THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Health-enhancing physical activity programme (HEPAP) for transient ischaemic attack and non-disabling stroke: recruitment and compliance

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Abstract

Aim To assess the feasibility of recruiting and retaining patients newly diagnosed with a Transient Ischaemic Attack (TIA) into an 8-week exercise programme.

Methods: The study was a single-centre, randomised-controlled trial. TIA was confirmed by a specialist stroke physician within 7 days of symptom onset. Following baseline assessment, participants were randomised to either an 8-week exercise intervention or control group (usual care). Participants completed a further assessment 2 months after baseline.

Results Of the 285 individuals diagnosed with TIA, 97 patients were invited to participate in the trial, of which 60 were successfully recruited (62%). Of those invited, 89% were identified within outpatient care. Individuals were typically of European descent (87%) and lived within 20km of the study site (81%). Distance to travel was considered the primary barrier for non-participation (46%). Three participants (5%) did not attend the follow-up assessment.

Conclusion Individuals with TIA were successfully recruited and retained into a RCT. A different approach is required to study interventions in Māori, Pacific Islanders, Asian and Indian populations. If the exercise intervention improves vascular risk factors and reduces recurrent vascular events, it could be applied to a large number of people who suffer a TIA or non-disabling stroke.

Stroke is a common cause of death and is the leading cause of disability in New Zealand (NZ), with approximately 7000 people suffering an initial or recurrent stroke each year.[1] Stroke has an enormous physical, psychological and financial impact on individuals' lives.[1,2] When symptoms of stroke resolve within 24 hours it is known as a transient ischaemic attack (TIA).

Individuals classified with a non-disabling stroke have minor residual symptoms which are managed by the same treatment paradigm as TIA. With the risk of stroke elevated soon after TIA and minor stroke, recurrent events are commonly fatal or disabling.[3,4] There will be major public health benefits if interventions are developed to reduce the burden of recurrent stroke and disability following TIA.

Many individuals presenting with a TIA have predisposing risk factors such as hypertension, tobacco use, diabetes mellitus, hyperlipidaemia, obesity and physical inactivity.[5] It has been suggested that 80% of recurrent vascular events could be prevented through a comprehensive multi-factorial strategy.[6] Exercise-based cardiac rehabilitation (CR) has been shown to improve each of these risk factors, and reduce morbidity and mortality among coronary artery disease (CAD) patients.[7]

Preliminary evidence suggests that TIA patients in the non-acute phase, within 12 weeks and 5 years of an event, can reduce vascular risk factors and improve their cardiovascular fitness by following a CR-type programme.[6,7] However, very little is known about when to engage new TIA patients in exercise and education programmes and whether these may reduce recurrent vascular events.

Participant recruitment is considered the most difficult aspect of the research process,[8] with trials typically unable to conclude on schedule due to low participant accrual and retention.[9] Evidence-based feasibility studies are conducted to ensure that difficulties associated with study design are avoided when completing future randomised controlled trials (RCT).[10] Feasibility studies are needed to validate recruitment and consent procedures, confirm effect sizes and power calculations for sample size, confirm study inclusion and exclusion criteria, test the appropriateness of questionnaires, and monitor the operational process of the study.[9]

Despite the integral role of recruitment in RCT, publication of data defining the recruitment effort is not routine in rehabilitation initiatives.[9,11] This information is vital in order to design definitive exercise intervention trials.

The purpose of the present study was to assess the feasibility of recruiting and retaining patients newly diagnosed with TIA or non-disabling stroke into an 8-week health enhancing physical activity programme (HEPAP).

Methods

Study design—The study was a single-centre, randomised, parallel-group clinical trial. TIA was confirmed by a specialist physician at Wellington Regional Hospital within 7 days of symptom onset, in accordance with the NZ TIA guidelines.[12] Following baseline assessment, participants were randomised to either an 8-week exercise and education intervention (HEPAP) or control group (usual care). All participants completed a further assessment 2 months after the baseline assessment (Table 1).

Sample size—To attain sufficient data to analyse the difference in treatment effect between HEPAP and control ($P<0.05$; effect size [ES] 0.80), which would enable an appropriate sample size calculation for a full RCT,[19,20] the study intended to recruit 60 subjects. It was postulated that 9 months would be required to complete participant recruitment, on the basis that one-to-two patients (out of the average 6-to-10 newly diagnosed TIA patients) would volunteer each week.

