Original Contributions

Stroke Trends in an Aging Population

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Background and Purpose: Trends in stroke incidence and survival determine changes in stroke morbidity and mortality. This study examines the extent of the incidence decline and survival improvement in the Netherlands from 1979 to 1989. In addition, it projects future changes in stroke morbidity during the period 1985 to 2005, when the country’s population will be aging.

Methods: A state-event transition model is used, which combines Dutch population projections and existing data on stroke epidemiology. Based on the clinical course of stroke, the model describes historical national age- and sex-specific hospital admission and mortality rates for stroke. It extrapolates observed trends and projects future changes in stroke morbidity rates.

Results: There is evidence of a continuing incidence decline. The most plausible rate of change is an annual decline of -1.9% (range, -1.7% to -2.1%) for men and -2.4% (range, -2.3% to -2.8%) for women. Projecting a constant mortality decline, the model shows a 35% decrease of the stroke incidence rate for a period of 20 years. Prevalence rates for major stroke will decline among the younger age groups but increase among the oldest because of increased survival in the latter. In absolute numbers this results in an 18% decrease of acute stroke episodes and an 11% increase of major stroke cases.

Conclusions: The increase in survival cannot fully explain the observed mortality decline and, therefore, a concomitant incidence decline has to be assumed. Aging of the population partially outweighs the effect of an incidence decline on the total burden of stroke. Increase in cardiovascular survival leads to a further increase in major stroke prevalence among the oldest age groups. (Stroke 1993;24:931-939)

KEY WORDS • aging • epidemiology • morbidity • mortality • The Netherlands

The dynamics of stroke morbidity and mortality are of major interest for clinicians as well as for epidemiologists and health policy makers. A changing stroke epidemiology results from changes in incidence and survival. The balance between these trends determines the numbers of short- and long-term stroke survivors within a population. Recently, the debate on the relative contribution of trends in incidence and survival to stroke mortality decline has intensified, complicated by different study methods and inconsistent results.1-4

In the Netherlands as well as in the United States, stroke mortality has been declining for all age groups since the early 1960s.1,3,6 In the Netherlands, the age-adjusted decline from 1979 to 1989 has been a constant 3.1% per year for men and 4.0% for women, whereas in the United States mortality decline has been 5.7% and 5.2%, respectively.5,5 An incidence decline has also been observed,7-9 ascribed to better hypertension control and a decline in smoking prevalence.7,8,10 Observed incidence trends are confounded by the introduction of computed tomography, improving the specificity of the diagnosis but also increasing case finding. Declines in short- and long-term case fatality have been documented for the last decades,7,9,11-13 explained mainly by a better prognosis after intracerebral hemorrhage, by increased hypertension control,7,10 and by better prevention and treatment of complications, especially of cardiac disease. However, the observed mortality decline started long ago and cannot be fully accounted for by observed changes in risk factors. Most likely, both incidence and case-fatality decline will remain largely unexplained.3,13

This study determines the most plausible range of incidence and fatality decline that explains the impressive observed reduction in stroke mortality in the Netherlands by means of a state-event model.14 In addition, the model is applied to project future changes in stroke incidence and prevalence using the calculated trend values.

Materials and Methods

Stroke mortality trends are determined by changes in stroke incidence, survival, recovery, recurrence, and mortality from other diseases. Given this complexity, a mathematical model is indispensable.14 We developed a state-event model that is based on the clinical course of stroke (Fig 1). Combining data from various sources, the model describes the epidemiology of stroke in the Netherlands.

The basic principle of a state-event model is that patients move from one particular state to another after experiencing a particular event.14,15 The likelihood of moving from one state to another, a transition probability, is independent from the preceding states or
events and depends only on the current state defined by disease stage, age, and sex during the event. All probabilities are age and sex specific. Five-year age groups range from 25 years to 90 years and older. The model combines a demographic component, containing the most likely national population projections\textsuperscript{16} and a stroke-specific component. Risk of death from other causes is accounted for in all states.

During computation the model annually generates first-incident cases from the demographic component. These enter the respective states within the stroke-specific component and follow the various flows with the model. Simultaneously, the model also annually updates all existing prevalent states for recurrences and their consequences.

