Rheumatic Heart Disease in Asia

Jonathan R. Carapetis, MBBS, PhD, FRACP, FAFPHM

A few years ago, my colleagues and I conducted a systematic review of data relating to the global burden of group A streptococcal diseases.\(^1,2\) Population-based data on rheumatic heart disease prevalence from 1985 through 2002 were included. We estimated that there were a minimum of 15.6 million people in the world with rheumatic heart disease, with 282,000 new cases each year and 233,000 resultant deaths each year; however, we also noted that the estimates of the number of cases in school-aged children in China (176,500) and Asia Other (102,000; Asia excluding South-Central Asia and China) were based on very few studies, none of which used echocardiography to confirm the presence of rheumatic heart disease lesions. Moreover, 5 of the 6 studies included in the Asia Other estimate came from 1 country, the Philippines. We therefore urged caution in interpreting these data from Asia, other than South-Central Asia, and concluded that there was an urgent need for more population-based data from this part of the world. In the 5 years since that review was compiled, more data have emerged to clarify the burden of rheumatic heart disease in Asia, which will be summarized here.

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Methods

The previous report included Medline searches and other searches to retrieve articles from 1980 to 2002 with population-based studies of rheumatic heart disease prevalence. To update these data for the present study, a Medline search was conducted with the terms "rheumatic fever" or "rheumatic heart disease" and Asia. The abstracts of all articles retrieved from 2003 through November 2007 were reviewed, and the manuscripts of relevant articles were reviewed in full. Population-based studies of the prevalence of rheumatic heart disease in school-aged children were used to update the regional prevalence estimates from the previous review. Additional studies in other age groups and non-population-based studies were also reviewed if they were thought to possibly offer insights into the burden of rheumatic heart disease in Asia.

Updated denominator data were obtained from the United Nations Population Division (available at http://esa.un.org/unpp/, accessed on February 15, 2008). Regions of Asia were divided in the same way as the previous review: South-Central Asia (Afghanistan, Bangladesh, Bhutan, India, Iran, Kazakhstan, Kyrgyzstan, Maldives, Nepal, Pakistan, Sri Lanka, Tajikistan, Turkmenistan, and Uzbekistan), China, and “Asia Other” (all other Asian countries). The author takes full responsibility for the integrity of the data and agrees to the manuscript as written.

Results

Five population-based prevalence studies of rheumatic heart disease in school-aged children were found from South-Central Asia since 2003,\(^3\)–\(^7\) along with 1 from China\(^8\) and 1 from Asia Other.\(^9\) Interestingly, 4 of 5 recent studies from South-Central Asia produced prevalence estimates substantially lower (range 0.68 to 1.3 per 1000) than the pooled estimate from this region in the previous review (2.2 per 1000), although 1 study from Pakistan gave a much higher estimate (between 7 and 12 per 1000).\(^4\) By contrast, the newer studies from China and Asia Other found prevalence rates higher than the previous estimate from those regions. The Chinese study reported a prevalence of 11 per 1000, which is dramatically higher than other estimates from Asia, but it is not clear whether echocardiographic confirmation was used in the study (Table 1).\(^8\)

The additional study from Asia Other is noteworthy. A school-based survey conducted in Phnom-Penh found a prevalence rate of echocardiographically confirmed clinical rheumatic heart disease (ie, in children with significant cardiac murmurs) of 2.2 per 1000.\(^9\) However, an additional feature of that study was that all children had echocardiography performed, with the result that many children without clinically significant heart murmurs were also diagnosed with rheumatic heart disease (the prevalence estimate increased almost 10-fold, to 21.5 per 1000, with the inclusion of these subclinical cases).

A household survey in rural Pakistan used rigorous methodology and found an all-age prevalence of echocardiographically confirmed rheumatic heart disease of 5.7 per 1000.\(^4\) Unfortunately, detailed data on age subgroups were not presented, but a graph of rheumatic heart disease prevalence indicated a prevalence of \(\approx7\) per 1000 in boys aged 5 to 14 years and 12 per 1000 in girls of the same age. The study also found that the highest prevalence of rheumatic heart disease in females occurred in those 45 to 54 years of age and in males in those 55 to 64 years of age.

