Progress Review

Frequency of Depression After Stroke
A Systematic Review of Observational Studies

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Background and Purpose—Although depression is an important sequela of stroke, there is uncertainty regarding its frequency and outcome.

Methods—We undertook a systematic review of all published nonexperimental studies (to June 2004) with prospective consecutive patient recruitment and quantification of depressive symptoms/illness after stroke.

Results—Data were available from 51 studies (reported in 96 publications) conducted between 1977 and 2002. Although frequencies varied considerably across studies, the pooled estimate was 33% (95% confidence interval, 29% to 36%) of all stroke survivors experiencing depression. Differences in case mix and method of mood assessment could explain some of the variation in estimates across studies. The data also suggest that depression resolves spontaneously within several months of onset in the majority of stroke survivors, with few receiving any specific antidepressant therapy or active management.

Conclusions—Depression is common among stroke patients, with the risks of occurrence being similar for the early, medium, and late stages of stroke recovery. There is a pressing need for further research to improve clinical practice in this area of stroke care. (Stroke. 2005;36:1330-1340.)

Key Words: depression ■ epidemiology ■ meta-analysis ■ stroke

Some form of depression is considered to occur in at least one-quarter of patients in the first year after acute stroke,1–4 with the period of greatest risk being the first few months after onset.2,5,6 However, such estimates vary considerably across studies because of differences in definitions, study populations and the timing of assessments, as well as complexities in the recognition, assessment, and diagnosis of abnormal mood in the setting of stroke-related disability.3,4,7 The results of studies may also depend on whether subjects are categorized on the basis of psychiatric interview using standard diagnostic criteria such as the Diagnostic and Statistical Manual of Mental Disorders (eg, DSM-IIIR,8 DSM-IV,9 or a psychiatric rating scale such as the Montgomery Åsberg Depression Rating Scale,10 or on the basis of a self-rating mood scale. The goal of this review was to determine the frequency, outcome, and management of depression after stroke from all high-quality published studies.

Materials and Methods

This review was restricted to published research articles, abstracts, and letters of patients with a clinical diagnosis of stroke in whom an assessment of mood was performed at a prespecified time point. The review included incidence studies and case series that had prospective consecutive patient recruitment within clearly defined geographical and time-limited boundaries. There were no restrictions on the basis of language, sample size, or duration of follow-up, but we excluded studies of mixed populations (such as stroke and head injury) unless separate results for stroke patients were identified. Studies were also excluded if they had any of the following: (1) limited to specific patient characteristics such as sex or location of stroke lesion; (2) convenience sampling; (3) retrospective recruitment; or (4) there was only unstructured assessment of mood. The primary endpoint was the proportion of patients who met the diagnostic category of depression as applied in a study, which included: (1) depressive disorder, depressive symptoms, or “psychological distress,” as defined by scores above a cut-point for abnormality on a standard mood scale; and (2) major depression or minor depression (or dysthymia) according to DSM-IIIR.8 DSM-IV,9 or other standard diagnostic criteria. Studies that reported mood outcomes only as a continuous variable, without a categorical diagnosis, were excluded.

Search Strategy and Data Extraction

Data for this review were identified from the following computerized databases: MEDLINE, EMBASE, CINAHL, PsychINFO, Applied Science and Technology Plus, Biological Abstracts, General Science Plus, Arts and Humanities Index, Science Citation Index, Social Sciences Citation Index, Sociofile, and Digital Dissertations using terms and strategy based on the Cochrane Stroke Group methodology (full details available on request; last searched June 2004). In some cases, similarities between study reports indicated the possibility of multiple publications from the...
same cohort. In the absence of explicit cross-referencing, we judged articles to be from the same cohort if they met the following criteria: there was evidence of overlapping recruitment sites, study dates, and grant funding numbers; and there were similar or identical reported patient characteristics in the studies.11 If several articles reported outcomes from the same study population, data were taken from the first publication that referred to each follow-up period. When a variety of methods of mood assessment were undertaken, we reported results for each scale/method. Because we were unable to obtain enough information on publications from one group of papers (the Iowa Group), we chose to present these studies separately.