Within the stroke disease component of the model two events can occur: a transient ischemic attack (TIA) or a stroke, both defined as in the Oxford Community Stroke Project (OCSP).\textsuperscript{17,18} We distinguished different states for the first year and for all subsequent years together. Because the flows in the model during the first year and the subsequent years are almost identical, these two states for each condition are depicted together to clarify the presentation. In both TIA states the patient has an increased risk of stroke. After the first year, patients with a history of a TIA enter the “subsequent-years” state and run a lower stroke risk. A separate first-month state after a first stroke allows for the acute phase with a high risk of disability and death. Patients enter this state after a first stroke. Patients surviving the first month are left either with a minor or major stroke as defined by Rankin grade 0 to 2 and 3 to 5\textsuperscript{19} respectively, and are divided between the two separate states. Patients with a history of stroke run a risk of recurrence. If this occurs, there is an excess risk of dying or having a major stroke. In the first-year state for major stroke, some patients recover, defined by Rankin grade 0 to 2. The recovered patients enter the minor stroke state. The remaining fraction moves to the major stroke state for all subsequent years. In both major stroke states a patient suffers a delayed death due to a first and disabling stroke.

One model assumption is that in the acute phase almost all deaths can be attributed to first stroke and only a few to other causes of death. In this phase, the risk of recurrence and the excess risk of death from heart disease are not accounted for because of an absence of recorded data. Also, a single state for all subsequent years together implies that the recurrence risk in the subsequent-years state is the same for all
following years. This is supported by recent Dutch data.20 In addition, we do not distinguish between strokes caused by intracerebral hemorrhage and those caused by cerebral infarction. From a patient-based view, these are different. At the aggregated population level a distinction is less useful because thrombotic infarctions constitute more than 80% of all stroke cases.17,21 Moreover, the survival after a hemorrhagic stroke is reaching the level of survival after an infarction as a result of improved prognosis and increased detection of smaller and less harmful hemorrhages.22

The origin of the crude data used to calculate the baseline input is summarized in Table 1. We have calculated the age-specific transition probabilities using the results of Dutch population-based studies, if available. If incomplete, they have been used to check selected comparable figures of other white populations as listed in the table. Relative risks are used when comparing risks for one patient category with another. Ratios are used as transition probabilities without further calculations. The choice of measure depends on the way the data have been made available.

The risk of a first TIA is calculated using the incidence figures from the OCSP.18 Age-specific probabilities are calculated by exponential interpolation and are comparable to data from the Nijmegen University Department of General Practice (NUHI)23 and also the Rochester study.24 The relative risks of stroke after a first TIA reported by the OCSP30 have been interpolated and are multiplied by the population risks from the Tilburg Epidemiological Study of Stroke (TESS) and the OCSP (see below)17,21 to calculate age-specific absolute stroke risks after a TIA.

Probabilities of a first stroke are calculated by averaging the results of the incidence studies by the OCSP and the TESS that have produced similar figures.17,21 Because the TESS included fewer age groups, the results of both studies are combined to have reliable incidence figures for as many age groups as possible. Results are consistent with the NUHI data.23,25 Age-adjusted all-stroke case-fatality rates from the TESS study have been corrected for recurrences by assuming a double recurrence death hazard. The resulting case-fatality ratios of the OCSP and TESS are nearly identical (19% and 20%). The probability of residual major disability after 1 month is assumed to be constant for age and sex.26

The recurrence risk for minor stroke patients is assumed to be the same as the first-stroke risk for TIA patients. The ratio of the risk of dying after a recurrence vs the risk after a first-ever stroke is 1.5.27 For the risk of a major stroke after a recurrence the same ratio is used. Recurrence risk in the subsequent-years state after a minor stroke is estimated at half the first-year risk,20 with the same risk of dying and of major stroke, given the recurrence, as during the first year.28

The probability of recovery from major stroke has been calculated by age group and is the same for both sexes.21 In agreement with various studies,9,21,27,29 recurrence risk and subsequent death after major stroke have been estimated by doubling the hazard ratio of the same parameter as found by Howard et al.27 for the minor stroke group. Late stroke mortality during subsequent years is half the risk in the first-year state. The recurrence risk in the subsequent-years state after a disabling stroke is half the first-year risk8,10 as assumed for minor stroke.

