

# Evidence-based care and outcomes of acute stroke managed in hospital specialty units

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EVIDENCE IS INCREASING that patients with stroke who are treated in specialised stroke units have better survival and functional outcome than those treated in general medical wards.<sup>1,2</sup> The main difference in outcome occurs within the first six weeks and is maintained at five years.<sup>1</sup> Treatment in specialised stroke units is associated with reduced risk of death, dependency and need for long-term institutionalisation.<sup>1-5</sup>

Dedicated stroke units differ from general medical wards in their care of patients with stroke, as they use clinical pathways for diagnosis, treatment, prevention of complications and rehabilitation. Interdisciplinary teams of physicians, therapists and nurses coordinate medical management, rehabilitative therapy and stroke education, aimed at reaching defined medical and functional goals before the patient is discharged.<sup>3,4</sup>

However, not all Australian hospitals have stroke units, and, even where these units exist, they may not care for all patients with stroke. The aim of our study was to describe management of patients with stroke and transient ischaemic attack (TIA) in a sample of large, metropolitan, tertiary-care hospitals in Australia, and to compare this management with evidence-based management recommended in a recent Australian review.<sup>6</sup> Furthermore, we aimed to compare management and outcomes between stroke and other types of specialty unit.

## METHODS

This was a multicentre, retrospective audit of patients admitted to hospital between 17 September 1999 and 23 May 2001. The hospitals were eight metropolitan tertiary care hospitals (Flinders Medical Centre [SA], Princess Alexandra Hospital and Royal Bris-

## ABSTRACT

**Objectives:** To assess the use of evidence-based investigations and treatments in patients with acute stroke in selected Australian hospitals and to compare management and outcomes between stroke and other types of hospital specialty unit.

**Design:** Retrospective, multicentre audit of hospital case files.

**Setting:** Eight metropolitan tertiary-care hospitals from five Australian States.

**Subjects:** 300 consecutive patients from each hospital admitted between 17 September 1999 and 23 May 2001 and having a discharge diagnosis of stroke or transient ischaemic attack.

**Main outcome measures:** Use of investigations and treatments supported by best available evidence; comparison of management and outcomes between stroke, neurology, general medical and geriatric units.

**Results:** 2383 patients were audited (median age, 72.7 years; 52% men); 72% had ischaemic events, and 28% haemorrhagic events. Use of investigations and treatments varied between hospitals and types of unit. Stroke units or teams cared directly for 23% of patients (range across hospitals, 0–100%). Although 47% of patients with ischaemic events presented within 3 hours of symptom onset (when thrombolysis might provide benefit), only nine (2%) received thrombolysis. Angiotensin-converting enzyme (ACE) inhibitors were given to 28% of survivors at discharge (range, 14%–38%). Stroke units were more likely to use diagnostic tests, while neurology units were more likely to prescribe heparin acutely for patients with ischaemic stroke (not recommended for patients in general), and geriatric units were less likely to discharge patients with atrial fibrillation on anticoagulation therapy. Outcomes also varied significantly between types of unit. In-hospital survival rates were 90% (stroke units), 91% (neurological units), 82% (general medical units) and 79% (geriatric units) ( $P < 0.001$ ). Stroke units and neurological units sent more patients home than the other units. Stroke units also sent fewer patients to rehabilitation and had longer mean length of stay.

**Conclusions:** Acute stroke care varies between Australian tertiary-care hospitals and types of specialty unit, with suboptimal use of many evidence-based interventions.

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For editorial comment, see page 309; see also pages 324, 329 and 333.