### TABLE 1. Frequency of Depressed Mood After Stroke: A Summary of the Population-Based Evidence

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>No. Assessed</th>
<th>Time Since Stroke</th>
<th>Depression Diagnosis/Criteria</th>
<th>Frequency (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Bristol Stroke Study25</td>
<td>UK</td>
<td>379</td>
<td>3 wk</td>
<td>WDI (score 19–36, depressed)</td>
<td>22 (18 to 26)</td>
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<tr>
<td>All strokes</td>
<td></td>
<td></td>
<td></td>
<td>WDI (score 15–18, probably depressed)</td>
<td>11 (8 to 14)</td>
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<tr>
<td>All strokes</td>
<td></td>
<td>377</td>
<td>6 mo</td>
<td>WDI (score 19–36, depressed)</td>
<td>20 (16 to 24)</td>
</tr>
<tr>
<td>All strokes</td>
<td></td>
<td>348</td>
<td>12 mo</td>
<td>WDI (score 15–18, probably depressed)</td>
<td>12 (9 to 15)</td>
</tr>
<tr>
<td>FINNSTROKE58</td>
<td>Finland</td>
<td>321</td>
<td>3 mo</td>
<td>BDI (score ≥10)</td>
<td>47 (42 to 53)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BDI (score 30–63 “severe”)</td>
<td>3 (1 to 5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BDI (score 19–29 “moderate”)</td>
<td>11 (8 to 14)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BDI (score 10–18 “mild”)</td>
<td>28 (23 to 33)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>311</td>
<td>12 mo</td>
<td>BDI (score ≥10)</td>
<td>47 (42 to 53)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BDI (score 30–63 “severe”)</td>
<td>2 (0 to 4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BDI (score 19–29 “moderate”)</td>
<td>15 (11 to 19)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BDI (score 10–18 “mild”)</td>
<td>25 (20 to 30)</td>
</tr>
<tr>
<td>Örebro Stroke Study24</td>
<td>Sweden</td>
<td>231</td>
<td>12 mo</td>
<td>GDS (score &gt;5)</td>
<td>37 (31 to 43)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>251</td>
<td>12 mo</td>
<td>DSM-IV depression</td>
<td>27 (22 to 33)</td>
</tr>
<tr>
<td>OCSP6</td>
<td>UK</td>
<td>89</td>
<td>1 mo</td>
<td>DSM-III: major depression</td>
<td>11 (5 to 18)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>DSM-III: dysthymic disorder</td>
<td>1 (0 to 3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>DSM-III: major depression</td>
<td>3 (0 to 6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>76</td>
<td>1 mo</td>
<td>BDI (score ≥10)</td>
<td>32 (22 to 43)</td>
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<td></td>
<td></td>
<td></td>
<td>BDI (score ≥13)</td>
<td>20 (11 to 29)</td>
</tr>
<tr>
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<td></td>
<td>119</td>
<td>6 mo</td>
<td>DSM-III: major depression</td>
<td>9 (4 to 14)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>DSM-III: dysthymic disorder</td>
<td>3 (0 to 6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>107</td>
<td>6 mo</td>
<td>BDI (score ≥10)</td>
<td>32 (23 to 41)</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>BDI (score ≥13)</td>
<td>18 (8 to 22)</td>
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<tr>
<td></td>
<td></td>
<td>112</td>
<td>12 mo</td>
<td>DSM-III: major depression</td>
<td>6 (2 to 11)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>DSM-III: dysthymic disorder</td>
<td>4 (0 to 8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>DSM-III: major depression</td>
<td>11 (5 to 17)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>88</td>
<td>12 mo</td>
<td>BDI (score ≥10)</td>
<td>16 (8 to 24)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BDI (score ≥13)</td>
<td>8 (2 to 14)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60</td>
<td>3–5 y</td>
<td>DSM-III-R major depression</td>
<td>18 (8 to 28)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>191</td>
<td>4 mo</td>
<td>DSM-III major depression</td>
<td>17 (12 to 22)</td>
</tr>
<tr>
<td></td>
<td>Australia</td>
<td></td>
<td></td>
<td>DSM-III minor depression</td>
<td>11 (7 to 15)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60</td>
<td>3–5 y</td>
<td>DSM-III-R major depression</td>
<td>18 (8 to 28)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>294</td>
<td>4 mo</td>
<td>DSM-III major depression</td>
<td>15 (11 to 19)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>DSM-III minor depression</td>
<td>8 (5 to 11)</td>
</tr>
<tr>
<td>SELSS63</td>
<td>UK</td>
<td>96</td>
<td>5 y</td>
<td>HADS (score &gt;10)</td>
<td>36 (26 to 46)</td>
</tr>
</tbody>
</table>

