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Research Article

Preventing Stroke Research Priorities Project: An Initiative of Synergies to Prevent Stroke (STOPstroke)

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Background: Research priority setting projects provide a method to engage stakeholders in the prioritisation of research activities. We conducted a priority setting project to identify priorities for research into the primary and secondary prevention of stroke.
Methods: A modified James Lind Alliance method was used for this project undertaken in Australia and New Zealand with two online surveys (September–November 2021 and May-June 2022) and an online workshop (August 2022). The main question addressed was 'What question about preventing stroke would you like to see answered by researchers?' Responses to Survey 1 were refined and reviewed to identify evidence uncertainties. Questions with uncertain evidence were presented in Survey 2 where participants rated the importance of questions. Quantitative analysis of the importance ratings identified highly rated questions. These questions were taken to the online workshop with two rounds of facilitated discussion to create a final list of priorities. A postworkshop evaluation questionnaire explored user's perceptions of the process.
Results: In Survey 1, 375 people proposed > 700 research questions. These were refined to 134 questions that were checked against evidence with 47 determined to be unanswered and distributed for consideration in Survey 2. Respondents to Survey 2 ($n = 97$) rated 24 of the 47 questions highly that were then discussed in the online workshop ($n = 16$ participants). There was agreement on the most highly rated question 'How can we improve early detection and measurement of stroke risk?' but limited agreement on the remaining questions. Participants favoured keeping all questions but presenting them thematically. The final list includes 22 questions under behavioural; pharmacological/clinical; structural; policy; individual; population and secondary prevention themes. Participants rated the workshop experience as acceptable.
Conclusion: A suite of research priorities for the primary and secondary prevention of stroke were identified by a broad range of stakeholders including people with lived experience of stroke, the public and health professionals.

1. Background

There is evidence that 90% of strokes are preventable [1]. This is because the population attributable risk for up to 90% of strokes is due to potentially modifiable risk factors, such as high blood pressure and smoking. Efforts to prevent stroke have been somewhat successful with the incidence and mortality rates for stroke generally decreasing over time [2].

However, there are several reasons why we cannot be complacent about stroke prevention. First, stroke incidence has plateaued in some age groups and even increased in younger people in some populations [3]. Second, although the rate of recurrent stroke has declined over time, it remains high at up to 25% within 5 years of the first event [4, 5]. Third, demographic changes with a shift to older populations and improved survival mean that the absolute numbers of strokes will increase by up to 70% in the coming decades [4]. We must, therefore, seek innovative ways to enhance the primary and secondary prevention of stroke.

The important role of the community in guiding health research priorities is increasingly recognised [6]. Most health research is funded by tax payers and, therefore, it is important to consider the priorities of the community when planning, conducting and translating health research. Research priority setting projects use a structured approach to canvass the opinions of stakeholders. Priority setting projects generally include the general public, policymakers and clinicians on areas requiring research [7]. Such projects in stroke research are scarce, with examples focussing on treatment and rehabilitation rather than prevention [8, 9]. Most recently, the UK Stroke Association used a James Lind Alliance Priority Setting Partnership (PSP) to explore research priorities for stroke in general [10, 11]. The outcomes included two 'Top 10' lists, one for 'prevention, diagnosis and hospital care' and the second for 'rehabilitation and long-term care.' One of the 'Top 10' priorities was 'identifying the best interventions for the primary prevention of stroke,' creating an opportunity to explore the specific community priorities for research into primary and secondary prevention of stroke.

We successfully obtained an Australian National Health and Medical Research Council Synergy Grant (Synergies TO Prevent stroke (STOPstroke)) in 2020 to address the urgent need to improve prevention of stroke. As part of the program's community engagement framework, we decided that a research priority setting project focused on stroke prevention was essential for guiding our research direction. Here, we describe the methods and results from our priority setting project for stroke prevention undertaken in Australia and New Zealand.