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## 1: Demographic characteristics and risk factors for stroke among 2383 patients with stroke or TIA

### Characteristic (number of patients with data available)\*

Median age (years) ( $n = 2383$ )	72.7
Sex (% men) ( $n = 2383$ )	52.2%
Previous stroke ( $n = 1863$ ) or TIA ( $n = 1744$ )	34.7%
Atrial fibrillation ( $n = 1778$ )	30.5%
Diabetes ( $n = 1929$ )	26.3%
Peripheral vascular disease ( $n = 1318$ )	20.3%
Current smoking ( $n = 1642$ )	25.0%
Past smoking ( $n = 1417$ )	37.7%
Hypertension (past or current) ( $n = 2173$ )	71.3%
Hyperlipidaemia (past or current) ( $n = 1619$ )	41.4%

TIA = transient ischaemic attack.

\* Not all data were documented for all patients. Percentages were calculated using the number of cases with data available as the denominator.

bane Hospital [QLD], Royal Melbourne Hospital and St Vincent's Hospital [VIC], Royal Perth Hospital [WA], Royal Prince Alfred Hospital and Westmead Hospital [NSW]). The audit was approved by the research ethics committee of each participating institution.

### Subjects

Patients with a discharge diagnosis of stroke or TIA were identified by reviewing hospital morbidity records and extracting case files for those with discharge diagnosis codes 430–438 (ICD-9<sup>7</sup>) or G45, G46, I60–I64 (ICD-10-AM<sup>8</sup>). Each hospital aimed to audit files for 300 consecutive patients identified with these codes after 17 September 1999.

### Data extraction and analysis

Case files were reviewed by research nurses using a standard, prospectively designed audit pro-forma. The nurses received specific training in data abstraction from case files from a clinical research associate (MEV). Data were extracted on use of investigations and treatments, length of hospital stay

and outcome (death or, for survivors, discharge location and functional ability). Data quality was checked by the clinical research associate during visits to each hospital.

Stroke type was classified as ischaemic or haemorrhagic based on the ICD code, and ischaemic strokes were subdivided using the criteria of TOAST (Trial of Org 10172 in Acute Stroke Treatment).<sup>6,9</sup>

Differences between groups were assessed by  $\chi^2$  tests or Kruskal–Wallis test (for length of stay). A  $P$  value  $< 0.05$  was considered statistically significant.

## RESULTS

A total of 2383 patients were audited from the eight hospitals. Events were classified as ischaemic for 1721 patients (72%) and haemorrhagic for 662 (28%). Patient demographic characteristics and risk factors for stroke are shown in Box 1.

### Management and outcomes

Mean length of hospital stay was 18 days (range, 10–37 days). Frequency of use of recommended investigations and treatments is shown in Box 2, along with outcomes.

**Investigations:** Almost all patients (91%) underwent neuroimaging with either computed tomography (CT) or magnetic resonance imaging (MRI), with 83% undergoing these investigations in the first 24 hours of admission. Although plasma biochemistry, full blood count and electrocardiography (ECG) were also performed for almost all patients within the first 24 hours, other routinely recommended tests, such as measurement of blood glucose level and erythrocyte sedimentation rate, and chest x-ray, were performed less often. Identifying a source of embolism with echocardiography and carotid ultrasound (recommended for patients with ischaemic stroke) was undertaken in only a minority of patients during the admission (data were not collected for tests performed after discharge).

**Treatments:** About a quarter (23%) of patients were directly cared for by a designated, multidisciplinary stroke

unit or team (range, 0–100% in different institutions).

Of the 834 patients with ischaemic events and a documented time of symptom onset, 136 (16%) presented within one hour and 393 (47%) within three hours, when thrombolysis might have been beneficial for selected patients. Thrombolysis was given to four patients (1% of the 393) and to another 5 patients who presented outside the recommended three-hour treatment period. Aspirin was given within the first 24 hours to 57% of the patients with ischaemic stroke. However, 29% of those with ischaemic stroke did not receive aspirin at all during the admission.

Of the 363 patients with ischaemic events and current or past atrial fibrillation, 83% received either warfarin (23%) or an antiplatelet agent (51%), or both (9%), at discharge. We did not determine reasons for giving or withholding thrombolysis, aspirin or other antithrombotic agents in individual cases.