BDI indicates Beck Depression Inventory; CI, confidence interval; DSM, Diagnostic and Statistical Manual of Mental Disorders; HADS, Hospital Anxiety and Depression Scale; OCSP, Oxford Community Stroke Study; PCSS, Perth Community Stroke Study; PSE, Present State Examination; SELSS, South East London Stroke Study; UK, United Kingdom; WDI, Wakefield Depression Inventory.
One reviewer (M.H.) extracted the data, and a second reviewer (C.Y.) cross-checked a selection of data extractions. Studies were grouped into 3 categories that represented degrees of case selection. The first group, “population-based studies,” considered to be of the highest (least biased) quality, consisted of studies that attempted to recruit all stroke patients, including those who were not admitted to hospital for acute care. Although not all of these studies fulfilled certain “ideal” criteria for population-based stroke incidence studies, we considered that these studies included stroke patients with the most representative characteristics.

The other 2 categories were “hospital-based” studies, which included all inpatients from acute care medical wards in general hospitals, and “rehabilitation-based” studies, which included patients from rehabilitation wards, or hospitals (including stroke units), with one study of patients recruited from an outpatient clinic and one study of patients from primary care general practices.

### Statistical Analysis

Studies were stratified by case selection, and according to the timing of mood assessment from stroke onset, defined as: “acute phase” (within 1 month and including date of admission to rehabilitation beds); “medium-term phase” (between 1 and 6 months and including date of discharge from rehabilitation); and “long-term phase” (6 months or more) after stroke. Studies with follow-up assessments that spanned 2 time points (e.g., 2 to 6 weeks after stroke) were included in the latter time category.

We used the depression category that included the most patients to determine the point estimate, together with 95% confidence intervals (CIs) for each study. Pooled estimates were calculated using both fixed and random effects. When one study contributed more than one endpoint to the pooled estimate, sensitivity analyses were undertaken using either the earliest or the latest assessment in that study, although data were presented herein only for the earliest assessment. Statistical heterogeneity was assessed using the standard Q statistic, with $P < 0.05$. When there was evidence of statistical heterogeneity, the random effects approach of DerSimonian and Laird was used to pool the frequencies.

### Results

More than 12,000 references were identified, of which 418 were retrieved to assess for inclusion/exclusion criteria, and a total of 96 reports (51 studies) were considered eligible for inclusion.

### Patient Characteristics

The 6 population-based studies included 2,869 patients from a base population of 1,338,981 between 1981 and 2000 (Table 2).
All these studies included patients with standard clinical criteria for stroke, although one excluded patients with subarachnoid hemorrhage in the assessment of mood outcomes, and between 38% and 92% of all stroke patients were managed in hospital. All studies excluded patients with communication difficulties (eg, aphasia, confusion, dementia), so that the proportion who completed mood assessments ranged from 61% (3-week assessment) to 99% (12-month assessment).