2. Methods

2.1. Design. The STOPstroke priority-setting method was informed by the James Lind Alliance methodology for PSP but was conducted independently using publicly available guidelines [12]. It was not possible to conduct a formal PSP with the James Lind Alliance due to resource constraints. Most PSP do not involve researchers in the conduct of the project. Given the nature of the funding for this program, we included some researchers in the design, implementation and interpretation of the priority setting activities.

The project incorporated terms of reference and an independent advisory group (see supporting information (available here)) comprising health professionals, researchers and people with lived experience of stroke or cardiovascular disease from across Australia and New Zealand. The project was approved by the University of Tasmania Human Research Ethics Committee (H0024539).

2.2. Participants. The target participants for the priority setting project were the general community of Australia and New Zealand. This included members of the public, health professionals (e.g., general practitioners, neurologists, physiotherapists, occupational therapists and nurses) and researchers. Participants were recruited through paid social media advertising, printed postcards in public locations (e.g., libraries) and through the networks of the research team and independent advisory group in Australia and New Zealand.

2.3. Structure. Broadly guided by the James Lind Alliance priority setting approach (Figure 1) and the Steering Group, we conducted two surveys and one workshop to prioritise the research questions provided by respondents on preventing stroke.

The two surveys were made available online through REDCap hosted by the University of Tasmania. The survey asked people to self-identify as being over 18 years of age and residing in Australia or New Zealand [13, 14]. Between September and November 2021, we distributed the first survey across Australia and New Zealand. In this survey (Survey 1—Unanswered questions about preventing stroke, see online Supporting Information (available here)), we asked participants 'What question about preventing stroke would you like to see answered by researchers?' Participants could provide up to three responses to these questions.

Between December 2021 and April 2022, we used the responses collected in the first survey to derive a list of unanswered summary questions based on two processes. First, we categorised and refined the initial questions to produce a list of in-scope and out-of-scope summary questions. In-scope questions were related to the primary and secondary prevention of stroke. Out of scope questions were about other topics related to stroke, e.g., rehabilitation and recovery. We then checked the in-scope summary questions against published evidence to determine whether they had already been answered by research. Based on previous priority setting projects [10], we considered that there was evidence for a particular question if it was addressed in management guidelines, scientific statements or systematic reviews/meta-analyses.

The second survey (Survey 2—Prioritisation of unanswered questions about preventing stroke—see supporting information (available here)) was distributed between May and June 2022. This involved prioritisation of the relevant in-scope questions, where participants were asked to indicate the importance of each question from a score of 1 (extremely important) to 5 (not important at all). We also included an option for 'do not know.' The research team then examined mean scores for each question, excluding the do not know responses, with a goal of reducing the number of questions to around 20–30, if more than 30 were provided, aligning with previous priority setting projects [12]. Examination of

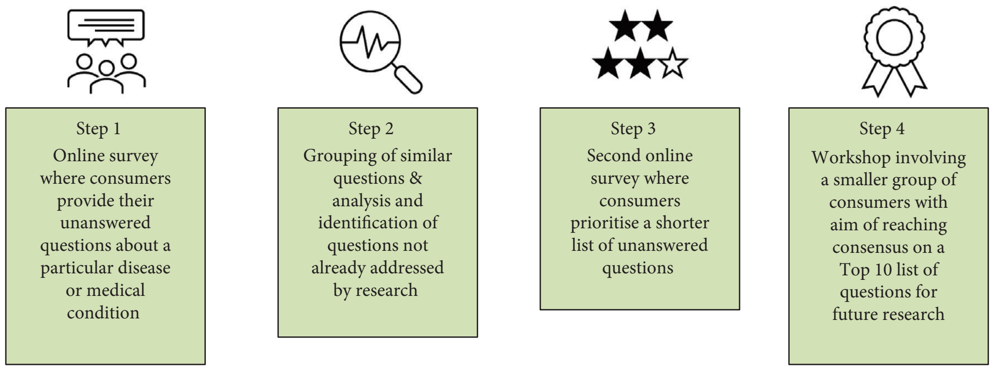

FIGURE 1: Overview of priority setting process using the modified James Lind Alliance method.

the scores according to the stakeholder group (i.e., health professionals, community and people with lived experience of stroke) also enabled us to consider whether there were large differences in priorities between groups, which could be considered in the workshop discussions.