The excess age-specific risk of death from ischemic heart disease (International Classification of Diseases [ICD] 410 to 414) in the prevalent states has been calculated by multiplying the hazard ratios for cardiac death27,28 with the age-specific risk of death from ischemic heart disease for the general Dutch population.6 Risk of death from other causes is calculated using the all-causes death rates from the national death registry corrected for the stroke-related figures (ICD 430 to 438).

**Table 1. Crude Literature Data Used to Calculate Baseline Transition Probabilities Within Stroke Model and Resulting Transition Probabilities for the Group of Patients Aged 70-74 Years**

<table>
<thead>
<tr>
<th>Event</th>
<th>Crude data</th>
<th>Probability (70-74 years)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First TIA</strong></td>
<td>Rate</td>
<td>0.42/1000</td>
<td>0.0037/0.0026</td>
</tr>
<tr>
<td><strong>First stroke</strong></td>
<td>Rate</td>
<td>1.62/1000</td>
<td>0.012/0.010</td>
</tr>
<tr>
<td><strong>Death from first stroke</strong></td>
<td>Ratio</td>
<td>0.20</td>
<td>0.21/0.21</td>
</tr>
<tr>
<td><strong>Major disability after first stroke</strong></td>
<td>Ratio</td>
<td>0.39</td>
<td>0.39</td>
</tr>
<tr>
<td><strong>Recovery from major stroke</strong></td>
<td>Ratio</td>
<td>0.76</td>
<td>0.22</td>
</tr>
<tr>
<td><strong>Stroke after TIA/minor stroke</strong></td>
<td>RR</td>
<td>First year &lt;75 years</td>
<td>13.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>First year &gt;75 years</td>
<td>4.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subsequent years</td>
<td>5.0</td>
</tr>
<tr>
<td><strong>Late death from major stroke</strong></td>
<td>Ratio</td>
<td>MHR*</td>
<td>0.17/0.42</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MHR†</td>
<td>1.261</td>
</tr>
<tr>
<td><strong>Death from cardiac disease after TIA or stroke</strong></td>
<td>RR</td>
<td>First-year recurrence</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RR‡</td>
<td>0.665</td>
</tr>
<tr>
<td><strong>Death from cardiac disease after major stroke</strong></td>
<td>RR‡</td>
<td></td>
<td>1.57</td>
</tr>
</tbody>
</table>

TIA, transient ischemic attack; RR, relative risk; MHR, multivariate hazard ratio; NUHI, Nijmegen University Department of General Practice; OCSP, Oxford Community Stroke Project; TESS, Tilburg Epidemiological Study of Stroke; DGP, Dutch general practices; N, North.

*Risk comparison: age (X+10)/X; †risk comparison: women-men; ‡risk comparison: major/minor stroke.
The stroke disease component of the model in combination with the demographic component describes the stroke epidemiology for the Dutch population in steady state. So far it has been presented with fixed transition probabilities. The model estimates stroke prevalence for the baseline year (Fig 2) after assuming the same transition probabilities during the preceding years.

The model allows for age-specific time trends for all the transition probabilities depicted in Fig 1. This allows for plausible projections over longer periods. The values of these trends are calculated by time-series analysis of available figures from comparable populations. A trend is defined as the annual percent change, which means an exponential change. To calculate this kind of trend, a log-transformation is first applied. The regression line, through the log-transformed figures of each time interval, is determined by a least-squares fit. The regression coefficient, or slope, of this line is the annual percent change of the time-series figures.

During computation two sets of trends are used. One set consists of all “attack” parameters: the risks of a TIA, first stroke, or recurrence. The other set includes all parameters regarding acute and late case-fatality of stroke accounting for the decreasing severity of stroke. This study focuses on the first-stroke incidence and case-fatality trends.