Blood pressure at discharge was documented in 97% of survivors (range, 85%–100%), with systolic pressure  $> 140$  mmHg in 41% (range, 31%–51%), and  $> 160$  mmHg in 13% (range, 9%–16%), while diastolic pressure was  $> 90$  mmHg in 14% (range, 11%–23%). Twenty eight per cent of survivors (range, 14%–38%) received angiotensin-converting enzyme (ACE) inhibitors at discharge.

### Comparison between unit types

Of the 2383 patients, 1664 were cared for in stroke, neurological, general medical or geriatric units, and were included in a subanalysis comparing management and outcome between different types of unit. (The other 719 were cared for in a wide variety of other units.)

**Patient characteristics:** Demographic characteristics and risk factors are compared between stroke units and the other three types of unit combined in Box 3. The only difference in these potential confounding factors was that stroke unit patients tended to be younger, with 55% aged under 75 years versus 46% for patients admitted to the other units ( $P = 0.003$ ).

## 2: Use of recommended\* investigations and treatments and outcomes among patients with stroke or TIA in eight Australian hospitals

	Mean frequency <sup>†</sup> (range)
<i>Recommended first-line investigations* (number with data available)</i>	
Neuroimaging (computed tomography or magnetic resonance imaging)	
Anytime during admission ( <i>n</i> = 2383)	91% (85%–95%)
In first 24 hours ( <i>n</i> = 2383)	83% (74%–94%)
Laboratory assessment in first 24 hours	
Blood glucose level ( <i>n</i> = 2383)	77% (41%–97%)
Full blood count ( <i>n</i> = 2378)	96% (94%–98%)
Erythrocyte sedimentation rate ( <i>n</i> = 2383)	21% (8%–39%)
Plasma biochemistry ( <i>n</i> = 2377)	96% (94%–97%)
Lipid profile ( <i>n</i> = 2383)	26% (14%–40%)
Electrocardiogram in first 24 hours ( <i>n</i> = 2383)	90% (78%–98%)
Chest x-ray in first 24 hours ( <i>n</i> = 2383)	66% (46%–76%)
Carotid doppler ultrasound anytime during admission <sup>‡</sup> (among 1721 patients with ischaemic stroke/TIA) ( <i>n</i> = 1721)	46% (27%–64%)
Echocardiography (transthoracic or transoesophageal) <sup>§</sup> (among 1721 patients with ischaemic stroke/TIA) ( <i>n</i> = 1721)	33% (21%–55%)
<i>Recommended treatments*</i>	
Stroke unit care	23% (0–100%)
Thrombolysis with tissue plasminogen activator (among 393 patients with ischaemic stroke presenting within 3 hours)	1% (0–2%)
Therapeutic heparin in ischaemic stroke/TIA (level 1 evidence against general use) <sup>¶</sup> (among 1721 patients with ischaemic stroke or TIA)	8% (2%–23%)
Aspirin immediately (within 24 hours) (among 1721 patients with ischaemic stroke or TIA)	57% (37%–80%)
Antiplatelet therapy (among 1546 survivors with ischaemic stroke/TIA)	78% (67%–88%)
Warfarin (among 363 patients with ischaemic stroke/TIA and past or present atrial fibrillation)**	33% (20%–56%)
Treatment of hypertension (among 1300 survivors with history of hypertension)	76% (52%–86%)
<i>Outcome of 1721 patients with ischaemic events (number with data available)</i>	
Death ( <i>n</i> = 1721)	10% (6%–12%)
Discharge to home	
All patients ( <i>n</i> = 1721)	55% (47%–65%)
Survivors ( <i>n</i> = 1546)	61% (52%–74%)
<i>Outcome of 662 patients with haemorrhagic events (number with data available)</i>	
Death ( <i>n</i> = 662)	29% (21%–38%)
Discharge to home	
All patients ( <i>n</i> = 662)	33% (23%–51%)
Survivors ( <i>n</i> = 472)	46% (34%–71%)

TIA = transient ischaemic attack.

