

# **Incidence of TIA & Stroke in Auckland, New Zealand**

## **Incidence of Transient Ischemic Attack in Auckland, New Zealand, in 2011-2012**

### **Cover title: Incidence of TIA in Auckland, New Zealand**

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**Title page** 260 words

**Abstract** 262 words

**Manuscript** 3,925 words

**References** 27

**Tables** 2

**Figures** 1

**Supplementary Appendix**

**Key words:** Cerebrovascular disorders; Ischemic attack, transient; Incidence

### ABSTRACT

**Background and Purpose:** There have been few recent population-based studies reporting the incidence (first ever) and attack rates (incident and recurrent) of transient ischemic attack (TIA).

**Methods:** The fourth Auckland Regional Community Stroke study (ARCOS IV) used multiple overlapping case ascertainment methods to identify all hospitalized and non-hospitalized cases of TIA that occurred in people  $\geq 16$  years of age usually resident in Auckland (population  $\geq 16$  years is 1.12 million), over the 12 months from 1<sup>st</sup> March 2011. All first-ever, and recurrent new TIAs (any new TIA 28 days after the index event), during the study period were recorded.

**Results:** There were 785 people with TIA [402 (51.2%) women, mean (SD) age 71.5 (13.8) years]; 614 (78%) of European origin, 84 (11%) Māori/Pacific and 75 (10%) Asian/Other. The annual incidence of TIA was 40 (95% CI 36 to 43), and attack rate was 63 (95% CI 59 to 68), per 100,000 people, age standardized to the WHO world population. Approximately two-thirds of people were known to be hypertensive and/or were being treated with blood pressure lowering agents, half were taking anti-platelet agents and just under half were taking lipid-lowering therapy before the index TIA. 210 (27%) were known to have atrial fibrillation at the time of the TIA, of whom only 61 (29%) were taking anti-coagulant therapy, suggesting a failure to identify or treat atrial fibrillation.

**Conclusions:** This study describes the burden of TIA in an era of aggressive primary and secondary vascular risk factor management. Education programs for medical practitioners and patients around the identification and management of atrial fibrillation are required.

### **INTRODUCTION**

There have been few recent population-based incidence studies of transient ischemic attack (TIA).<sup>1-4</sup> Such studies are difficult to perform as TIA diagnosis relies on expert clinical assessment and they require regular and comprehensive case-ascertainment from multiple overlapping sources of information in the whole population.<sup>5</sup> Many of the earlier TIA incidence studies were performed before widespread use of medications to lower cholesterol levels and blood pressure, and surgical intervention in patients with significant internal carotid artery stenosis. Even fewer population-based studies have examined the effect of ethnicity on the burden of TIA in the same community.<sup>6,7</sup>

We examined the incidence of TIA in a large population-based TIA and stroke incidence study. The aim was to determine the burden of TIA in an ethnically diverse community in an era of aggressive primary and secondary vascular risk factor management.

### **METHODS**

The fourth Auckland Regional Community Stroke study (ARCOS IV) utilized a population-based register of first ever, or first ever and recurrent, TIA and stroke events, over the 12 months from 1<sup>st</sup> March 2011, in people aged 16 years or older in the resident population of the Auckland region (in 2011-2012 the population aged  $\geq 16$  was 1,119,192).<sup>8</sup> Detail on the ARCOS IV methodology of case-ascertainment has been provided elsewhere.<sup>8</sup> In brief, all new hospitalized and non-hospitalized cases of TIA and stroke were identified using multiple overlapping methods of case ascertainment.<sup>9, 10</sup> Daily checks were made of all public hospitals, emergency departments, hospital discharge registers and CT/MRI records; weekly checks of all private hospitals, rest homes and community health services (general practices,

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hospital outpatient clinics and rehabilitation centers); monthly checks of coroner/autopsy records; quarterly checks of New Zealand Health Information Service data and death certificates (from the Registrar of Births, Deaths and Marriages).

The study population is ethnically diverse comprising those of European origin (56% of the population), Māori/Pacific [25%; the indigenous people of New Zealand and people originating from the Pacific Islands, ethnically Polynesian] and Asians/Others (19%).<sup>11</sup> The region has been consistently served by four large public acute care hospitals, two main private medical care hospitals and many long-stay residential care facilities. The Regional Ethics Committee approved the study.

Trained clinical researchers and nurses undertook face-to-face interviews with patients or the next-of-kin where necessary, as soon as possible after notification of TIA. A structured questionnaire was used to obtain information regarding demographics, clinical features, investigations, management and health status (Supplementary Appendix). Both known and newly diagnosed risk factors were documented. Ethnic group was defined by self-identification and prioritized as European, Māori/Pacific, Asian/Other using corresponding New Zealand census definitions. Information on ethnic group was not available in 12 study participants who were excluded from the ethnicity analyses.