The hospital-based studies included 16,302 patients (see Table 2), and the rehabilitation-based studies included 6,036 patients (Table 3) at the initial assessment. One study accounted for the majority (86%) of patients in the hospital-based studies, with the remaining studies ranging in size from

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### TABLE 3. Frequency of Depressed Mood After Stroke: A Summary of the Rehabilitation-Based Evidence

<table>
<thead>
<tr>
<th>First Author, Year, Source of Patients</th>
<th>Country</th>
<th>No. Assessed</th>
<th>Time of Assessment</th>
<th>Depression Criteria</th>
<th>Frequency (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Åstrom, 1993 Stroke unit</td>
<td>Sweden</td>
<td>76</td>
<td>Discharge from hospital</td>
<td>DSM-III-R major depression</td>
<td>25 (15 to 35)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>73</td>
<td>3 mo after stroke</td>
<td></td>
<td>31 (20 to 42)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>68</td>
<td>1 y after stroke</td>
<td></td>
<td>16 (7 to 25)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>57</td>
<td>2 y after stroke</td>
<td></td>
<td>19 (9 to 29)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
<td>3 y after stroke</td>
<td></td>
<td>29 (16 to 42)</td>
</tr>
<tr>
<td>Bacher, 1990 Rehabilitation hospital</td>
<td>Canada</td>
<td>48</td>
<td>Admission to hospital</td>
<td>ZDS (score ≥60)</td>
<td>4 (0 to 10)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>43</td>
<td>6 wk after admission</td>
<td>ZDS (score ≥60)</td>
<td>9 (1 to 18)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>42</td>
<td>6 mo after admission</td>
<td>ZDS (score ≥60)</td>
<td>17 (5 to 28)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>39</td>
<td>1 y after admission</td>
<td>ZDS (score ≥60)</td>
<td>21 (8 to 33)</td>
</tr>
<tr>
<td>Bendesen, 1997 Rehabilitation hospital</td>
<td>Denmark</td>
<td>128</td>
<td>1.5 mo after stroke</td>
<td>DSM-III-R major depression</td>
<td>16 (10 to 22)</td>
</tr>
<tr>
<td>Carod-Artal, 2000 Stroke unit</td>
<td>Spain</td>
<td>90</td>
<td>1 y after stroke</td>
<td>HDRS (cut-point not stated)</td>
<td>38 (28 to 48)</td>
</tr>
<tr>
<td>Daily, 1983 Stroke unit</td>
<td>USA</td>
<td>32</td>
<td>Admission to unit</td>
<td>HDRS &amp; BDI (cut-point not stated)</td>
<td>16 (3 to 29)</td>
</tr>
<tr>
<td>Diamond, 1995 Geriatric rehabilitation unit</td>
<td>USA</td>
<td>14</td>
<td>Admission to unit</td>
<td>GDS (score &gt;10)</td>
<td>36 (11 to 61)</td>
</tr>
<tr>
<td>Folstein, 1977 Rehabilitation hospital</td>
<td>USA</td>
<td>20</td>
<td>30 d after stroke</td>
<td>PSE (≥ 8 items on the 8th edition)</td>
<td>45 (23 to 67)</td>
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<tr>
<td>Gainotti, 1999 Neurology department &amp; rehabilitation center</td>
<td>Italy</td>
<td>153</td>
<td>&lt;2 mo after stroke</td>
<td>DSM-III-R major depression/ HDRS (score ≥17)</td>
<td>27 (20 to 34) / 32 (25 to 39)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2–4 mo after stroke</td>
<td>DSM-III-R major depression/ HDRS (score ≥17)</td>
<td>40 (32 to 48) / 60 (52 to 68)</td>
</tr>
<tr>
<td>Gillen, 2001 Inpatient rehabilitation</td>
<td>USA</td>