\* Investigations and treatments were those recommended by Hankey<sup>6</sup> based on best available evidence, including, for treatments, Level I [E1] evidence from systematic review of all relevant randomised controlled trials.

<sup>†</sup> As not all data were documented for all patients, percentages were calculated using the number of patients with data available or number of eligible patients as the denominators.

<sup>‡</sup> To assess suitability for carotid endarterectomy in non-disabling carotid ischaemic event.

<sup>§</sup> To identify embolic source in non-lacunar ischaemic event.

<sup>¶</sup> Heparin is not recommended generally, as it has no net effect on death and dependency, despite reducing venous thromboembolism.

\*\* Atrial fibrillation, recent myocardial infarction, valvular heart disease.

**Investigations:** Those which differed significantly in frequency of use between stroke and other units are shown in Box 4. Significant differences were noted in use of chest x-ray, carotid doppler ultrasound examination and transthoracic echocardiography, which were all used more in stroke units, but not in use of CT and MRI, transoesophageal echocardiography or ECG.

Significantly more patients in stroke units than in other units had their blood glucose levels and lipid profiles measured. There were no significant differences in use of other laboratory investigations (full blood count, erythrocyte sedimentation rate and plasma biochemistry).

**Treatments:** Those which differed significantly in frequency of use between stroke and other units are shown in Box 4. Percentages of patients with ischaemic stroke who received aspirin differed only slightly between the units (76% in stroke units v 67%, 71% and 74% in geriatric, general medical and neurological units, respectively; *P* = 0.08).

Thirteen percent of ischaemic stroke patients who were treated by a neurology unit received therapeutic doses of heparin (low molecular weight or unfractionated), compared with only 7.5% of those who were treated in a stroke unit, and 3.6% and 7.4% in the geriatric and general medical units, respectively (*P* = 0.002).

There were no significant differences between units in the percentages of patients with past or current atrial fibrillation who were taking warfarin or an antiplatelet agent (aspirin, clopidogrel or dipyridamole) on admission (warfarin: range, 18%–28%; *P* = 0.4; antiplatelet agent: range, 42%–50%; *P* = 0.7). However, fewer of these patients were discharged taking warfarin from stroke units than from other units. Patients from stroke units were more likely to be discharged taking an antiplatelet agent.

There were no significant differences between units in percentages of patients with hypertension who were taking anti-hypertensive drugs on admission (69%–75%; *P* = 0.36 for differences across units), but patients in stroke units were more likely to have their medication changed. At discharge, systolic blood pressure was similar across units, with

41%–46% of patients having systolic blood pressure > 140 mmHg ( $P=0.5$ ). However, diastolic blood pressure at discharge differed across units, with 14% of patients discharged from both geriatric and general medical wards having diastolic blood pressure > 90 mmHg versus 18% and 22% of patients from stroke and neurological units, respectively ( $P=0.02$ ).

**Outcomes:** In-hospital survival was 90% and 91% for patients cared for by stroke and neurological units, respectively, compared with 82% and 79% for those cared for by general medical and geriatric units, respectively ( $P<0.001$ ).

Among survivors, discharge destinations varied significantly between units. Stroke and neurological units sent more patients home than general medical and geriatric units, while geriatric units sent more to nursing homes than the other three types of unit. Stroke units sent fewer patients to another acute hospital and to rehabilitation than other units.

More stroke unit patients were able to dress themselves at discharge, but more geriatric unit patients were able to feed themselves, shower, and transfer unassisted at discharge than patients from other units and had longer mean length of stay.

## DISCUSSION

Our study found considerable variability in investigation and treatment of patients with stroke between hospitals and between different types of clinical specialty unit. Reasons for the observed variability are not clear. However, we believe our findings reflect real differences in practice and suboptimal use of some recommended investigations and treatments. Patient mortality and outcomes also varied between different types of unit.

