of how aphasia is assessed and determined across stroke trials. Also, although many outcome measures have been developed specifically for people with aphasia,[110] many broader stroke outcome measures, for example, the Stroke Impact Scale,[111] do not have validated aphasia-friendly versions, leading to potential consequences for stroke trials, as researchers may need to choose between (1) substantially altering standardized measures (if permission is provided), compromising the validity and reliability of the outcome measure and the perceived rigor of the trial, potentially compromising publication; (2) administering an unmodified outcome measure to individuals with aphasia, compromising their ability to respond meaningfully and/or potentially masking their true abilities; (3) omitting the chosen measure for participants with aphasia, resulting in missing data and reduced participant numbers on analysis; and (4) excluding people with aphasia. Therefore, research is needed to develop a range of stroke outcome measures that are communicatively accessible, psychometrically valid, and reliable for people with aphasia.

At present, there appears to be minimal application of the adaptations and accommodations required to enable the meaningful and valid inclusion of people with aphasia across stroke trials. In addition, this review identified that when such adaptations were made, they were never made across all elements of the research process. Adaptions were mainly focused on consent (element 3), and the collection, use and management of data and information (element 4). This is concerning as people with aphasia can face barriers to meaningful inclusion at any stage of the research process that requires language and communication. Without making "reasonable accommodations" researchers may be unintentionally excluding people who are communicatively vulnerable,[14(p531)] restricting the rights of this population to express their opinions about what matters to them.[14] Working collaboratively with speech and language therapists and people with aphasia from the beginning of the research process could help to address this issue.

Little information is provided in stroke trials regarding how consent procedures are conducted and how capacity for those with communication difficulties, including aphasia, is determined. Consistent with the findings of Bunning et al,[112] this review found that greater focus was placed on how consent was documented (for example, signed consent forms) rather than the interactive process required in the consent procedure. The most common adaptation to the consent procedure was use of proxy consent, most commonly in hyper-acute and acute trials. This may relate to instances where proxy consent is indeed the most appropriate option, such as when consent needs to be obtained quickly in a hyper-acute setting or for an unconscious patient. However, the use of proxies should be considered carefully—in addition to the burden placed on the proxies themselves, many people with aphasia do not agree with proxies being used.[113] Wherever possible, all individuals should be empowered and given the autonomy to make their own choices about participation in research.[114] Prior to using proxy consent, all practical steps should be taken, using aphasia-accessible communication, to determine whether a person with aphasia has capacity.[96,115,116] Once capacity has been established, consent procedures should apply.[112] This process, and the adaptations and accommodations used to appropriately support this process, should be clearly documented,[112,114] as informed consent is "not a one size fits all".[114(p23)]

Due to the lack of clarity in reporting regarding the inclusion of people with aphasia in stroke trials, it is possible and perhaps likely that some people with aphasia have been included in these studies, but without adaptations and accommodations needed to support their inclusion. Such unsupported inclusion leads to a high risk of invalid results, attrition, and potential ethical violations. Adapting research processes to support the meaningful inclusion of people with aphasia will require an investment of time and resources up front but will likely result in savings with improved recruitment, retention, and applicability of findings. Current guidance, resources, and materials to support the inclusion of people with aphasia in research are outlined in the supplementary files of the companion paper by Shiggins et al.[15] Further work is required to develop training, resources, outcome measures, and guidelines that can support stroke researchers to include people with aphasia meaningfully in their studies, and thereby enhance the internal and external validity of stroke research.

The key issues identified in this review are (i) aphasia is rarely discussed or documented in either the protocols or the published findings of stroke trials, (ii) the number of people with aphasia included in stroke trials is not consistently documented and/or reported; (iii) there are low inclusion rates of people with aphasia in stroke trials across topics, disciplines, and the continuum of stroke care, (iv) justification for excluding people with aphasia (either total or partial exclusion) is absent or limited, (v) the terms "speech", "language", "communication", and "cognition" are often conflated, (vi) aphasia is often assessed inadequately and inappropriately for the purposes of determining eligibility, (vii) there is minimal application of the adaptations and accommodations required for the meaningful and valid inclusion of people with aphasia across stroke trials, and when these are made, they are mainly made at the consent stage of the research process, and (viii) little information is provided in stroke trials on how the consent procedure is conducted and how capacity for those with communication difficulties, including aphasia, is determined.

Limitations and strengths

A limitation of this review is the focus on stroke trials from only 1 reference year. However, this allows us to provide a detailed snapshot of practice. In addition, as the completed RCTs may have been conceptualized and conducted many years prior to publication, it is likely that we have captured inclusion practices across many years, and by including the RCT protocols, we aimed to capture inclusion practices in ongoing trials. Further limitations of this review are that we only included studies written in English, a limited search strategy was used and only 1 database was searched and, therefore, some stroke RCTs published in 2019 may have been missed. In addition, only 1 author (C.S.) screened articles for inclusion. A significant strength of this paper is that it contributes the first comprehensive investigation of inclusion practices for people with aphasia in stroke trials across topics, disciplines and the continuum of care; an issue of great importance to the stroke and aphasia populations.

Future directions

The intention of this review was to highlight an important issue in stroke trials and to raise awareness in stroke researchers about the need for aphasia-inclusive research practices in the design and conduct of stroke research. Like Bunning et al,[112] we believe that a more nuanced approach to including people with communication difficulties in research is needed. We acknowledge that there are challenges associated with including people with aphasia in stroke research that can make the process difficult for stroke researchers. What remains unclear from this review is the nature of these barriers and what might best enable inclusion from the perspective of stroke researchers. Future research could explore these questions with stroke researchers in order to develop training, guidelines and resources that reduce researcher burden and increase participant inclusion and positive research experience.

Conclusion

Despite the high prevalence of aphasia among stroke survivors, the significant negative impacts of aphasia on a person's life, and the fact that people with aphasia have poorer outcomes than stroke survivors without aphasia, people with aphasia are regularly excluded from stroke research. This review is consistent with findings of previous research indicating a lack of clear reporting on the inclusion of people with aphasia in stroke research and the supports provided to enable their inclusion. This review has highlighted a significant issue in stroke research, which has the potential to affect the validity of stroke research, and its generalizability to the whole stroke population. There is a pressing need to improve reporting in stroke trials and protocols to benefit stroke researchers and all stroke survivors. We call for the increased inclusion of people with aphasia in stroke research, and for this inclusion to be supported and meaningful.

Keywords

Aphasia; Clinical trials; Ethics; Inclusion; Rehabilitation; Research; Stroke

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