<td>243</td>
<td>15 d after stroke</td>
<td>GDS (score ≥15)</td>
<td>13 (9 to 17)</td>
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<tr>
<td>Gottlieb, 2002 Inpatient rehabilitation</td>
<td>Israel</td>
<td>65</td>
<td>3 mo after stroke</td>
<td>GDS (≥50% items endorsed)</td>
<td>63 (51 to 75)</td>
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<tr>
<td>Jürgensen, 1999 Geriatric rehabilitation center</td>
<td>Germany</td>
<td>77</td>
<td>6 mo after discharge</td>
<td>DSM-IV major depression</td>
<td>20 (11 to 29)</td>
</tr>
<tr>
<td>Kauhanen, 1999 Stroke unit</td>
<td>Finland</td>
<td>101</td>
<td>3 mo after stroke</td>
<td>DSM-III-R major depression</td>
<td>9 (3 to 15)</td>
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<tr>
<td></td>
<td></td>
<td>92</td>
<td>1 y after stroke</td>
<td>DSM-III-R major depression</td>
<td>44 (34 to 54)</td>
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<td></td>
<td></td>
<td></td>
<td>DSM-III-R major depression</td>
<td>15 (8 to 22)</td>
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<td></td>
<td>DSM-III-R major depression</td>
<td>26 (17 to 35)</td>
</tr>
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<td>Kellermann, 1999 Stroke unit</td>
<td>Hungary</td>
<td>82</td>
<td>1 wk after admission</td>
<td>BDI (score &gt;10)</td>
<td>20 (11 to 28)</td>
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<td>Kim, 2002 Outpatient clinic</td>
<td>Korea</td>
<td>145</td>
<td>3–12 mo after stroke</td>
<td>DSM-IV depression (≥5 items), BDI (score &gt;13)</td>
<td>15 (9 to 21)</td>
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<tr>
<td>King, 2002 Rehabilitation units and general hospital</td>
<td>USA</td>
<td>53</td>
<td>Discharge from unit</td>
<td>CES-D (score ≥16)</td>
<td>30 (8 to 42)</td>
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<td></td>
<td>6–10 wk after discharge</td>
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<td>26 (14 to 38)</td>
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<td></td>
<td>1 y after discharge</td>
<td></td>
<td>17 (7 to 27)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 y after discharge</td>
<td></td>
<td>23 (12 to 34)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Prevalence over 2 y</td>
<td></td>
<td>51 (38 to 65)</td>
</tr>
</tbody>
</table>
The criteria used to define depression (or depression symptom burden) also varied across studies. In the main, DSM criteria were used to define depression (in 19 studies) using information from completed mood scales, and occasionally from structured interviews, although the criteria for dysthymia were modified by excluding the requirement for symptoms to be present for at least 2 years. There was also variation in the cut-points used on the standardized mood scales, whereas there was consistency for the Montgomery Åsberg Depression Rating Scale (≥7) and the Zung Depression Scale (≥50), these scales were used in only a minority (6) of studies, whereas multiple cut-points were used for the Beck Depression Inventory (≥10, >10, >13, and ≥17), the Geriatric Depression Scale (>5, >10, ≥15, >50% items positively endorsed), and the Hamilton Depression Rating Scale (>8, ≥12, ≥13, ≥17, ≥18).