The study has been powered to assess for a secondary rather than a primary outcome measure (i.e., blood pressure) as insufficient data is currently available to estimate a potential treatment effect of exercise on recurrent stroke and TIAs.

Ethics approval—Ethical approval was ascertained from the Central Regional Health and Disabilities Ethics Committee (NZ).

Participants—Individuals residing within New Zealand's Capital and Coast District Health Board (CCDHB) catchment area and who were diagnosed with new TIA or non-disabling stroke were eligible to participate. Exclusion criteria included oxygen dependence, uncontrolled angina, unstable cardiac conditions, uncontrolled diabetes mellitus, severe claudication, febrile illness, significant cognitive impairment and immobility. All participants were required to comply with drug treatment and standardised therapy in accordance with recommendations from the stroke physician as per the NZ TIA treatment guidelines.[12]

Patient identification and recruitment—Following stroke physician approval, TIA patients were provided written information and a verbal explanation of the purpose of the study, and were invited to participate. Patients provided verbal consent to the clinical team to release their contact details to the study team at the local academic institution (AI). Potential recruits were contacted by telephone to identify whether they were interested in participating in the study. Non-respondents to the initial telephone call were phoned until contact was achieved.[21]

Patients who declined to participate were given the opportunity to provide a reason why. For those agreeable for baseline assessment, a suitable date and time was arranged at the AI. Written consent was obtained at this stage.

Table 1. Trial assessments and intervention

Baseline assessment	8 week intervention		Follow-up assessment
	HEPAP	Normal care	
Health History Questionnaire[13] Physical Activity Questionnaire[13] Coronary Artery Disease (CAD) risk stratification[13] • Total lipid profile – Total cholesterol (TC), high-density lipoproteins (HDL); TC:HDL ratio[b] • Fasting blood glucose[b] • Seated/standing/supine systolic & diastolic blood pressure[c] • Smoking history • Family history of CAD • Waist & hip girth • Height, weight, Body Mass Index Peak or symptom limited exercise ECG stress test on a treadmill[d] • Modified Bruce protocol[13] Cycle ergometry test to provide submaximal estimates of oxygen consumption[e] • 2 x 3min stages (30 & 60 W) Psycho-social questionnaires • Short-form 36[14] • Profile of Mood States[15] • Stanford Medical Centre Stroke Awareness Questionnaire • Hospital Anxiety and Depression Scale[16] • International Physical Activity Questionnaire[17]	*Exercise* 2 x 90 minute exercise sessions per week • 15 min walking & 15 min cycling • 60 min of resistance training (alternate arm biceps curl & shoulder press, pec-dec, dumbbell press), core-stability and postural exercises using buso and swiss balls, and flexibility exercises • Blood pressure, heart rate and ratings of perceived exertion (RPE)[18] monitored throughout exercises *Education* 1 x 30 min group discussion each week concerning the following issues: Stroke facts, understanding stroke, risk of stroke after TIA, stroke prevention, dietary advice, blood pressure, physical activity participation, coping with stress, fatigue after stroke	Monthly telephone calls	See baseline assessments

[a]CardioChek, Hannover, Germany; [b]Optium, Abbott Diabetes Care, Victoria, Australia; [c]Accoson Works, London, England; [d]Schiller, Baar, Switzerland; [e]Monark Ergometer, Sweden

Distance between patients' residential address and the assessment site were calculated for each individual, whether recruited or not. The assessment and intervention site was at the AI, located within 1 km of the hospital.

Randomisation—Randomisation to the HEPAP or control group occurred after baseline assessment. Allocation to groups was by means of sealed envelopes drawn by the participants, designed for a 50:50 allocation between groups. Due to the nature of the intervention, it was not feasible to blind patients or researchers to group allocation.

Statistical analysis—Independent sample t-tests were used to assess the effect of residential locality on participant recruitment, and whether there were any differences in the demographic characteristics of randomised and non-randomised participants. Levenes' test for equality of variance was used to assess the variance in values between conditions. All data were analysed using the statistical package SPSS for Windows (version 18).