These trends in transition probabilities are not very well documented. The Rochester study is the only study that produces age- and sex-specific data on the secular changes in both stroke incidence and fatality. We applied the Rochester incidence and case-fatality trends to the respective attack and case-fatality sets of trends within the model. This can be done because the Dutch incidence figures for TIA and stroke as well as case-fatality ratios for a single 2-year period agree with comparable Rochester data. We ignored the recent, most likely temporary, incidence increase for Rochester caused by increased case-finding because of the introduction of computed tomography. Trends in the two remaining transition probabilities, the risk of major stroke after stroke and the chance of recovery from a major stroke, are not known and are assumed constant. The application of the Rochester incidence and survival trends appears to reproduce almost identical sex-specific mortality trends as observed in the Netherlands from 1979 to 1989 (Table 2). This seems logical because both populations are mainly white and comparable in most other aspects. Other combinations of trend values for incidence and case-fatality, however, can also account for the observed mortality decline. The difficulty is that trend values are reported mostly separately from each other and without corresponding overall mortality trend.

To solve this we used a two-way sensitivity analysis of incidence and case-fatality trends to determine a plausible set of values.


<table>
<thead>
<tr>
<th>Scenario</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Annual trend (%)</td>
<td>Fit</td>
</tr>
<tr>
<td></td>
<td>Incidence</td>
<td>Case-fatality</td>
</tr>
<tr>
<td>Upper</td>
<td>−1.7</td>
<td>−1.7</td>
</tr>
<tr>
<td>Rochester</td>
<td>−1.9</td>
<td>−1.3</td>
</tr>
<tr>
<td>Lower</td>
<td>−2.1</td>
<td>−1.0</td>
</tr>
</tbody>
</table>

*df=10 [(number of age groups−1)⋅(number of categories−1)].
†P>.5 indicates a good fit.
sible ranges of values (Fig 3). In the analysis, for each value of one set of trends we calculated the corresponding value of the other set that, in combination, leads to the same mortality decline. Under the condition of a fixed mortality decline, the incidence and case-fatality trends are inversely proportional. When the incidence rates decrease, the case-fatality rates have to increase five times as rapidly to outweigh the decreasing mortality decline. The main reason for this is that the case fatality after a first stroke is 20%. This inverse relation leads to the isomortality lines in Fig 3. The area above the lines includes those values of trends that lead to a larger mortality decline. The area below includes the values that lead to a lesser mortality decline. The range of reported values for case-fatality trends is small.9,12 As a result, it defines a much narrower range of values for a possible incidence decline than is reported in the literature.

Statistical testing of the results of the computations is done by comparing model results with the observed national data. A $\chi^2$ goodness-of-fit test is used (see “Appendix”). A value of $P>.5$ for this test indicates a good fit of the computed results and the observed data. The goodness-of-fit of the model age-specific stroke mortality rates and stroke admission rates (first and recurrent strokes together) is given as well as that of the trends in the model mortality rates.

**Results**

The stroke model produces nationwide projections regarding the stroke epidemiology including first-stroke incidence, stroke recurrences, and stroke mortality and prevalence. Fig 2 shows the model outcome regarding national stroke hospital rates, including both fatal and nonfatal cases, and national stroke mortality rates for the 1985 baseline year. There is a good fit for the age groups up to 80 years between model outcomes and the national data of the same year: the $\chi^2$ for men is 8.10 and 6.37, respectively, and for women is 6.21 and 8.15, respectively (all $P>.5$, df=11). These $\chi^2$ values support the validity of the model. The national admission rate for the group aged 85 years and older from the hospital registry is lower than the model admission rate, because the latter refers to the group aged 85 to 89 years only. The lower model stroke death rates of the same age group are most probably due to an overregistration of stroke deaths for this age group in general practice and/or a possible underregistration of incidence in the OCSP and TESS.

Table 3 lists the aggregated model results for 1985 and relative change of output results for the year 2005. Here trend values are used assuming a continuing Rochester-like scenario and therefore a continuing mortality decline. All rates are decreasing, and there are no major sex differences. Because all attack rates, including risk of recurrence, are assumed to decrease, all-stroke rates decrease more than first-stroke rates. Because of improved survival, the drop in prevalence rates is considerably less. The projected decline in stroke death rate is the same as during the past 20 years in the Netherlands.5,6 This has been the basic assumption of this projection.

The effect of the aging of the postwar baby boom population is shown in the shifts in absolute numbers: less decline in all-stroke cases and an increase in prevalent cases. The longer life expectancy of Dutch women is reflected in a smaller decrease of first-stroke cases and stroke deaths. In general, the incidence decline outweighs the expected increase in absolute numbers of acute stroke episodes with the aging of the postwar generation. Nevertheless, increased survival increases the absolute number of prevalent cases considerably.