**Frequency of Depression**

Although there was considerable variation in the reported frequency of depression after stroke across individual studies,
<table>
<thead>
<tr>
<th>First Author, Year</th>
<th>Assessed/Alive Time Since Stroke</th>
<th>Topic</th>
<th>Depression Criteria</th>
<th>Frequency</th>
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</thead>
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<tr>
<td><strong>Cohort 1</strong></td>
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<tr>
<td>Robinson, 1982</td>
<td>103/154 Acute assessment</td>
<td>Prevalence and severity of depression</td>
<td>GHQ-28 ≥5</td>
<td>29</td>
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<tr>
<td></td>
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<td>GHQ-28 ≥6</td>
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<td></td>
<td></td>
<td></td>
<td>GHQ-28 ≥8</td>
<td>17</td>
</tr>
<tr>
<td>Robinson, 1983</td>
<td>103 2 wk Predictors of depression</td>
<td>DSm-III Major D</td>
<td>27</td>
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<tr>
<td>Robinson, 1984</td>
<td>40/154 3 mo Prevalence and duration of depression</td>
<td>DSm-III Major D</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>50/154 6 mo</td>
<td></td>
<td>DSm-III Minor D</td>
<td>27</td>
</tr>
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<td>Robinson, 1987</td>
<td>37/154 12 mo Prevalence of depression</td>
<td>DSm-III Major D</td>
<td>14</td>
<td></td>
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<tr>
<td></td>
<td>48/154 2 y</td>
<td></td>
<td>DSm-III Minor D</td>
<td>19</td>
</tr>
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<td>Parikh, 1990</td>
<td>63 2 y Recovery over 2 y</td>
<td></td>
<td>DSm-III Major D</td>
<td>24</td>
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<td></td>
<td></td>
<td></td>
<td>DSm-III Minor D</td>
<td>6</td>
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<td><strong>Cohort 2</strong></td>
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<td></td>
</tr>
<tr>
<td>Castillo, 1993</td>
<td>288/309 2 wk Generalized anxiety disorder and depression</td>
<td>HDRS (no cutpoint), PSE (no cutpoint)</td>
<td>38</td>
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<tr>
<td>Downhill, 1994</td>
<td>140/309 Baseline Depression and cognitive impairment</td>
<td>DSm-IV Major D</td>
<td>40</td>
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<td></td>
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<td>DSm-IV Minor D</td>
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<tr>
<td>Castillo, 1995</td>
<td>142/215 Baseline Correlates of early and late onset GAD</td>
<td>‘Depression’</td>
<td>51</td>
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<td></td>
<td>78 3 mo</td>
<td></td>
<td>DSm-III-R GAD</td>
<td>27</td>
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<td></td>
<td>80 6 mo</td>
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<td></td>
<td>70 12 mo</td>
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<td>36</td>
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<tr>
<td></td>
<td>66 2 y</td>
<td></td>
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<td>Kishi, 1996</td>
<td>301 Baseline Validity of observed depression</td>
<td>DSm-IV Major D</td>
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<td>DSm-IV Minor D</td>
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<tr>
<td>Paradiso, 1997</td>
<td>142 Baseline Psychological symptoms associated with depression</td>
<td>HDRS (no cut-point), PSE (no cut-point)</td>
<td>42</td>
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<tr>
<td></td>
<td>76 3 mo</td>
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<td></td>
<td>79 6 mo</td>
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<td></td>
<td>69 12 mo</td>
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<td>29</td>
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<td></td>
<td>66 2 y</td>
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<td>Schultz, 1997</td>
<td>142 Baseline GAD and depression and recovery</td>
<td>DSm-IV GAD</td>
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<td>77 3 mo</td>
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<td>66 2 y</td>
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<td>Shimoda, 1998</td>
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<td>DSm-IV Major D</td>
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<td>Shimoda, 1998</td>
<td>142 Baseline Social functioning and depression on recovery</td>
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<td>301 2 wk Gender differences in depression</td>
<td>DSm-IV Major D</td>
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GAD indicates generalized anxiety disorder; GHQ, General Health Questionnaire.

*Funding numbers: MH00163, NS15178, NS16332, NS18622, NS9–2032, recruitment period 1.5 years, or between January 1980 and July/August 1981; populations had similar demographic characteristics.

†Did not report funding number NS9-2032.

‡Funding numbers: MH00163, MH40355; populations had similar demographic characteristics.
the pooled estimate indicates that depressive symptoms are present in 33% (95% CI, 29% to 36%) of all stroke survivors at any time during follow-up (Figure). The pooled estimate from the population-based studies was 33% in the acute and medium-term phases, with a slight increase to 34% in the long-term phase of recovery after stroke. There was modest variation in the pooled frequencies in the hospital-based (acute 36%, medium-term 32%, and long-term 34%) and rehabilitation-based studies (acute 30%, medium 36%, and long-term 34%) over time, but the 95% CIs around all pooled frequencies overlapped.

There was, however, more variation in the pooled frequencies when studies were grouped by method of mood assessment (data not presented). The 2 studies that used a single simple question to determine depression status had a pooled frequency of 14% (95% CI, 14% to 15%). The smallest pooled frequency with standardized questionnaires was from studies that used the Hamilton Depression Rating Scale (26%; 95% CI, 11% to 42%), whereas the highest frequency was in studies that used the Montgomery Åsberg Depression Rating Scale (41%; 95% CI, 23% to 60%) or the Zung Depression Scale (41%; 95% CI, 34% to 48%). The estimates again varied when studies were grouped by type of mood scale and timing of assessment.