TIA was defined as an acute loss of focal cerebral or ocular function with symptoms lasting <24 hours, and that after adequate investigation was presumed to be due to embolic or thrombotic vascular disease, as previously defined.<sup>6</sup> Patients with isolated vertigo, diplopia, bilateral blindness, drop attacks, non-focal symptoms, and features suggesting migraine, epilepsy or transient global amnesia, were excluded. Brain imaging was used to exclude disorders mimicking TIA. To enable comparison with earlier studies, brain imaging was not used to reclassify patients with transient symptoms and evidence of acute infarction as stroke

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and not TIA. Therefore, this sample likely includes some patients with ‘minor stroke’ using a tissue-based definition of cerebral infarction. All first-ever and recurrent new TIAs (any new TIA event 28 days after the index event) during the study period were recorded.

A diagnostic committee of study physicians (PB, VF, YR) classified all TIA cases using medical history, clinical and laboratory findings (Supplementary Appendix). The diagnostic committee optimized case ascertainment by meeting regularly to review the clinical features, medical records and imaging results of all recently referred patients. Difficult cases were classified by consensus. Only patients in whom the diagnostic committee agreed met the above criteria were included.

Crude annual age-, sex- and ethnic-specific annual incidence (first-ever-in-a-lifetime events) and attack (first ever and recurrent events) per 100,000 people with 95% confidence intervals (CI) were calculated assuming a Poisson distribution. Age-standardized rates were derived by the direct method with WHO world population as the reference.<sup>12</sup> In order to facilitate comparisons with previous studies, summary rates were also age-standardized to the European population.<sup>13</sup> Ethnic specific rates were calculated using the proportion of residents belonging to each of the specific ethnic groups.

For categorical variables, statistical significance of trends was assessed using the Cochran-Armitage trend test; and for continuous variables, analysis of variance or the Kruskal-Wallis test was used. Completeness of case ascertainment was determined using log-linear (capture-recapture) modelling assuming a Poisson distribution,<sup>14</sup> and used the three main sources of notification: hospital, general practitioner and other sources.  $P < 0.05$  was considered statistically significant in all analyses.

### RESULTS

There were 785 people who presented with TIA [402 (51.2%) women, mean (SD) age 71.5 (14) years, of whom 732 had a first ever TIA and 53 had a recurrent TIA (Table 1). There were 614 (78.2%) people who identified as European, 84 (10.7%) as Māori/Pacific and 75 (9.6%) as Asian/other. Six hundred and forty-five (82%) people were seen in an acute hospital setting such as an emergency department or acute medical assessment unit, and most of the remainder were seen in an outpatient clinic setting. The estimated number of missing cases was low as determined by the capture-recapture analysis (13/785; 1.5%). Brain imaging was obtained in 594 (76%) people within 24 hours and 621 (79%) within 28 days, of symptom onset. TIA was diagnosed solely on the basis of clinical presentation by the diagnostic committee in those people in whom brain imaging was not obtained.

Prior to presentation, 172 (23%) of 785 people were known to have had a stroke. Five-hundred and thirteen (65%) were known to have hypertension (with 61% treated with anti-hypertensive therapy), and an additional 57 (7%) had a first blood pressure recording greater than 140/90 mmHg. Three hundred and sixty nine (47%) had been diagnosed as having elevated lipids, with a similar proportion (45%) treated with lipid lowering therapy. Four-hundred and fourteen (53%) were taking anti-platelet agents. 210 (27%) were known to have atrial fibrillation, of whom only 61 (29%) were taking anti-coagulant therapy at the time of the TIA. An additional 69 (9%) were first diagnosed as having atrial fibrillation at presentation.

There were ethnic differences in vascular risk factors. Māori/Pacific and Asian/Other people had double the rates of known diabetes mellitus at presentation compared to Europeans, and there was a trend for Māori/Pacific people to be less likely to be known to have elevated

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lipids. There was also a trend for Māori/Pacific people to be more likely to be seen in an acute hospital setting than other ethnic groups.

The annual incidence of TIA was 40 (95% CI 36 to 43) per 100,000 people, age-standardized to the WHO world population (Table 2). The annual TIA incidence rates increased with age in all groups, and were similar in men (41, 95% CI 36 to 46) and women (38, 95% CI 34 to 43). When age-standardized to the European population to enable comparisons with earlier studies, the annual incidence of TIA was 73 (95% CI 67 to 80) per 100,000 people per year (“Figure” DELETED”).