Resulting prevalence rates for major stroke are given in Fig 4 and agree with the population-based rates found in Finland and Rochester.34 The same figure also demonstrates the trend dynamics by a stepwise inclusion of the two attack and case-fatality sets of trends that are based on the time-series analysis of the Rochester data. A decreasing incidence of stroke results in a decreasing major stroke prevalence and also a decreasing minor stroke prevalence (data not shown). This decreasing effect on prevalence is nearly halved by an
increase in survival, especially of major stroke patients and, to a lesser extent, of minor stroke and TIA patients who live longer with the risk of suffering a debilitating stroke. The effect of survival improvement on stroke prevalence increases with age. This results in an increase in stroke prevalence among the older age groups.

The two-way sensitivity analysis determines the plausible range of values for the incidence trend that explains Dutch stroke mortality decline, given the reported survival improvement. Fig 3 shows that the values for the incidence trend range between 1.7% and 2.1% per year for men and between 2.3% and 2.8% per year for women. The figure also demonstrates that, if one supposes no incidence decline, a reported annual improvement of survival of more than 5% would be necessary to effect the observed mortality decline. On the other hand, an incidence decline of more than 3% for men would likewise imply an unreported absence of survival improvement or even a deterioration.

In Table 2, the results of a goodness-of-fit test of the model mortality trends and the empirical trend are given for three plausible scenarios: one with the highest case-fatality improvement, one with the lowest case-fatality improvement, and a Rochester-like scenario that turns out to be in between these two case-fatality declines. Assuming no incidence decline and the highest known annual case-fatality improvement results in a mortality decline that does not fit to the national figures.

Fig 5 shows the projected age-specific absolute changes in prevalence rate during the 20-year period. The decrease of age-specific stroke mortality is greatest for persons in their late 60s and 70s. Case-fatality decline within these age groups has also been limited, and therefore for these persons a rather large incidence decline has to be assumed. Consequently, stroke morbidity among these groups is decreasing remarkably, for men at a younger age than for women. Later in life, the increase in survival results in a large increase in stroke prevalence, offsetting a relatively small incidence decline. In Fig 5, an upper and lower limit of the age-specific prevalence changes is given. These limits are determined by the extreme values of the plausible ranges for incidence decline and case-fatality decline as reported in Fig 3. A smaller incidence decline results in a smaller prevalence decline among the younger patients and a higher morbidity among the older groups. The resulting prevalence changes in these alternative scenarios, again assuming a constant mortality decline, however, are on only slightly different.

**Discussion**

Downward trends in the occurrence of ischemic heart disease and stroke characterize changes in health within the aging population: reduced disease-specific mortality results in a relatively limited increase in life expectancy but might cause a longer period of severe disability from the same disease. In the case of stroke, the major question is whether declining mortality rates are resulting in a paradoxically increasing burden of disease, especially among the oldest age groups. The answer depends on whether one supposes mortality and morbidity to be compressed against an alleged fixed biological upper limit to the life span, or whether one supposes a mortality decrease in the oldest age groups and a parallel expansion of morbidity. In the former scenario, health care provision results in a decrease of morbidity, but in the latter it may well result in an increase of chronic morbidity.

Our analysis is based on empirical data from different sources. None of the large population-based studies or clinical trials has been comprehensive enough to be able to assess the extent of incidence decline and survival improvement in relation to stroke mortality decline. The results show a plausible range of a considerable incidence decline for the Netherlands. Because mortality decline in the United States has been much higher, most likely incidence decline has also been higher. For the Netherlands, consequently, Fig 5 confirms a likely scenario for stroke with a compression of morbidity in
the near future but with an increase of major stroke prevalence among the very old. At a younger age dominant incidence decline results in a decrease in morbidity. For the oldest age groups, however, the decrease in case fatality is larger than the calculated incidence decline, and therefore the resulting mortality decrease is small, ie, approximately 1% annually. At these ages the result is, indeed, a trade-off of stroke mortality for morbidity. The projected changes in morbidity are supported by recent observations: age-adjusted admission rates for stroke are decreasing in the Netherlands and in the United States among whites. In both countries the average age of stroke patients is increasing. In the Netherlands, the average age of patients admitted to long-term care institutions, which is indicative of the prevalence of major stroke, is increasing, as is the average disability score. This confirms the changes toward a higher major stroke prevalence among higher age groups, as reported in Fig 5. Similarly, the average stay of severely disabled patients in nursing institutions is increasing, and consequently Dutch mortality statistics are showing a parallel increase of late cerebrovascular deaths (ICD code 438) among the oldest. The increase in institutionalization is not explained by social factors, as the intensive home care program has been expanding during the last 5 years to cope with waiting lists of long-term patients with major stroke.