The data from these population-based prevalence studies in school-aged children were used to estimate the total number of rheumatic heart disease cases in Asia (Table 2). The estimate from South-Central Asia (\(\approx450,000\) cases) should be considered the most reliable, because it relied on 16 studies that used echocardiography. The estimate from China is based on 2 studies, neither of which could be confirmed as...
having used echocardiography. The estimate from Asia highlights the variability of the overall estimate depending on whether all studies are included (≈150 000 cases) or the 1 echocardiography-based study is used (≈390 000 cases). The overall estimate is between 1.96 and 2.21 million cases of rheumatic heart disease in Asian children 5 to 14 years of age.

In the previous review, we detailed 4 studies that allowed an estimate of the proportion of rheumatic heart disease cases in the total population that could be expected to be found in the 5- to 14-year-old age group. We concluded that number of cases in school-aged children should be multiplied by 5.5 to 7.2 to estimate the total cases in all ages. The recent

### Table 1. Studies Since 1985 of Rheumatic Heart Disease Prevalence in School-Aged Children in Asia

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year of Study</th>
<th>Place</th>
<th>Age, y</th>
<th>RHD Prevalence (per 1000)</th>
<th>No. Screened</th>
<th>No. of Cases</th>
<th>Echo</th>
<th>Type of Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kumar et al&lt;sup&gt;11&lt;/sup&gt;</td>
<td>1988–1990</td>
<td>India: Rajasthan</td>
<td>3.5–18</td>
<td>3.3</td>
<td>10 168</td>
<td>34</td>
<td>Yes</td>
<td>School survey</td>
</tr>
<tr>
<td>Patil et al&lt;sup&gt;13&lt;/sup&gt;</td>
<td>1986</td>
<td>India: Anand</td>
<td>5–15</td>
<td>1.8</td>
<td>11 069</td>
<td>20</td>
<td>?</td>
<td>Yes</td>
</tr>
<tr>
<td>WHO&lt;sup&gt;14&lt;/sup&gt;</td>
<td>1986</td>
<td>Pakistan: Islamabad</td>
<td>5–15</td>
<td>0.26</td>
<td>11 700</td>
<td>3</td>
<td>?</td>
<td>No</td>
</tr>
<tr>
<td>Avasthi et al&lt;sup&gt;15&lt;/sup&gt;</td>
<td>1987</td>
<td>India: Ludhiana</td>
<td>6–16</td>
<td>1.3</td>
<td>6005</td>
<td>8</td>
<td>?</td>
<td>Yes</td>
</tr>
<tr>
<td>Thakur et al&lt;sup&gt;17,18&lt;/sup&gt;</td>
<td>1990s</td>
<td>India: north</td>
<td>5–16</td>
<td>2.9</td>
<td>15 080</td>
<td>44</td>
<td>Yes</td>
<td>School survey</td>
</tr>
<tr>
<td>Gupta et al&lt;sup&gt;19&lt;/sup&gt;</td>
<td>1991</td>
<td>India: Jammu City</td>
<td>6–16</td>
<td>1.4</td>
<td>10 263</td>
<td>14</td>
<td>Yes</td>
<td>School survey</td>
</tr>
<tr>
<td>Shrestha et al&lt;sup&gt;20&lt;/sup&gt;</td>
<td>1991</td>
<td>Nepal (rural)</td>
<td>5–16</td>
<td>1.4</td>
<td>4452</td>
<td>6</td>
<td>Yes</td>
<td>School survey</td>
</tr>
<tr>
<td>Ahmed et al&lt;sup&gt;21&lt;/sup&gt;</td>
<td>1991</td>
<td>Bangladesh (rural)</td>
<td>5–15</td>
<td>1.3</td>
<td>5923</td>
<td>8</td>