The annual attack rate (incident and recurrent) of TIA was 63 (95% CI 59 to 68) per 100,000 people, age-standardized to the WHO world population. The annual attack rates also increased with age in all groups and were similar in men (69, 95% CI 63 to 76) and women (58, 95% CI 53 to 64). Ethnic differences were also seen with Asian/Others having almost half the incidence and attack rates than the other two ethnic groups (Supplementary Table I).

### **DISCUSSION**

This study found that over a 12 month period there were 40 first ever TIAs (95% CI 36 to 43), and an acute cerebrovascular service could expect 63 (95% CI 59 to 68) people with first ever or recurrent TIA per 100,000 people at risk. When standardized to the European population, the annual TIA incidence was 73 (95% CI 67 to 80). This was higher than that found in the Oxford Vascular Study (OXVASC) study, where the annual TIA incidence was 58 (95% CI 46 to 69) per 100,000 people,<sup>15</sup> but in the middle of the range when compared with other populations studied since 2000 (Figure).<sup>1-4, 6, 16-20</sup> This likely reflects higher stroke incidence in our population compared to other developed countries.<sup>21</sup>

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Ethnic differences were seen with Asian/Others having half the incidence of TIA compared to the other ethnic groups. This difference may be related to the large influx of younger, presumably generally healthy, Asian immigrants into New Zealand over the last two decades.<sup>11</sup> TIA incidence rates in Māori/Pacific were slightly, albeit not statistically significantly, lower than that in European people. This finding is at odds with the ARCOS IV stroke incidence study where Māori/Pacific had higher age-standardized stroke incidence rates.<sup>8</sup> We speculate that this discrepancy between TIA and stroke incidence may be due to a failure to seek medical attention for transient neurologic symptoms in these ethnic groups.<sup>22</sup>

A large number of individuals were identified as having, and were taking treatment for, vascular risk factors. Approximately two-thirds were known to be hypertensive and were being treated with blood pressure lowering agents, half were taking anti-platelet agents, just under half were taking lipid-lowering therapy and there were low current tobacco smoking rates. However what appears to have been aggressive management of vascular risk factors did not seem to have had a marked impact on TIA incidence, when compared with earlier studies. A possible explanation is the low use of anti-coagulant therapy. Just over two thirds (71%) of the patients known to have atrial fibrillation at the time of presentation were not being treated with oral anti-coagulants. This finding is not isolated to our cohort with low rates of anti-coagulation therapy noted in other populations of stroke and TIA patients presenting with atrial fibrillation.<sup>23, 24</sup> Education strategies that focus on increasing community and physician awareness of the need for guideline based atrial fibrillation treatment may lead to reductions in the numbers of people presenting with TIA and stroke

Most TIA patients were seen in hospital emergency departments or were admitted to hospital. The four public hospitals serving the study region have acute medical assessment units where patients can be admitted and assessed urgently, with outpatient TIA clinics used for lower

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risk patients. This high rate of inpatient hospital care is in contrast to the OXVASC study where almost two-thirds of patients were managed as outpatients.<sup>15</sup> Rapid access TIA clinics improve outcomes and are cost effective but the provision of such clinics may be challenging in some healthcare settings.<sup>25-27</sup> There is unlikely to be a one size fits all solution with the provision of TIA services varying depending on local factors.

This study has several strengths. ARCOS IV was the fourth in a series of 'ideal' population-based stroke incidence studies carried out every decade since 1981. There was prospective case ascertainment in a well-defined population with multiple overlapping sources of information and using standard WHO definitions. New Zealand has a public health system available to all residents, with provision of a government part subsidy for primary care practice visits and free hospital care, reducing but not eliminating barriers to patients seeking medical care.

This study also has several limitations. Most notifications came from medical practitioners or hospitals with few from other sources. It is likely that many people with transient neurologic symptoms fail to seek medical care and were therefore not identified. This is a problem that faces all TIA incidence studies. In addition, only people who met strict study diagnostic criteria were included. The numbers of patients referred with suspected TIA may be up to six times greater than those with definite TIA and needs to be borne in mind when planning acute cerebrovascular services.<sup>15</sup>

In conclusion, the incidence of TIA in this study sits in the middle range when compared to earlier reports from a range of other countries. The high use of anti-hypertensive, anti-platelet and lipid-lowering therapy is reassuring. However, management of atrial fibrillation remains a problem. Most patients who were known to have atrial fibrillation at the time of the TIA were not being treated with anti-coagulants. We speculate that comprehensive education

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programs for medical practitioners and patients, and increased use of newer fixed dose oral anticoagulants, may lead to reductions in TIA incidence.