Our study had some limitations. As it was a retrospective audit in a limited number of hospitals, there were many potential confounding variables. Documentation was variable and incomplete, and we did not assess care after hospital discharge. Rea-

sons that investigations or treatments were used or not used in individual patients were not available. There may have been differences between units in the complexity and severity of cases that we did not assess, while the younger age of patients in stroke units may have improved their outcomes. However, a strength of the study was that it was one of the largest hospital-based audits of stroke care to be undertaken and included large, metropolitan teaching hospitals from most Australian states.

We recognise that some recommended diagnostic and therapeutic strategies are not suitable for individual patients (eg, carotid doppler ultrasound examination is not suitable for patients with cerebral haemorrhage or posterior circulation ischaemia). Nevertheless, some recommended investigations and treatments seemed to be underused. Blood pressure management was suboptimal, although it is increasingly recognised as important in secondary prevention of stroke and other athero-

sclerotic vascular disease.<sup>10-12</sup> Furthermore, use of ACE inhibitors was low (28% of patients). It was recently shown that use of these drugs after stroke reduces the risk of a second stroke, even if antihypertensive therapy would not normally be indicated.<sup>10,11</sup> For example, the PROGRESS trial demonstrated that perindopril-based therapy reduced the relative risk of second stroke by 28% in patients with pre-existing stroke or TIA.<sup>10,11</sup> These studies were published during and after the audit period, respectively, which might explain the low use of ACE inhibitors in the audit group.

Of particular interest, while almost half the patients with ischaemic events presented within three hours of symptom onset (when thrombolysis might have provided benefit),<sup>6</sup> only 1% of these patients (and 2% of those with ischaemic events) received this treatment. We did not determine the reasons that thrombolysis was given or withheld in individual cases, but note that stroke seems not to be a widely accepted indication for thrombolysis in Australia.

Other strategies were better implemented, with 83% of patients in atrial fibrillation treated with warfarin or antiplatelet therapy. Likewise, more than half the patients with ischaemic stroke were given aspirin within 24 hours of symptom onset. As the retrospective audit did not assess contraindications to treatments (eg, dysphagia is a relative contraindication for aspirin therapy), rates in patients without contraindications were probably higher.

The prevalence of direct care by stroke units or teams was low, despite such units being known to reduce mortality and improve outcomes.<sup>1,2</sup> Management and outcomes varied between patients treated by different types of hospital specialty unit. Those treated in stroke or neurology units had a survival advantage over those treated in general medical or geriatric units. Survival varies with type of stroke and age. The Framingham Heart Study found that, after an initial stroke, 22% of men and 25% of women die within a

### 3: Comparison of characteristics of 1664 patients treated in different types of specialty unit

	Stroke unit (n=536)	Other units* (n=1128)	$\chi^2$	P†
Age (years)			11.87	0.003
< 55	71 (13.3%)	129 (11.4%)		
55–74	222 (41.4%)	386 (34.2%)		
≥ 75	243 (45.3%)	613 (54.3%)		
Sex			2.98	0.08
Men	297 (55.4%)	574 (50.9%)		
Women	239 (44.6%)	554 (49.1%)		
Stroke type			0.02	0.9
Ischaemic	456 (85.1%)	957 (84.8%)		
Haemorrhagic	80 (14.9%)	171 (15.2%)		
Number of risk factors‡			7.4	0.3
0	58 (10.8%)	91 (8.1%)		
1	145 (27.1%)	287 (25.4%)		
2	159 (29.7%)	369 (32.7%)		
3	125 (23.3%)	270 (23.9%)		
4	37 (6.9%)	92 (8.2%)		
5	12 (2.2%)	17 (1.5%)		
6	0	2 (0.2%)		

\*Other units = geriatric, general medical and neurological units.