<td>Yes</td>
<td>Community survey</td>
</tr>
<tr>
<td>Haque et al&lt;sup&gt;22&lt;/sup&gt;</td>
<td>1992</td>
<td>Bangladesh: Dhaka and Dhamrai</td>
<td>5–15</td>
<td>2.2</td>
<td>15 798</td>
<td>36</td>
<td>Yes</td>
<td>School survey</td>
</tr>
<tr>
<td>Joardar et al&lt;sup&gt;23&lt;/sup&gt;</td>
<td>1992</td>
<td>Bangladesh: Rajbari</td>
<td>5–20</td>
<td>1.45</td>
<td>686</td>
<td>1</td>
<td>No</td>
<td>Community survey</td>
</tr>
<tr>
<td>Begum et al&lt;sup&gt;24&lt;/sup&gt;</td>
<td>1993</td>
<td>Bangladesh: Dhaka</td>
<td>5–15</td>
<td>2.4</td>
<td>10 538</td>
<td>25</td>
<td>Yes</td>
<td>School survey</td>
</tr>
<tr>
<td>Rizvi et al&lt;sup&gt;6&lt;/sup&gt;</td>
<td>1993–1994</td>
<td>Pakistan: Rahim Yar Khan</td>
<td>5–14</td>
<td>7 to 12*</td>
<td>NK*</td>
<td>NK*</td>
<td>Yes</td>
<td>Household survey</td>
</tr>
<tr>
<td>Regmi and Pandey&lt;sup&gt;24&lt;/sup&gt;</td>
<td>1997</td>
<td>Nepal: Kathmandu</td>
<td>5–16</td>
<td>1.2</td>
<td>4736</td>
<td>6</td>
<td>Yes</td>
<td>School survey</td>
</tr>
<tr>
<td>Bahadur et al&lt;sup&gt;8&lt;/sup&gt;</td>
<td>2002</td>
<td>Nepal: Kathmandu Valley</td>
<td>5–18</td>
<td>1.2</td>
<td>9420</td>
<td>11</td>
<td>Yes</td>
<td>School survey</td>
</tr>
<tr>
<td>Jose and Gomathi&lt;sup&gt;9&lt;/sup&gt;</td>
<td>2001–2002</td>
<td>India: Vellore</td>
<td>6–18</td>
<td>0.68</td>
<td>229 829</td>
<td>157</td>
<td>Yes</td>
<td>School survey</td>
</tr>
<tr>
<td>Periwal et al&lt;sup&gt;10&lt;/sup&gt;</td>
<td>2005</td>
<td>India: Bikaner</td>
<td>5–14</td>
<td>0.67</td>
<td>3002</td>
<td>2</td>
<td>Yes</td>
<td>School survey</td>
</tr>
<tr>
<td>WHO&lt;sup&gt;14&lt;/sup&gt;</td>
<td>1986</td>
<td>Guangdong Province</td>
<td>5–15</td>
<td>0.8</td>
<td>31 180</td>
<td>25</td>
<td>?</td>
<td>No</td>
</tr>
<tr>
<td>Chen et al&lt;sup&gt;8&lt;/sup&gt;</td>
<td>1993–1994</td>
<td>Sichuan Province</td>
<td>5–18</td>
<td>11</td>
<td>46 595</td>
<td>512</td>
<td>Unknown†</td>
<td>Community survey</td>
</tr>
<tr>
<td>WHO&lt;sup&gt;14&lt;/sup&gt;</td>
<td>1986</td>
<td>Thailand: Bangkok and Nakornrajasima</td>
<td>5–15</td>
<td>0.2</td>
<td>55 465</td>
<td>9</td>
<td>No</td>
<td>School survey</td>
</tr>
<tr>
<td>Guzman&lt;sup&gt;25&lt;/sup&gt;</td>
<td>1987–1990</td>
<td>Philippines: Laguna</td>
<td>5–15</td>
<td>0.8</td>
<td>91 694</td>
<td>72</td>
<td>?</td>
<td>No</td>
</tr>
<tr>
<td>WHO&lt;sup&gt;14&lt;/sup&gt;</td>
<td>1986</td>
<td>Philippines: Laguna</td>
<td>5–15</td>
<td>1.6</td>
<td>17 320</td>
<td>27</td>
<td>?</td>
<td>No</td>
</tr>
<tr>
<td>Marijon et al&lt;sup&gt;9&lt;/sup&gt;</td>
<td>2001–2002</td>
<td>Cambodia: Phnom-Penh</td>
<td>6–17</td>
<td>2.2‡</td>
<td>3677</td>
<td>8</td>
<td>Yes</td>
<td>School survey</td>
</tr>
</tbody>
</table>

RHD indicates rheumatic heart disease; WHO, World Health Organization; ?, not clear from publication if echocardiography was used (response likely inferred from manuscript); and NK, not known.