### **ROLE OF FUNDING SOURCE**

The Health Research Council of New Zealand, Neurological Foundation of New Zealand and the Auckland Medical Research Foundation funded the study but had no input into the design, performance, analysis or reporting of the study and did not see the manuscript prior to final acceptance for publication.

**DISCLOSURES: None**

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### FIGURE 1 LEGEND

Annual incidence of transient ischemic attack per 100,000 people per year in different populations,<sup>1-4, 6, 16-20</sup> age-standardized to the European population.<sup>13</sup>

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**Table 1. Summary of baseline variables for TIA by ethnicity groups\***

	Total n=785	European n = 614	Maori/Pasifika n = 84	Asian/Other n = 75	P-value
Age [mean (SD) years]	71.5 (14)	73.7 (12.9)	60.2 (13.8)	68 (12.6)	<0.0001
Female n (%)	402 (51)	309 (50)	58 (62)	34 (45.3)	0.068
<b>Medical history n (%)</b>					
High blood pressure	513 (65)	398 (65)	60 (64)	55 (73)	0.320
Ischaemic heart disease	194 (25)	152 (25)	20 (21)	22 (29)	0.484
Previous stroke	172 (23)	129 (22)	24 (27)	19 (26)	0.418
Previous TIA **	185 (25)	154 (26)	20 (23)	11 (16)	0.132
Current smoker	51 (7)	36 (6)	12 (14)	3 (4)	0.639
Diabetes	158 (20)	92 (15.0)	35 (37)	31 (41)	<0.0001
Atrial fibrillation	210 (27)	170 (28)	19 (20)	21 (27)	0.327
Elevated blood lipids	369 (47)	295 (48)	34 (36)	38 (51)	0.078
<b>Prior medications n (%)</b>					
Anti-hypertensives	480 (61)	371 (60)	56 (60)	53 (71)	0.213
Anti-platelet agents	414 (53)	327 (53)	42 (45)	45 (60)	0.129
Lipid lowering agents	353 (45)	278 (45)	38 (40)	37 (49)	0.502
Anti-coagulants	61 (8)	44 (7)	12 (13)	4 (5)	0.120
* <b>Acute assessment ***</b>	645 (82)	503 (82)	84 (89)	57 (76)	0.070

\* Participants with missing ethnicity data have been excluded from the ethnicity sections.

\*\* Information on prior TIA was only recorded in 75 patients.

\*\*\* Includes patients managed in hospital emergency departments and acute medical assessment units.

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**Table 2.** Annual incident (first ever) and attack rates (first ever and recurrent) age specific TIA per 100,000 people, age standardized to the WHO world population.

	N	n	Incidence Rate (95% CI)	n	Attack rate Rate (95% CI)
<b>Total</b>					
16-54	808869	81	10 (8; 12)	126	16 (13; 18)
55-64	147171	105	71 (58; 85)	152	103 (87; 120)
65-74	95190	122	128 (105; 151)	202	212 (183; 241)
75-84	48387	155	320 (270; 371)	259	535 (470; 600)
85+	19578	102	521 (420; 622)	167	853 (724; 982)
Total	1119195	565	50 (46; 55)	906	81 (76; 86)
<b>Age-standardized</b>			<b>40 (36; 43)</b>		<b>63 (59; 68)</b>
<b>Male</b>					
16-54	390354	31	8 (5; 11)	55	14 (10; 18)
55-64	71058	63	89 (67; 111)	97	137 (109; 164)
65-74	45678	69	151 (115; 187)	115	252 (206; 298)
75-84	21759	72	331 (254; 407)	124	570 (470; 670)
85+	6807	27	397 (247; 546)	51	749 (544; 955)
Total	535656	262	49 (43; 55)	442	83 (75; 90)
<b>Age- standardized</b>			<b>41 (36; 46)</b>		<b>69 (63; 76)</b>
<b>Female</b>					
16-54	418518	50	12 (9;15)	71	17 (13; 21)
55-64	76110	42	55 (38; 72)	55	72 (53; 91)
65-74	49509	53	107 (78; 136)	87	176 (139; 213)
75-84	26628	83	312 (245; 379)	135	507 (421; 593)
85+	12771	75	587 (454; 720)	116	908 (743; 1074)
Total	583536	303	52 (46; 58)	464	80 (72; 87)
<b>Age- standardized</b>			<b>38 (34; 43)</b>		<b>58 (53; 64)</b>