Results

Participant recruitment—97 TIA patients met study inclusion criteria and were invited to participate in the trial. Of these 62% (n=60) attended baseline assessment and were randomised (Figure 1).

Figure 1. Patient recruitment to HEPAP study

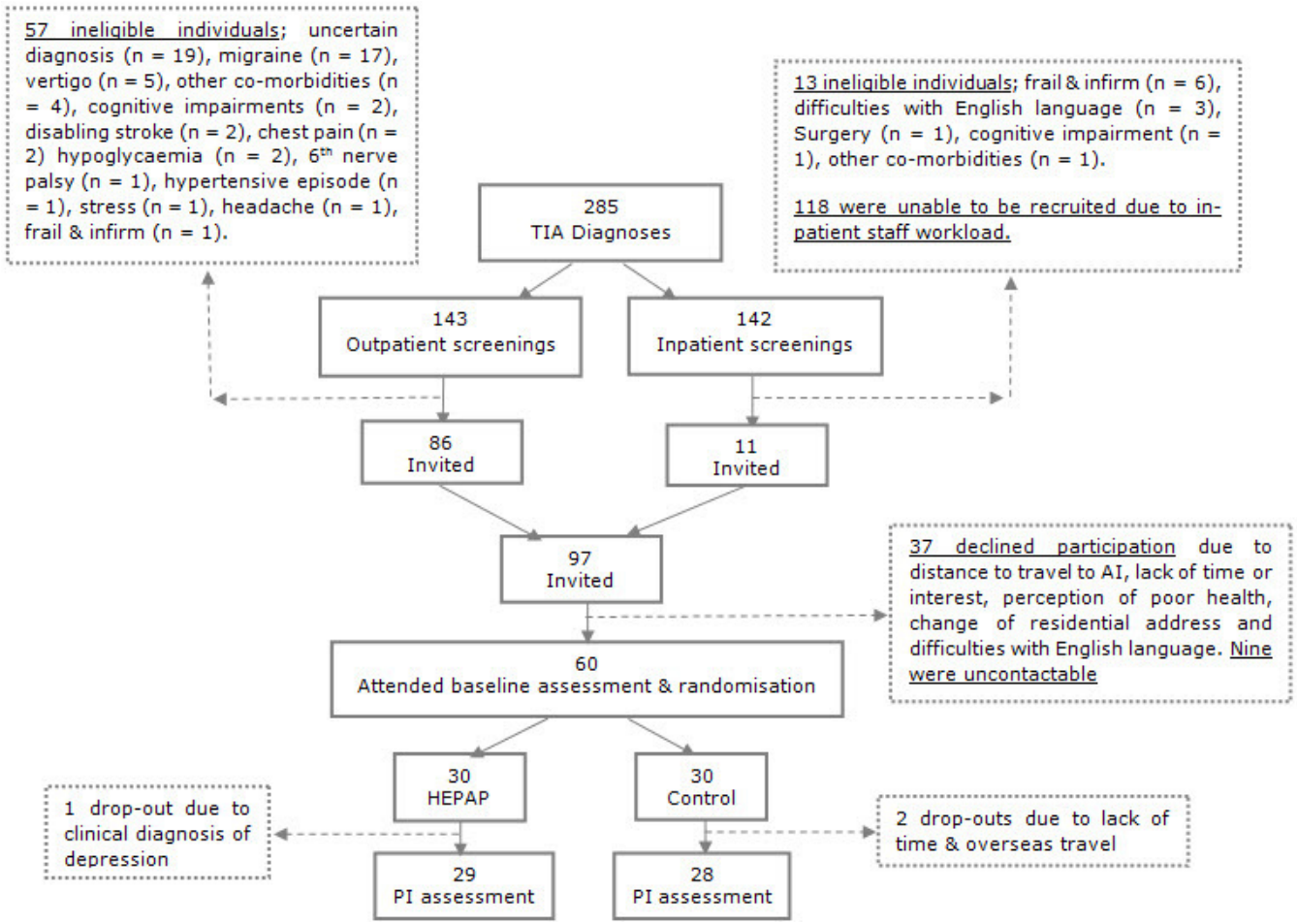

Table 2 describes participant characteristics between randomised and non-randomised participants. There were no significant differences between the age, gender, ethnicity or diagnosis category of randomised and non-randomised participants (all P>0.05).