*Household survey of all ages. Data not presented separately for school-aged children, except for graphical depiction of rheumatic heart disease prevalence, by gender.

†Article in Chinese; only the English abstract was reviewed.

‡Prevalence estimate for those diagnosed clinically with echocardiographic confirmation. Separate estimate presented for screening of all children with echocardiography: 79 cases, prevalence 21.5 per 1000 (ie, 90% of rheumatic heart disease cases were subclinical).
study from Pakistan supports this: Although sufficient data were not presented to make the same calculation, the graphical illustration of rheumatic heart disease prevalence by age group confirms that there was no decrease in prevalence (in fact, rates peaked in older age groups) between the 5- to 14-year-olds and the 55- to 64-year-olds. Applying these multiplication factors to the estimates in Table 2, one can estimate that the total number of rheumatic heart disease cases is between 10.8 million (lower estimate based on 5.5 multiplication factor and all studies) and 15.9 million (upper estimate based on 7.2 multiplication factor and echocardiographic studies only).

In the previous review, we pointed out that accurate estimates of mortality due to rheumatic heart disease are not possible because of the lack of data from developing countries. Our best estimates were based on an expected mortality of 1.5% per year in rheumatic heart disease patients, which was based on prospective studies from North America and the United Kingdom during the 1960s.29–32 However, a 12-year cohort study from India published in 2002 found a mortality rate among rheumatic heart disease patients of 3.3% per year.33 Applying this to the estimates in Table 2, we estimate that rheumatic heart disease is directly responsible for 356 000 to 524 000 deaths each year in Asia.

Other Data
A number of recent publications added information regarding rheumatic heart disease in Asia. A cross-sectional study of 8080 middle-aged to elderly people in China during 2001 to 2002 found a prevalence of 2 cases of echocardiographically proven rheumatic heart disease per 1000 people.34 A 50-year retrospective study from 2 hospitals in Shanghai, China, found that cardiovascular admissions increased 3-fold over this period but that the proportion due to rheumatic heart disease declined 5-fold (from 50% to 10% of cardiac admissions).35 A prospective study conducted in Lebanon from 1999 to 2005 found that rheumatic heart disease was the most common acquired heart disease in children (36% of cases).36

Endocarditis
In the last review, all of the data published globally since 1980 documenting the association of infective endocarditis and rheumatic heart disease had come from Asia. This interest in endocarditis persisted: An additional 8 studies37–48 from Asia were found during the preparation of the present

Table 2. Estimated Number of Rheumatic Heart Disease Cases in Children 5 to 14 Years of Age in Asia

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>South-Central Asia</td>
<td>18 (16)</td>
<td>1.4</td>
<td>392 078</td>
<td>1.2</td>
<td>379 692</td>
<td>1.2</td>
<td>365 731 000</td>
<td>444 946</td>
<td>455 608</td>
</tr>
<tr>
<td>China</td>
<td>2 (0)</td>
<td>5.9</td>
<td>77 775</td>
<td>6.9</td>
<td>NA</td>
<td>NA</td>
<td>198 485 000</td>
<td>1 370 446</td>
<td>NA</td>
</tr>
<tr>
<td>Asia Other</td>
<td>7 (1)</td>
<td>1.2</td>
<td>247 345</td>
<td>0.8</td>
<td>3677</td>
<td>2.2</td>
<td>178 694 000</td>
<td>149 547</td>
<td>388 782</td>
</tr>
<tr>
<td>Total</td>
<td>74</td>
<td></td>
<td>742 910</td>
<td></td>
<td>1 964 939</td>
<td>2 214 836*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Echo indicates echocardiography; RHD, rheumatic heart disease; and NA, not applicable because there were no echocardiographic studies. Prevalences are per 1000.

*Includes all-studies estimate for China, because no echocardiographic studies were available.