To obtain a final 'Top 10' set of questions, on the 2nd of August 2022, we ran a half-day online prioritisation workshop to discuss and rank the higher priority questions from the second survey. Participants for the workshop were selected from expressions of interest from both survey rounds. We purposively selected people to have diversity of gender, location (e.g., country and regions) and type of lived experience (e.g., health professional, community member and person that had a stroke). Prior to the workshop, participants were given a list of questions to consider and do their own preworkshop ranking (see supporting information (available here)). However, workshop participants were not provided with the rankings from the second survey. The workshop was structured to have two rounds of prioritisation. We completed the first round of prioritisation sorting questions into highest, middle and lowest priority. The second round of prioritisation was designed to rank the highest priority questions into a Top 10. Participants in the workshop were sent an evaluation survey that included seven questions about their workshop experience (e.g., technology and facilitators) and free-text responses to provide any additional comments having reflected on the workshop event (see supporting information (available here)).

3. Results

3.1. Survey 1—Unanswered Questions About Preventing Stroke. In the initial survey, 375 respondents proposed over 700 unanswered research questions about preventing stroke (Table 1). The questions broadly fell into the following themes: (1) age and risk; (2) surveillance and assessment; (3) pre-existing medical conditions and medication risks; (4) medication for prevention; (5) lifestyle, environment and cultural risk factors; (6) hereditary risk factors and (7) education. After refinement to remove duplicates and create summary questions, 134 questions were checked against evidence. This resulted in 47 questions identified as unanswered by research.

TABLE 1: Characteristics of participants in surveys and workshop for preventing stroke research priority project.

Characteristics	Survey 1 $n = 375$	Survey 2 $n = 97$	Workshop $n = 16$
Gender			
Male	68 (18.1%)	25 (25.8%)	7 (43.7%)
Female	289 (77.1%)	70 (72.2%)	9 (56.3%)
Not reported	18 (4.8%)	2 (2.1%)	—
Age group (years)			
18–29	7 (1.9%)	3 (3.1%)	—
30–49	65 (17.3%	20 (20.6%)	—
50–69	163 (43.5%)	49 (50.5%)	—
70+	124 (33.1%)	22 (22.7%)	—
Not reported	16 (4.3%)	3 (3.1%)	—
Group*			
General community	213 (56.8%)	38 (39.2%)	4 (25.0%)
Lived experience	92 (24.5%)	23 (23.7%)	6 (37.5%)
Health professional	33 (8.8%)	28 (28.9%)	4 (25.0%)
Researcher	14 (3.7%)	6 (6.2%)	2 (12.5%)
Not reported	23 (6.1%)	2 (2.1%)	—
Location			
Australia	263 (70.1%)	78 (80.4%)	15 (93.7%)
New Zealand	112 (29.9%)	19 (19.6%)	1 (6.3%)

*Participants could select up to two categories. We collapsed response to a single category prioritising lived experience over all other categories, followed by health professional and researcher.

3.2. Survey 2—Prioritisation of Unanswered Questions About Preventing Stroke. A total of 97 respondents participated in the second survey to rate the importance of each question (Table 1). At a mean score of 2.16, 24 highly rated questions were identified (Table 2). The rank of the top-rated questions by community, health professionals and researchers was generally consistent. The top-rated question in Survey 2 based on the mean score was 'How can we improve early detection and measurement of stroke risk?,' although researchers scored this substantially lower than the community or health professionals.