In addition to incidence and survival, stroke morbidity rates are determined by the risk of residual disability after stroke and the chance of recovery. In this respect, some groups are running larger risks after a stroke because of concomitant debilitating disease, such as atherosclerotic heart disease, or other risk factors, such as hypertension. It is hoped that ongoing empirical studies may be able to answer questions regarding stroke trends in these patient groups now that their

FIG 4. Graphs showing age-specific prevalence rates of major stroke for 1985 and 2005, after computation for a period of 20 years. For the 2005 projection, the results of two runs are shown. During the first run, only the Rochester incidence trend (a decline) is applied to all “attack” parameters. During the second run, the Rochester case-fatality trend (also a decline) on all stroke case-fatality parameters is added.

FIG 5. Graphs showing projected age-specific absolute change in prevalence rate in the Netherlands for the period 1985-2005. The most plausible trends in incidence and case-fatality are assumed, resulting in continuation of a Rochester-like scenario. Upper and lower limits have been calculated using the most extreme values of the range of plausible incidence and case-fatality trends found through sensitivity analysis.
survival is improving.\textsuperscript{15} Also, empirical studies will have to answer related questions on comorbidity and disability from other diseases among the aged.

An important question is whether stroke mortality will continue to decline. Because most of the mortality decline is unexplained, no one can be sure of the answer, nor does the stroke model answer this question. In its projections it assumes the same continuing mortality decline, because this decline has been very constant in the Netherlands. Our model demonstrates the dynamics of stroke morbidity change. Both in the Netherlands and the United States there are still benefits to be gained from large-scale hypertension control\textsuperscript{13,37,38} and reduction of smoking.\textsuperscript{15,37,38} Better intervention possibilities might further improve prognosis. Population benefits from recurrence prevention are limited because of the relatively high first-stroke fatality and relatively low recurrence risk. The effects of increasing cardiac disease prevention and treatment are already evident and will further increase survival.

The influence of demographic changes differs between the Netherlands and the United States. Stroke prevalence will increase less in the United States because of less extreme aging of the population. Stroke incidence and morbidity rates are higher for blacks. However, for this group mortality decline parallels the decline for whites.\textsuperscript{4} With a mortality trend of the same magnitude, similar dynamics in stroke morbidity might be taking place. These issues can only be dealt with after including population-specific transition probabilities and demographic and epidemiological trends in the state-event model, which is possible.

In conclusion, this study supports evidence of a further decline in stroke incidence.\textsuperscript{3} It also supports the observation\textsuperscript{29} that a further increase in survival of the older age groups as a result of therapeutic interventions may result in a longer period of severe disability before death. The findings are of importance for setting health care priorities for the aged, especially in regard to the nursing needs of stroke patients during the acute, rehabilitative, and chronic phases of their illness.

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Appendix

Testing the Goodness-of-Fit
Age-specific computed stroke figures are compared with the national registry figures. This is done by using the standard formula for the chi\textsuperscript{2} test for larger tables: \(\chi^2 = \sum \frac{(O-E)^2}{E}\).\textsuperscript{39} Here \(O\) represents the observed figure in both groups of data and \(E\) the expected figure. \(E\) is based on the calculation \((R-N)/T\) where \(R\) is the sum of the computed and the registry figure for the age group involved, \(N\) is the total of all age groups, and \(T\) the total for all age groups of the computed and registry figures together. \(C\) is the number of age groups. The number of degrees of freedom is the product of the number of age groups minus 1 and the number of categories (ie, computed and observed) minus 1.

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