Table 3. Studies Since 1980 Documenting the Association of Rheumatic Heart Disease and Infective Endocarditis in Asia

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year of Study</th>
<th>Country</th>
<th>Proportion of IE With RHD as Predisposing Factor</th>
<th>Rank of RHD as Predisposing Factor</th>
<th>Notes/Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cetinkaya et al37</td>
<td>1974–1999</td>
<td>Turkey</td>
<td>65%</td>
<td>Most common</td>
<td>Incidence IE 1.2 per 100 000 in 1990s; deduced incidence of RHD-related IE=0.44 per 100 000</td>
</tr>
<tr>
<td>Borer et al38</td>
<td>1980–1994</td>
<td>Israel</td>
<td>37%</td>
<td>Most common</td>
<td>Mortality 25%</td>
</tr>
<tr>
<td>Choudhury et al39</td>
<td>1981–1991</td>
<td>India</td>
<td>42%</td>
<td>Most common</td>
<td>Mortality 25%</td>
</tr>
<tr>
<td>Dhawan et al40</td>
<td>1984–1990</td>
<td>India</td>
<td>49%</td>
<td>Most common</td>
<td></td>
</tr>
<tr>
<td>Kanafani et al41</td>
<td>1986–2001</td>
<td>Lebanon</td>
<td>33%</td>
<td>Most common</td>
<td></td>
</tr>
<tr>
<td>Lertsapcharoen et al42</td>
<td>1987–2004</td>
<td>Thailand</td>
<td>12%</td>
<td>2nd most common</td>
<td>Congenital heart disease in 74%</td>
</tr>
<tr>
<td>Agarwal et al43</td>
<td>1987–1988</td>
<td>India</td>
<td>68%</td>
<td>Most common</td>
<td>Mortality 21%</td>
</tr>
<tr>
<td>Garg et al44</td>
<td>1992–2001</td>
<td>India</td>
<td>47%</td>
<td>Most common</td>
<td></td>
</tr>
<tr>
<td>Heper and Yorukoglu45</td>
<td>1995–2000</td>
<td>Turkey</td>
<td>66%</td>
<td>Most common</td>
<td>Incidence IE 2.8 per 100 000</td>
</tr>
<tr>
<td>Yiu et al46</td>
<td>1995–2005</td>
<td>Hong Kong</td>
<td>18%</td>
<td>2nd most common</td>
<td></td>
</tr>
<tr>
<td>Khanal et al47</td>
<td>1995–1997</td>
<td>India</td>
<td>56%</td>
<td>Most common</td>
<td>Mortality 30%</td>
</tr>
<tr>
<td>Liew et al48</td>
<td>1997–2004</td>
<td>Singapore</td>
<td>4%</td>
<td>Rare</td>
<td>Congenital heart disease in 89%</td>
</tr>
</tbody>
</table>

IE indicates infective endocarditis.
report (Table 3). The recent studies from India, Turkey, and Lebanon all found that rheumatic heart disease was the most
common underlying factor in endocarditis (range 33% to 66%),
whereas studies from Hong Kong and Thailand found rheumatic heart disease in 18% and 12% of cases, respectively,
and a study from Singapore found rheumatic heart disease in only 4% of endocarditis cases.

**Stroke**

A population-based stroke registry in Iran found an incidence of ischemic stroke of 43 per 100,000 population, with 11.8% due
to cardioembolism, in 45% of whom rheumatic heart disease was detected. The authors concluded that rheumatic
heart disease caused 4.3 preventable strokes per 100,000 people per year in Iran.

**Pregnancy and Rheumatic Heart Disease**

An 18-year study in Taiwan found that stroke occurred in
46.2 of 100,000 pregnancies, and 44% of cases had underlying
rheumatic heart disease. Rheumatic heart disease was the
most common underlying condition (27% of cases) found
in pregnant patients admitted to the intensive care unit in a
Saudi Arabian hospital between 1997 and 2002. In an
Indian hospital between 1994 and 2000, rheumatic heart
disease accounted for 88% of cardiac diseases in pregnant
women.

**Discussion**

It is often claimed that the burden of some infectious
diseases in Asia may be different from that in other parts of the world.