Table 2. Demographic characteristics and diagnostic categories of randomised and non-randomised participants

Variables		Total	Randomised	Non-randomised
Age (y)		68.5 ± 10.4	67.3 ± 10.5	70.8 ± 10.1
Gender (male; n)		51	31	20
Ethnicity (n)	European NZ	84	53	31
	Māori	3	1	2
	Pacific Islands	5	3	2
	Asian	3	2	1
	Indian	2	1	1
Diagnostic category (n)	Ant Cir*	49	32	17
	Post Cir*	26	18	8
	Uncertain territory	22	10	12

*Ant Cir (Anterior Circulation); Post Cir (Posterior Circulation)

Residential location—Participant recruitment was more likely when residential addresses were within 20 km (n=38/47; 81%) of the study site and lowest for individuals living greater than 30 km from the study site (n=10/27; 37%; Table 3). Randomised participants lived closer to the study site than non-randomised participants (21.3 ± 20.3 cf. 36.6 ± 22.6 km, respectively; $t_{(95)}$=-3.38, P <0.001; ES 0.37; Cohen d=0.67).

Table 3. Number of randomised and non-randomised participants and corresponding residential location from study site

Distance (km)*	Total number of referred patients	Randomised participants (n)	Non-randomised participants (n)
< 10	24	20	4
< 20	23	18	5
< 30	23	12	11
≥ 30	27	10	17

*Distance of residential address from AI (assessment & HEPAP site)

Barriers to recruitment—Thirty-seven eligible patients were not randomised. Of these patients, nine were unable to be contacted. Twenty-eight patients declined to take part in the study. Distance of travel to the AI (46.2 ± 16.6 km) was cited by 13 patients as the primary reason for non-participation. Other reasons for non-randomisation included lack of time (n=5), patient perception of poor health (n=4), lack of interest in exercise participation (n=2), language difficulties (n=2) and patient migration out of study area (n=2).

Adverse events & participant adherence to HEPAP—There were three recurrent TIAs between the baseline and follow-up assessment (n=1, HEPAP; n=2 control). Participant retention was 95% at the follow-up assessment. Three participants (5%) were unable to be

re-assessed due to a clinical diagnosis of depression (n=1; HEPAP), lack of patient time (n=1; control) and overseas travel (n=1; control).

For individuals randomised to HEPAP, participants attended 94% of the available exercise sessions. Twenty-four (83%) participants attended all of the available exercise sessions.

Discussion

This study has demonstrated that it is possible to successfully recruit and retain newly diagnosed TIA patients to a health enhancing physical activity programme (HEPAP). This is important as participant accrual is the primary predisposing factor determining the feasibility of clinical rehabilitation trials.[22]

In the present study, 62% of eligible TIA patients (60 out of 97 patients) were recruited; far greater than the 6 to 17% that has previously been reported for acute stroke-focused research trials.[9,23,24] It is of practical significance that the intended sample (60 participants) was obtained within the anticipated timeframe (9 months). These findings are of relevance to those considering designing and conducting larger, multi-site RCTs of this nature for newly diagnosed TIA patients.

Studies that have restrictive entry criteria may prohibit successful patient recruitment and minimise the number of individuals eligible for randomisation. A pragmatic research design was used to improve the generalisability of the trial. A large number of ineligible individuals was expected at hospital screening (inpatient & outpatient) due to the high proportion of diagnoses encountered within TIA services.[25,26]

Of the 285 individuals diagnosed with TIA or non-disabling stroke at WRH, 97 (34%) were invited to participate in the trial (Figure 1). Of these invited participants, 89% were identified within outpatient care, whereas only 11% were identified from inpatient care. This value was lower than anticipated and is likely attributed to the high in-patient staff workload. To increase participant recruitment, it may be important to ensure adequate staff resourcing within inpatient care so that a greater number of participants may be actively recruited.

Participant recruitment was superior when residential location was within 20 km of the assessment site, with 81% of eligible patients accepting the opportunity to participate in the study. This is intuitive as participants were required to travel to and from a centralised AI frequently. Nevertheless, 46% of all non-randomised participants cited ‘distance to travel’ as the most critical barrier to participation, as previously demonstrated,[9,21] due to living in outlying recruitment areas. For these individuals, an additional study site for this RCT, perhaps 20-30 km away from the AI, may have increased interest in trial participation. For those planning TIA focused research, this is a vital consideration.