†P for overall data as shown.

‡Comprising past stroke or transient ischaemic attack, hypertension, diabetes, smoking, atrial fibrillation or hyperlipidaemia.

#### 4: Comparison of use of investigations, treatments and outcomes of 1664 patients treated in different types of specialty unit

	Geriatric unit (n=195)	General medical unit (n=604)	Neurological unit (n=329)	Stroke unit (n=536)	$\chi^2$	P*
<b>Investigations</b>						
Chest x-ray	156/195 (80%)	461/604 (76%)	209/329 (64%)	432/536 (81%)	35.48	<0.001
Carotid doppler ultrasound (ischaemic stroke/TIA only)	28/166 (17%)	228/517 (44%)	154/274 (56%)	304/456 (67%)	134.83	<0.001
Echocardiography, transthoracic or transoesophageal (ischaemic stroke/TIA only)	13/166 (8%)	143/517 (28%)	94/274 (34%)	234/456 (52%)	120.39	<0.001
Blood glucose level	141/195 (72%)	415/604 (69%)	263/329 (80%)	497/536 (93%)	56.65	<0.001
Lipid profile	54/195 (28%)	306/604 (51%)	209/329 (64%)	346/536 (65%)	92.76	<0.001
<b>Treatments</b>						
Therapeutic heparin (low molecular weight or unfractionated)	6/166 (4%)	38/517 (7%)	36/274 (13%)	34/456 (7%)	14.53	0.002
Antithrombotic treatment on discharge (patients with past or current atrial fibrillation only)						
Warfarin	9/54 (17%)	46/118 (39%)	24/49 (49%)	29/112 (26%)	16.74	<0.001
Antiplatelet therapy	24/54 (45%)	78/118 (67%)	21/49 (43%)	67/112 (60%)	11.83	0.008
Antihypertensive medication changed (patients with hypertension only)	29/138 (21%)	144/399 (36%)	72/229 (32%)	189/357 (53%)	54.97	<0.001
<b>Outcomes</b>						
In-hospital survival	155/195 (79%)	496/604 (82%)	298/329 (91%)	480/536 (90%)	25.56	<0.001
Median hospital stay (days) (range; IQR)	7 (1–362; 4–16)	8 (1–123; 4–14)	7 (1–371; 4–12)	10 (1–406; 5–26)	54.01 <sup>†</sup>	<0.001
Discharge destination						
Home	58/155 (37%)	281/498 (57%)	191/298 (64%)	305/480 (65%)		
Acute hospital bed	16/155 (10%)	16/498 (3%)	16/298 (5%)	13/480 (3%)		
Nursing home	42/155 (27%)	67/498 (14%)	13/298 (4%)	64/480 (14%)		
Rehabilitation unit	39/155 (25%)	131/498 (26%)	77/298 (26%)	91/480 (19%)		
Ability to perform activities of daily living						
Dress	51/138 (37%)	289/485 (60%)	209/294 (71%)	325/476 (68%)	56.32	<0.001
Feed	85/137 (62%)	380/478 (79%)	246/290 (85%)	384/473 (81%)	31.4	<0.001
Shower	50/144 (34%)	277/487 (57%)	205/294 (70%)	316/476 (66%)	60.1	<0.001
Transfer alone	61/147 (43%)	308/491 (73%)	213/294 (72%)	342/477 (72%)	53.59	<0.001

TIA = IQR = interquartile range. \*P for overall data. †Kruskal–Wallis test.

year, and that these percentages rise with age.<sup>13</sup> In our audit, stroke types did not differ significantly between types of unit, and therefore did not explain survival differences, but patients in stroke units were younger, possibly contributing to their better survival.