3.3. Final Prioritisation Workshop. Table 1 describes the attendees of the final priority-setting workshop. This included people with lived experience of stroke ($n = 6$), general interest in stroke ($n = 4$), healthcare professionals ($n = 4$) and researchers ($n = 2$). There was agreement across all groups

Table 2: Priority rating of 47 questions to derive the top 24 questions about preventing stroke from Survey 2.

Question	Ranking by stakeholder group				
	Overall	Community	Health professionals	Researchers	People with lived experience
How can we improve early detection and measurement of stroke risk?	1	2	2	17	1
What can be done to improve the translation of research on stroke prevention into clinical practice?	2	4	1	2	2
What is the role of modifiable risk factors (like diet and exercise) in preventing stroke in people with a family history of stroke?	3	1	9	37	2
How effective is an education program, based on a cardiac rehabilitation model, for preventing a second or subsequent stroke?	4	8	4	5	2
How can people living in regional or remote areas best receive information about stroke prevention strategies?	5	9	8	10	10
What are the exercise guidelines to reduce the risk of stroke?	6	4	17	17	14
How can we ensure people have access to up-to-date and evidence-based health information for stroke prevention?	7	3	24	16	17
For people with pre-existing cardiac conditions, what is the optimal level of exercise to prevent stroke?	8	7	17	25	7
Does informing people of their risk of stroke increase their engagement in risk factor management to prevent stroke?	9	10	4	25	9
Are there different interventions (e.g., diet or exercise recommendations) at different ages to reduce the risk of stroke?	10	6	12	17	17
What are the dietary guidelines to reduce the risk of stroke?	11	11	15	4	17
What can be done to motivate people to manage their stroke risk factors?	12	12	11	3	22
If prescribed treatments are not followed by patients (i.e., taking blood pressure medication), how many will go on to suffer a stroke?	13	18	19	5	12
Can improved perioperative management reduce the incidence of stroke in high-risk patients?	14	20	16	11	5
What is the burden of stroke associated with poor management of atrial fibrillation?	15	14	12	11	11
What is the safety and effectiveness of a cardiovascular polypill for stroke prevention?	16	15	19	5	13
What are the effective components of community-based programs for the prevention of stroke?	17	17	3	11	22
What are effective policy interventions to reduce the risk of stroke (e.g., health promotion, advertising restrictions, taxation, health screening)?	18	16	25	1	21
How can secondary prevention be improved for people with communication disabilities (e.g., aphasia, difficulty reading)?	19	22	4	17	6
What clinical training/information/guidelines are required for the treatment of refractory hypertension to reduce the risk of stroke?	20	13	23	9	20
If a young adult (i.e., under 65 years old) has had a stroke, is the chance of subsequent stroke different to that of an older person?	21	23	21	31	8
How do genetics and the environment interact to reduce stroke risk?	22	24	4	5	31
What is the role of screening for PFO in young adult stroke patients (i.e., under 65 years old) to prevent second or subsequent stroke?	23	25	14	35	15
Across different ethnicities and races, do the causes of stroke and risk factors for stroke differ?	24	28	9	11	34

Note: Green shading represents questions within the top third as ranked by an individual group. Orange shading represents questions in the bottom third as ranked by an individual group. The 24 questions included in the second survey included the entire top third for all groups except for 'Researchers' where one question ranked equal 11th was not included in the final 24.

that the top-rated question was 'How can we improve early detection and measurement of stroke risk?' We were unable to gain consensus on the remaining top 9 or their ranking. In the final group discussion, it was decided to proceed with all 24 questions but to group them thematically. We subsequently used a framework recently developed by Bam et al.

[15] to group the questions thematically (Figure 2) into (1) behavioural, (2) pharmacological/clinical, (3) structural, (4) policy, (5) individual and (6) population. We also distinguished between questions focused on primary compared with secondary prevention. We collapsed some questions together to create a final list of 22 questions under these themes. We have provided a description of each question including evidence uncertainties in the online supporting Information (see supporting table (available here)).