The Oxfordshire Community Stroke Project, conducted nearly 20 years ago, is the only population-based study to date that recruited controls to allow estimates of the relative risks of depression after stroke. Using Beck Depression Inventory (scores ≥10) and the Present State Examination psychiatric interview schedule (scores ≥5) to determine “caseness,” the study showed that the frequency of depression in stroke survivors (20% Beck Depression Inventory; 11% Present State Examination) was twice that in controls, although this difference only reached statistical significance at the 6-month follow-up assessment. In addition, 4 hospital-based studies have compared mood data in cases with controls, although only 1 study had controls selected from the community. However, this latter study only assessed patients with new episodes of depression within the 6 months after stroke, yet still included patients with depression that had been present for ≥1 year. Despite this anomaly, the 5% proportional frequency of “new” depression was similar in stroke patients and controls. Another study showed no difference in the cumulative 1-year incidence of depression after

The meta-analyses of proportions are presented stratified into subgroups on the basis of case selection (population-based ○, hospital-based □, rehabilitation-based △) and timing of mood assessment from the onset of stroke (acute phase: within one month, and including date of admission to rehabilitation beds; medium-term phase: between one and six months, and including date of discharge from rehabilitation; and long-term phase: six months or more after stroke). The circles, triangles, squares and diamonds are centered around the pooled estimate of effect; their size is large where samples are larger, reflecting the relationship between the inverse of the variance. Horizontal lines represent 95% confidence intervals (CI). The solid diamond represents the pooled frequency and 95% CI for all contributing studies.

Observational studies of the proportional frequency of depression after stroke.
stroke compared with a randomly selected control group of patients with first-ever myocardial infarction (in contrast to consecutive recruitment of stroke patients). Different results were found in 2 other studies; one study in which controls were randomly selected from the neighboring hospital community and including spouses of stroke patients showed more depression in stroke survivors (11%) than controls (5%) at 3 months after stroke (odds ratio [OR], 2.52; 95% CI, 1.35 to 4.80); and the other study that did not provide any details on the selection of controls, reported that depression was also more common in stroke patients than controls (OR, 3.16; 95% CI, 1.48 to 4.12).

Another robust examination of the relative frequency of depression in stroke survivors was undertaken in The Framingham Study, a prospective, observational, community-based study that enrolled middle-aged subjects who have been followed-up biennially since the middle of the past century. When data from 74 of the 251 subjects who experienced a stroke between 1982 and 1994 were isolated and compared with data from 74 control subjects matched for age and sex, significantly more stroke survivors (38%) were depressed at 6 months after stroke than controls (10%). In a separate analysis of ≥20-year outcomes from 148 subjects with a stroke between 1972 and 1974, only 1 (11%) of 9 stroke survivors met the criteria for depression compared with 3 (15%) of 20 nonstroke controls.

**History of Depression, Antidepressants, and Psychotherapy**

Only 2 population-based studies have assessed the natural history of depression within individual stroke patients. Both found that only a small proportion of patients had depressive symptoms that persisted for most of the first year after stroke, despite the relatively constant overall frequency of depression among the total study population during this time. Although some patients recovered spontaneously from depression within a few months, others had depressive symptoms for the first time later after stroke. Similar results were found in 1 hospital-based, and 4 rehabilitation-based studies, and are further confirmed by this review.

It is well-recognized that personal or family history of depression may place an individual at increased risk of depression. Although no population-based studies excluded patients with a history of depression from analyses, 17 hospital-based and rehabilitation-based studies excluded patients with recent or severe depression, including 6 studies in which patients using antidepressants at entry were also excluded. Use of antidepressants at entry or during follow-up was assessed in less than half of the included studies, and ranged from 0% in the first few weeks to 31% at 2 years after stroke. The highest proportion of “adequately treated” patients (ie, those using antidepressants who did not fulfill criteria for depression) at the time of assessment in any one study was 84%. The highest proportion of participants receiving antidepressants who were “inadequately treated” (ie, those on antidepressants who still fulfilled criteria for depression) was 71%. No data were available on the proportion of stroke patients who had received psychotherapy.