Rates of investigations also varied between unit types. Generally, more patients had blood glucose and lipid profiles measured in stroke and neurology units than in the other units. Clearly, all stroke patients should have blood glucose level measured, not only because hypoglycaemia can mimic acute stroke, but also because diabetes is a

risk factor for stroke. Lipid profiles may also be important, as hyperlipidaemic therapy has been found to reduce the risk of stroke in patients with previous myocardial infarction<sup>14</sup> and is currently under study for secondary prevention of stroke.

Use of heparin in stroke is controversial. Neurology units prescribed more heparin at therapeutic doses for acute treatment of ischaemic stroke than other units. An ongoing Cochrane review of the effect of anticoagulation therapy (including low molecular weight and unfractionated heparin) in early treatment of patients with acute

ischaemic stroke found that it did not reduce the odds of death from all causes.<sup>15</sup> Sensitivity analyses identified no particular regimen or patient characteristic associated with net benefit. In contrast, the TOAST trial suggested a higher rate of favourable outcomes in patients with large-artery atherosclerotic stroke treated with low molecular weight heparin.<sup>16</sup> Heparin is often prescribed for patients with continuing neurological deterioration in the first hours or days after stroke (“stroke in evolution”), but the TOAST trial found no improvement in outcomes in such patients. These findings do not

support a role for therapeutic doses of heparin in halting neurological deterioration after stroke. However, low dose, prophylactic heparin is often recommended to prevent venous thromboembolism.<sup>17</sup>

Our results were consistent with previous results showing that specialised stroke units improve outcome compared with general medical wards.<sup>1-5</sup> We found more favourable outcomes in neurological and stroke units than in general medical and geriatric units. This was accompanied by a small, statistically significant increase in length of stay in stroke units. Nevertheless, care in stroke units can still be improved. A Norwegian study in 2000 found that patients were more likely to be independent if they received extended service from a stroke unit (including early supported discharge, further rehabilitation and follow-up from a mobile team in close cooperation with the primary healthcare team) rather than standard service.<sup>18</sup>

Clearly, management of acute stroke in Australia does not always follow recommended practice, but identifying areas for improvement is only the first step. Clinicians and administrators must realise that evidence-based strategies exist for improving care after stroke.<sup>19</sup> Systematic assistance with practice improvement is needed. Improving the outcome of first stroke and reducing the incidence of second events with optimal secondary prevention would have clear benefits for the health of the nation.

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#### COMPETING INTERESTS

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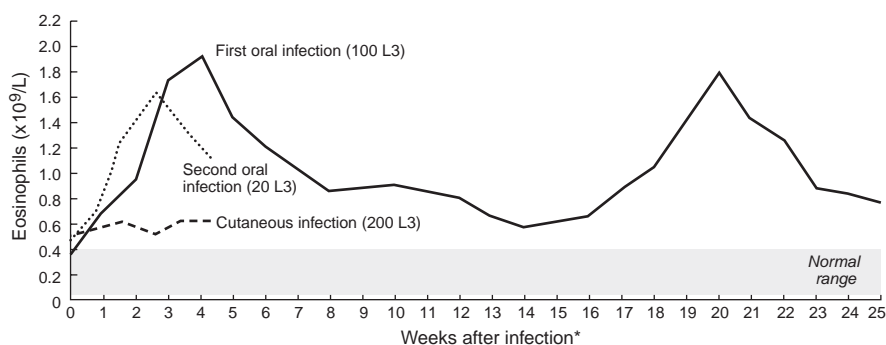
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#### Correction

Re: "Experimental human infection with the dog hookworm, *Ancylostoma caninum*", the Research article by Juergen K Landmann and Paul Procriv in the 20 January issue of the Journal (*Med J Aust* 2003; 178: 69-71), in which the labels for the second oral infection and cutaneous infection in the Figure in Box 2 were accidentally reversed. The corrected Figure is reproduced here.

#### 2: Peripheral blood eosinophil levels after exposure to infective larvae of *Ancylostoma caninum*



\* The three separate experiments were run consecutively over a period of one year.