The evaluation of the workshop demonstrated that the online approach was accessible for all participants and the platform (Zoom) was easy to use. Participants reported that the workshop was too long and that management of breakout groups could be reviewed (data not shown).

4. Discussion

We have generated a comprehensive list of contemporary research priorities for stroke prevention developed in consultation with the community, health professionals and researchers. The priority setting activity identified 22 priorities for research across primary and secondary prevention. The framework for stroke prevention recently developed by Bam et al. [15] allowed us to group research questions under six themes: behavioural, pharmacological/clinical, structural, policy, individual and population. The diversity in the questions across this range of themes was not surprising given the number of potential mechanisms for stroke and the potential leverage points for intervention at the level of the individual, the health system and policy. This list of potential unanswered research questions will be of use to a broad range of stakeholders including researchers, health professionals, service providers and policymakers.

The question that was identified as the highest priority was 'How we can improve the early detection and measurement of stroke risk?' Addressing this question requires interdisciplinary action across disciplines including epidemiology, health services research, public health, primary care and specialist areas such as general practice, cardiology and neurology. It will also require the use of quantitative and qualitative methods. The currently recommended process for measurement and management for cardiovascular disease (including stroke) risk in Australia and New Zealand, as well as other countries, is based on absolute cardiovascular risk. While the equations differ somewhat between the countries, the objective is to identify and manage people at 'high' risk [16, 17]. One limitation of these risk prediction equations in the context of stroke prevention is that they provide estimated risk of all cardiovascular diseases combined, potentially limiting the ability to raise awareness of stroke specifically. They may also be restricted to use in people under a certain age (e.g., 79 years in Australia or 84 years in the UK). This has implications for prediction of the risk of strokes, which are more common in older people than cardiac events. The appropriateness of this 'high risk' approach is debated by some due to the lack of empirical evidence [18]. There is also low (about 20%) uptake of the absolute cardiovascular risk approach by primary care health professionals [19], with a high cost of the screening programmes [20]. There is also debate about whether the 'high' risk approach deprives people with low to moderate cardiovascular risk, in whom a large proportion of strokes and myocardial infarctions occur, from effective prevention [21].

The strategies to enhance early detection and measurement of stroke risk may include primary care and digital health. In Australia, the 'heart health check' for people aged 45 years and over provides a rebate to general practitioners to do a comprehensive cardiovascular risk assessment [22]. While uptake is increasing, the use of this assessment is still suboptimal [19], possibly due to limited engagement with general practitioners in its design and implementation. The branding of the assessment as the 'heart' health check may reduce opportunities to raise awareness of the links between cardiovascular risk factors and stroke in the community. There are other longer assessments available through general practice in Australia and New Zealand that attract government rebates that also provide opportunities for comprehensive risk assessment and preventive healthcare on an annual basis. Future research may explore alternative models and optimisation of delivery at scale including the benefits of raising awareness of available screening or assessments among the community or health professionals. Digital health approaches using mobile applications (mHealth) or web-based approaches (eHealth) may also address this issue at a population level, for example, the Stroke Riskometer. The evidence for digital health interventions for stroke prevention is emerging [23], with several ongoing trials [24]. The growing access to smartphones and internet, even in low resource settings, makes digital health approaches for stroke prevention appealing.

Many of the top priorities related to areas that have considerable evidence for preventing stroke, e.g., diet or physical activity, but with nuances (e.g., benefit of *specific* diets or *types* of physical activity), meant we included them as uncertainties. For example, there were questions regarding the effectiveness of interventions in subgroups, e.g., those with a family history or specific comorbidities. When checking the evidence in this priority setting project, we used the methods from the recent UK Stroke Association PSP where clinical guidelines, systematic reviews or meta-analyses and scientific statements were deemed to be certain 'evidence.' It is possible that there is evidence for some of the priorities in individual studies that were not captured using these sources. A first step for the research community may be to explore the questions in systematic reviews and meta-analyses.