For those randomised to the intervention group, participation in the first 8 weeks of the trial amounted to approximately 1680 minutes (28 hours) for each individual (Table 1). This is a considerable time commitment for participants. It is reassuring that once recruited the vast majority regularly attended the available exercise and education sessions.

Furthermore, participant retention was successful with 95% of randomised participants attending the 8-week post-intervention assessment. This is consistent with other research that shown approximately 90% participant retention following 2 weeks of physical therapy[9] or a 12-week home-based exercise programme.[27]

Communication, support, symptom management and supervision are important characteristics that may influence patient retention. Retention of participants randomised to the exercise group was expected to be high due to the anticipated rapport that would develop between participants and project staff during the intervention.[28] However, for a RCT to examine intervention efficacy it is vital for individuals randomised to the control condition to stay within the trial despite meeting project staff much less frequently. This study demonstrates that similarly high retention rates in the control group can be achieved.

We feel that the responsiveness, friendliness and approachability of the project staff within the baseline assessment was important to create a trusting and empathetic environment that would encourage control participants to return for their second assessment. Previous research also suggests that a clinician educated within the area of research may have a positive effect on recruitment and retention and this was a factor in the present study.[8] This trial is ongoing and we will continue to examine retention in the further assessments planned 3 and 12 months following completion of the intervention.

In this study there were no differences in age, gender, ethnicity or TIA diagnosis classification between randomised and non-randomised participants. However, particular races and ethnicities were found to be disproportionately represented. Eighty-seven percent of all invited participants were NZ European, whereas only 13% in total were Māori, Pacific Islanders, Asian or Indian (Table 2). This is of particular interest as ~35% of the NZ population is of the above 'minority groups',[29] and as previous research has demonstrated that Māori and Pacific peoples are at higher risk of stroke than NZ Europeans.[30]

The disproportionate representation is likely due to differences in socioeconomic and environmental vascular risk factors between these groups.[30] A longer recruitment period and consideration of additional, culturally sensitive recruitment methods may be necessary to achieve a more heterogenous and representative participant sample.[9] It is also of interest to note that 22 of the 97 TIA or non-disabling stroke diagnoses were classified as being of uncertain territory. This is likely due to more than one vascular territory having been responsible for the TIA diagnosis, although there is the possibility that some of the participants may not have suffered a TIA or non-disabling stroke.

In conclusion it is possible to recruit and retain a large proportion of people into a RCT to examine the effects of exercise and education in TIA and non-disabling stroke. Recruitment from outpatient care was more successful than inpatient care. Distance to travel was the most frequently reported reason for non-participation.

Māori, Pacific Islanders, Asian and Indian patients were disproportionately under-represented and a different approach may be required to study interventions in these groups. To date, management strategies post-TIA discharge are largely aligned with lifestyle advice and pharmacotherapy. If the present intervention is efficacious with regards to improving vascular risk factors and reducing recurrent vascular events, it could be applied to a large number of people who suffer a TIA or non-disabling stroke.

Competing interests: None known.

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Acknowledgements: Funding for this study was provided by the Massey University Research Fund and the Wellington Medical Research Foundation.

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References:

1. Gommans J, Barber A, Hanger C, et al. Rehabilitation after stroke: changes between 2001 and 2007 in services provided by district health boards in New Zealand. N Z Med J. 2008;121:26–33.
2. Feigin VL, Lawes CM, Bennett DA, et al. Stroke epidemiology: a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. Lancet Neurology.2003;2:43–53.
3. Coull AJ, Lovett JK, Rothwell PM. Population based study of early risk of stroke after transient ischaemic attack or minor stroke: Implications for public education and organisation of services. BMJ. 2004;328:326–328.
4. Brownlee WJ, Fergus L, Bennett P, et al. Transient ischaemic attack services in New Zealand. N Z Med J. 2009;122: 21–27.
5. Wolf PA, Clagett GP, Easton JD, et al. Preventing ischemic stroke in patients with prior stroke and transient ischemic attack: A statement for healthcare professionals from the Stroke Council of the American Heart Association. Stroke. 1999;30:1991–1994.
6. Prior PL, Hachinski V, Unsworth K, et al. Comprehensive cardiac rehabilitation for secondary prevention after transient ischemic attack or mild stroke: I: Feasibility and risk factors. Stroke. 2011;42:3207–3213
7. Lennon O, Carey A, Gaffney N, et al. A pilot randomized controlled trial to evaluate the benefit of the cardiac rehabilitation paradigm for the non-acute ischaemic stroke population. Clin Rehabil. 2008;22:125–133.
8. Watson JM, Torgerson DJ. Increasing recruitment to randomised trials: a review of randomised controlled trials BMC Medical Research Methodology. 2006;6:34.
9. Blanton S, Morris DM, Prettyman MG, et al. Lessons Learned in Participant Recruitment and Retention: The EXCITE Trial. Phys Ther. 2006;86:1520–1533.
10. Elkins JS, Khatabi T, Fung L, et al. Recruiting Subjects for Acute Stroke Trials. Stroke. 2006;37:123–128.
11. Fitzgerald GK, Delitto A. Considerations for Planning and Conducting Clinic-Based Research in Physical Therapy. Phys Ther. 2001;81:1446–1454.
12. New Zealand guidelines for the assessment and management of people with recent transient ischaemic attack (TIA). 2008. Stroke foundation of New Zealand http://www.stroke.org.nz/pdfs/TIA_GuidelineForweb.pdf
13. ACSM's guidelines for exercise testing and prescription. 8th Wd. Philadelphia: Lippincott Williams & Wilkins; 2010.
14. Ware JE, Sherbourne CD. The MOS 36-item Short-Form health survey (SF-36): I. Conceptual framework and item selection. Med Care. 1992;30:473–83.
15. Shacham S. A shortened version of the Profile of Mood States. J Pers Assess. 1983;47;305–306.
16. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67:361–70.
17. Craig CL, Marshall AL, Sjöström M, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc. 2003;35:1381–95.
18. Borg G. Borg's Perceived exertion and pain scales. Champaign, IL: Human Kinetics; 1998.
19. Cohen J. A power primer. Psychol Bull. 1992;112:155–159.

20. Hulley SB, Cummings SR, Browner WS, et al. Designing Clinical Research. An Epidemiologic Approach.2nd Ed. London: Lippincott Williams and Wilkins; 2001
21. Patel MX, Doku V, Tennakoon L. Challenges in recruitment of research participants. Adv Psychiatr Treat. 2003;9:229–238.
22. Bell-Syer SEM, Klaber Moffett JA. Recruiting patients to randomised trials in primary care: principles and case study. Fam Pract. 2000;17:187–91.
23. Werner RA, Kessler S. Effectiveness of an intensive outpatient rehabilitation program for postacute stroke patients. Am J Phys Med Rehabil. 1996;75:114–120.
24. Studenski S, Duncan PW, Perera S, et al. Daily Functioning and Quality of Life in a Randomized Controlled Trial of Therapeutic Exercise for Subacute Stroke Survivors. Stroke. 2005;36:1764–1770.
25. Stead LG, Vaidyanathan L, Bellolio MF, et al. Knowledge of signs, treatment and need for urgent management in patients presenting with an acute ischaemic stroke or transient ischaemic attack: a prospective study, Emerg Med J. 2008;25:735–739.
26. Alberts MJ, Bertels C, Dawson DV. An Analysis of Time of Presentation After Stroke. JAMA. 1990;263:65–68.
27. Duncan P, Richards L, Wallace D, et al. A randomized, controlled pilot study of a home-based exercise program for individuals with mild and moderate stroke. Stroke. 1998;29:2055–2060.
28. Dias L, Schoenfeld E, Thomas J, et al. Reasons for high retention in pediatric clinical trials: comparison of participant and staff responses in the Correction of Myopia Evaluation Trial. Clin Trials. 2005;2:443–452.
29. Statistics New Zealand. Demographic trends: 2011. Wellington: Statistics New Zealand; 2012.
30. Feigin V, Carter K, Hackett M, et al. Ethnic disparities in incidence of stroke subtypes: Auckland Regional Community Stroke Study, 2002–2003. The Lancet Neurology. 2006;5:130–139.