For example, there has been considerable discussion as to
whether there is evidence that *Haemophilus influenzae* type b
infections are less common in Asian children than in children in
other less-developed regions. Similarly, with the exception of a few countries in South-Central Asia (India, Bangladesh, and Pakistan most prominently), there has been little concern about rheumatic heart disease in most Asian countries.

The data presented here suggest that rheumatic heart
disease is indeed an ongoing problem in Asia. Although the
regional estimates for prevalence in school-aged children
may not be as high as, for example, in sub-Saharan Africa, the
total burden of cases (between 10.8 and 15.9 million cases in
all ages) and deaths (356,000 to 524,000 each year) warrants
attention. Moreover, the 2 most rigorously performed studies,
from Pakistan and Cambodia, confirm that careful research
methodology will uncover many more cases than would
otherwise have been detected, which suggests that the true
number of rheumatic heart disease cases may be even greater
than presented here.

The estimates presented here are only for clinically signif-
icant rheumatic heart disease, ie, for cases that as a minimum
have a murmur of rheumatic valvular disease. The Cambod-
ian study suggested that universal echocardiographic screen-
ing will uncover 10 subclinical rheumatic heart disease cases
for every clinical case. If this can be confirmed in other
studies, and if the significance of these subclinical cases is
found to be similar to clinical cases, then there is an immense
unrecognized burden of rheumatic heart disease in Asia that
requires urgent attention.

The Pakistan and Cambodia studies also highlight the
importance of high-quality epidemiological studies in devel-
opung countries. Such studies, using echocardiography to
cr confirm the diagnosis of rheumatic heart disease, are possi-
ble. Moreover, they are invaluable for providing the robust
estimates of disease burden on which public health strategies
must be based. It is clear from the studies outlined in Table 1
that there is a need for more and better studies from China and
the Asia Other countries, and accordingly, the summary
estimates from these places should be interpreted with
cautions.

The studies on infective endocarditis confirm that in most
Asian countries, at least half of all cases of this severe and
often fatal disease are due to underlying rheumatic heart
disease, although in some countries with emerging middle
classes, this proportion is probably lower. Similarly, the
prospective stroke registry data from Iran support those in the
previous report that indicate that a substantial proportion of
strokes in developing countries are due to rheumatic heart
disease. If the incidence of strokes due to rheumatic heart
disease in Iran (4.3 per 100,000 people per year) were to be
applied to the population of Asia (3.9 billion), it could be
estimated that rheumatic heart disease causes 167,000 pre-
ventable strokes each year in Asia.

The compelling point about the data presented here is that
almost all of these cases, severe complications and deaths, are
preventable. Rheumatic heart disease can be prevented and
controlled with the establishment of register-based coordi-
nated control programs, the major focus of which is delivery
of secondary prophylaxis to prevent recurrences of rheumatic
fever. There is ample evidence that this strategy is cheap,
cost-effective, and practical in developing countries. With
the exception of some parts of a few countries in South-
Central Asia, I am not aware of coordinated control programs
in any Asian countries. Surely, it is time for health authorities
in Asian countries and international organizations such as the
World Health Organization to act on rheumatic heart disease
in this region.

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There are no other conflicts of interest to report.

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1. Carapetis JR. *The Current Evidence for the Burden of Group A Strepto-
coccal Diseases.* Geneva, Switzerland: World Health Organization; 


CLINICAL PERSPECTIVE

With the exception of India, there have been few population-based studies of the burden of rheumatic heart disease in Asian countries; however, recent studies suggest that as with other developing regions of the world, rheumatic heart disease is an underappreciated cause of morbidity and mortality in children, adolescents, and adults in low- and middle-income countries of Asia. More importantly, it is likely that many cases of mild rheumatic heart disease remain undetected in Asian children, with the risk that these lesions will progress to clinical significance as these children enter adulthood. Aside from highlighting the need for better-quality data from Asia, the implications of these findings are that clinicians should have a high index of suspicion of rheumatic heart disease when seeing children in this region, even if they are asymptomatic. Moreover, the need for institution of formal rheumatic heart disease control programs and even for echocardiography-based screening of school-aged children should be considered.
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