During the evidence checking process, there was often evidence for the prevention of cardiovascular diseases broadly (e.g., major adverse cardiovascular events including stroke) or for specific cardiac events, e.g., myocardial infarction, but less often for stroke specifically. Whether it is necessary to gather new evidence or reanalyse previous studies to determine the stroke-specific effects is unclear. One approach could be to adapt and implement interventions for stroke prevention that are effective for the primary or secondary prevention of myocardial infarction. Also relevant is that scientific statements or clinical guidelines may not include up to date evidence. The advent

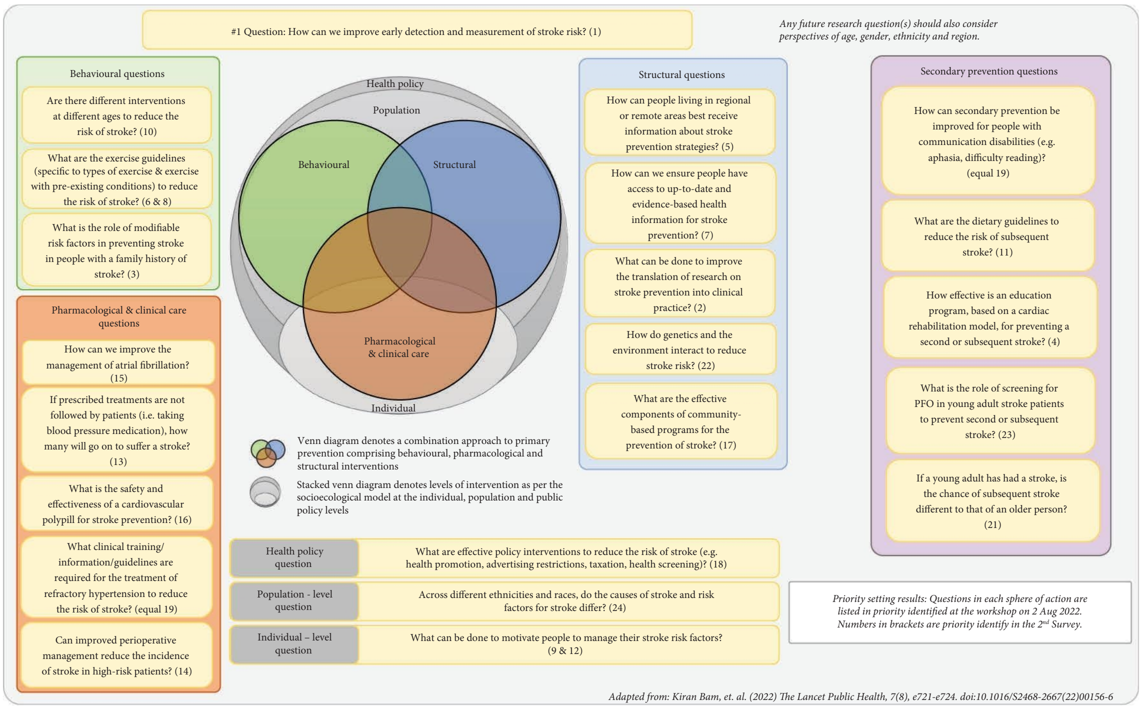

Figure 2: Preventing stroke research priorities.

of 'living' guidelines should circumvent this in the future, but the living Clinical Guidelines for Stroke Management coordinated by Stroke Foundation in Australia include only secondary prevention of stroke, not primary prevention [25, 26]. While the American Heart Association's guidelines for stroke do include primary prevention of stroke, these guidelines have not been updated since 2014 [27]. We recommend that these international primary prevention guidelines are updated, particularly using a living model. This will ensure clinicians, policymakers and the community can have access to up-to-date information on how to prevent stroke.