**Discussion**

We report that one third of all people experience significant depressive symptoms at some time after the onset of stroke. We recognize, however, that this is likely to be a conservative estimate because of potential under-reporting (or under-recognition) of abnormal mood, and the difficulties inherent to the assessment of mood in patients with neurological disability, particularly when there are communication problems caused by dysphasia and/or dementia. Given the importance of mood, which along with cognition, motivation, and social support is a key factor influencing recovery from stroke, it is surprising that there is much misconception over the epidemiology of stroke-associated depression, although the generally poor quality of studies has obviously contributed to this situation.

Whereas previous reports have acknowledged wide variation in the frequency of depression after stroke across studies largely because of differences in patient characteristics and study designs, they have also suggested that the lowest and highest frequency of depression is found among patients in population-based and rehabilitation-based studies, respectively, potentially reflecting selection bias toward the inclusion of more disabled stroke survivors in the latter studies. Moreover, the time period of greatest risk of depression has traditionally been considered to be the first few months of stroke onset. Our review, conversely, showed consistency in the overall frequency of depression across the 3 different types of studies and in relation to the time periods from stroke onset, thus raising doubts about specific biological theories related to an acute stroke lesion as the major cause of depression in this condition. In addition, we found that few stroke patients receive effective management (antidepressants or psychotherapy) for their depression, although the limited data would suggest that these symptoms are self-limited in most after several months.

Because the design of observational studies, by their very nature, may differ in a number of important ways, it is useful to explore and quantify the reasons for such heterogeneity. We identified variation in the cut-points used to determine “caseness” in the standardized mood scales as one key source of variability in the data. It would appear that many studies failed to consider that older people, and those with physical illnesses, might require higher cut-points on these scales. Two other problems were that multiple methods were often used to diagnose depression, with few investigators clearly identifying an a priori primary endpoint in their study, so that the endpoints reported varied between “any depression,” “first-ever depression,” and “severity” of depression. Without greater uniformity or standardization of such methodological issues, it will remain difficult to determine whether heterogeneity in study findings represent true differences in characteristics of populations or simply artifact caused by measurement bias and other error.

Of course, heterogeneity across studies can also be attributed to differences in case mix, including variation in stroke features, clinical characteristics, source of patient recruit-
ment, and the timing of assessment. In this review, we have attempted to minimize heterogeneity by grouping studies by source of case selection. It is particularly noteworthy that a number of studies excluded patients at the greatest risk for depression, that is those with a history of depression. Although a systematic review with meta-analysis can overcome some of the shortcomings of unstructured examination of individual studies, the gold standard review would include an individual patient data analysis with adjustment for potential confounding factors to calculate frequency estimates, but this is complex and challenging to undertake.

There are other problems of study design that limit the reliability of the comparisons of frequency estimates between stroke patients and controls. It is important to note that stroke patients are generally older, female, and more likely to have concomitant illnesses and to have experienced some bereavement or other major life event than that of the general population. In this respect, controls need to be matched by age and sex, because these factors are associated with depression at any age. Yet the selection of controls in 3 of the 5 case-control studies did not account for such factors. Although it may appear likely that stroke-associated depression is no more common than other types of depression in the general population, there have been no direct comparisons between stroke patients and people with other disabling and potentially life-threatening illnesses.

Although we attempted to adhere to the guidelines for reporting meta-analyses of observational studies, this review does have several limitations. First, we did not hand-search journals and made no attempt to identify unpublished studies, raising the possibility that some studies have been missed. Second, only one person extracted most of the data. Ideally, 2 people should complete data extraction to reduce the possibility of errors when transcribing study results. Even so, all the data were checked for accuracy on multiple occasions and all analyses were conducted twice. Finally, it is possible that some ‘multiple publications’ have been missed altogether. We have paid particular attention to addressing this source of publication bias, because the lack of cross-referencing of data from some cohorts has only served to mislead the research community, specifically in reference to the amount of information available on the development of depression after stroke.

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Maree L. Hackett, Chaturangi Yapa, Varsha Parag and Craig S. Anderson

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