A strong theme was questions regarding differences in the effectiveness of interventions in particular subgroups, many of whom are under-represented in research [28, 29]. This includes effectiveness according to gender, age, race, ethnicity and rural or remote settings. We would also argue that this should include people experiencing social disadvantage, even though this was not specifically identified in our activity. PROGRESS-Plus provides a framework whereby researchers can consider the drivers of health inequalities [30]. Our overarching recommendation for all further research into stroke prevention is that these factors should be considered in the development and evaluation of all research. This could be in the form of stroke prevention research focussing on specific groups or study designs that ensure subgroup analyses are included, and reported, a priori. Considering codesign with the community in the development of stroke prevention research will ensure that subgroups are considered in meaningful ways. Including these considerations in future research on stroke prevention is essential for ensuring the inclusiveness of interventions to reduce the risk of stroke across the population.

This priority setting project was done to inform the specific research for STOPstroke, which is a 5-year grant including researchers and health professionals from five Australian and New Zealand institutions. The aim of STOPstroke is to reduce the burden of stroke by improving the evidence base for primary and secondary prevention. The questions from this priority setting project will feed into the program's three themes: (1) better prediction of who will have a stroke; (2) improved management of people at risk of stroke and (3) developing a national platform for stroke surveillance and cost-effective intervention modelling. This project adds to the most recent priority setting projects led by the Stroke Association in the United Kingdom, where they identified questions presented in two 'Top 10' lists: (1) stroke prevention, diagnosis, prehospital and hospital care and (2) stroke rehabilitation and long-term care. The top priority in the 'stroke prevention, diagnosis, prehospital and hospital care' priorities was 'What are the best interventions to stop stroke happening for the first time (i.e., primary prevention)?' Other relevant questions were on the risks, benefits and timing of 'blood thinning treatments.' There is clear alignment between our top-rated question and that in the recent UK-based project. However, as our priority setting project was executed to directly inform the STOPstroke programme solely on stroke prevention, it provided a deeper insight into research priorities.

The limitations of this project include the lack of representativeness in the participants in each stage of the project. We had a reasonable sample size in Surveys 1 and 2 but these were mostly older women, meaning the questions provided initially may be focused on the priorities of that group. There were some discrepancies between the highest priorities for researchers and the other participants, noting that there were few participants who were researchers. We purposefully recruited to the workshop that provided a balance of genders, location and stakeholder groups, thereby providing some confidence that the final questions are priorities across a broader range of people. However, we did not collect the age or ethnicity of workshop participants, so we cannot comment on the generalisability of our findings by age and ethnicity. With that said, one of our recommendations for research that came from the surveys and workshop was that research should consider these aspects of diversity, equity and inclusion in their design, analysis and reporting. The use of only certain types of evidence may be a limitation, as noted earlier. The strengths include that the project was overseen by an independent advisory committee with membership balanced by gender, age, location and stakeholders. The use of online surveys and workshops meant that people from across Australia and New Zealand in any location could participate. While we asked people to self-identify as living in Australia or New Zealand, the survey was distributed by a public link. It is, therefore, possible that people outside of these countries responded. We do not think this has affected the validity of our findings as although we were interested in people from these two countries due to our setting, it is likely that people in other countries have similar priorities regarding stroke prevention research. This will not have affected the workshops, which were done online with participant locations known.

In conclusion, this research priority setting project identified a broad range of novel, unanswered research questions about stroke prevention. The resulting questions fall under broad themes that can be addressed by the stroke research community both in Australia and New Zealand and globally and that align with the needs of a diverse range of stakeholders.

Data Availability Statement

The data underlying these analyses may be provided by the authors with appropriate ethics and governance approvals in place.

Conflicts of Interest

The authors declare no conflicts of interest.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. *(Supporting Information)*

The supporting information provided in the PDF contains the terms of reference for the steering group for the project; the REDCap data collection tool for Survey 1; the REDCap data collection tool for Survey 2; the prereading provided to workshop participants; the feedback survey provided to workshop participants and a supporting table containing each of the final priority setting questions including specific examines of questions provided by respondents, evidence that the question is unanswered and the respondent groups that provided each question.

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