Pneumosil introduction in Timor-Leste

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& Researcher at Menzies School of Health Research, Darwin, Australia

Ndjamena, Chad, 14 September 2023
OUTLINE

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Background
Brief story of Timor-Leste
Background: About Timor-Leste

- Timor-Leste regained independence in 2002, following years of occupation
- Estimated 1.3 million population and 39% are of 1-14 years old (TL 20022 population census)
- Timor-Leste has 12 main municipalities located on the eastern half of Timor Island and one autonomous municipality (Oecusse) which is an enclave inside West Timor.
Photo credit: Australian National Museum
Background: National Health Service Delivery in Timor-Leste

- Process of nation-building is ongoing
- Free universal health coverage to Timorese citizen is implemented
- Major advancement are seen but gaps remaining
- Maternal and under five mortality still occur
- Health seeking behaviour and access to health care are poor
- High burden of undernutrition, TB, Hepatitis B and other infectious diseases.
Background – few milestones

From malaria control to elimination within a decade: lessons learned from Timor Leste, a newly independent country

A. M. G. Manel Yapabandara, Maria do Rosario de Fatima Mota, Raul Sarmento, Johannes don Bosco and Rajitha Wickremasinghe

Bhutan, Timor-Leste eliminate rubella; Achieve 2023 target of measles and rubella elimination

21 July 2023 | News release | New Delhi

The World Health Organization South-East Asia Region today announced Bhutan and Timor-Leste have eliminated rubella, a highly contagious disease that causes serious illness and irreversible birth defects in newborns of women infected during pregnancy, but preventable through vaccination.

Bhutan and Timor-Leste had eliminated measles in 2017 and 2018 respectively, and now join Maldives and Sri Lanka to achieve elimination of measles and rubella by 2023, a flagship priority program of WHO South-East Asia Region.
History EPI Program in Timor-Leste

EPI Programme commenced in 1978

DPT-HepB vaccine introduction in 2007

MR1, IPV, DT, DPT4 and MR2 vaccine Introduction in 2016

Pneumococcal vaccine introduction in 2023

Re structuring after independence in 2002

Pentavalent vaccine introduction in 2007

Rota Virus Vaccine introduction in 2012

Human Papilloma Vaccine Introduction in Q4 2023

NITAG-TL cMYP in 2015
Current immunization schedule in Timor-Leste

- **At birth**: BCG, OPV-0 dose (Up to 14 days) & Hepatitis B birth dose
- **6 weeks**: Pentavalent-1, OPV-1 and RVV-1, PCV-1
- **10 weeks**: Pentavalent-2, OPV-2 and RVV-2, PCV-2
- **14 weeks**: Pentavalent-3, OPV-3, IPV and RVV-3, PCV-3
- **9 months**: Measles Rubella (MR)-1
- **18 months**: Measles Rubella-2 dose and Diphtheria Pertussis Tetanus (DPT)-4
- **6 Year**: Diphtheria Tetanus (DT)-5
Background
Pneumonia and malnutrition in Timor-Leste
Background: Pneumonia mortality

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Value</th>
<th>Latest year with data</th>
<th>Progress towards global target</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.2.1 Under-five mortality rate (deaths per 1,000 live births)</td>
<td>42</td>
<td>2020</td>
<td></td>
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<tr>
<td>3.2.2 Neonatal mortality rate (deaths per 1,000 live births)</td>
<td>19</td>
<td>2020</td>
<td></td>
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<tr>
<td>3.3.1 (HIV Incidence) — New HIV infections per 1,000 uninfected population [Children &lt;5]</td>
<td>0</td>
<td>2020</td>
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<tr>
<td>3.3.2 (HIV Incidence) — New HIV infections per 1,000 uninfected population [Adolescent GIRLS 15-19]</td>
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<td>2020</td>
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<td>3.5.1 (HIV Incidence) — New HIV infections per 1,000 uninfected population [Adolescent BOYS 15-19]</td>
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<tr>
<td>3.1.1 Maternal mortality ratio (deaths per 1,000,000 live births)</td>
<td>142</td>
<td>2017</td>
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<td>3.1.2 Proportion of births attended by skilled health personnel (%)</td>
<td>56</td>
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<td>3.7.2 Adolescent birth rate per 1,000 women</td>
<td>41</td>
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<td>3.8.1 Coverage of essential health services (index)</td>
<td>53</td>
<td>2019</td>
<td></td>
</tr>
<tr>
<td>2.2.1 Prevalence of stunting among children under 5 (%)</td>
<td>48</td>
<td>2020</td>
<td></td>
</tr>
<tr>
<td>2.2.2a Prevalence of wasting among children under 5 (%)</td>
<td>9</td>
<td>2013</td>
<td></td>
</tr>
<tr>
<td>2.2.2b Prevalence of overweight among children under 5 (%)</td>
<td>12</td>
<td>2020</td>
<td></td>
</tr>
<tr>
<td>3.3.1b Proportion of surviving infants receiving measles-containing vaccine first-dose (MCV1) (%)</td>
<td>79</td>
<td>2020</td>
<td></td>
</tr>
<tr>
<td>3.3.1c Proportion of surviving infants receiving 3 doses of diphtheria-tetanus-pertussis (DTP3) (%)</td>
<td>86</td>
<td>2020</td>
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</tr>
</tbody>
</table>

Source: L Liu et al. The Lancet 2015 385, 430-440 DOI: (10.1016/S0140-6736(14)61698-6)
Background: Pneumonia in Children Under 5 in ASEAN Countries

Lower respiratory infection including pneumonia in children under five years in 2016
Background:
Malnutrition in ASEAN Countries

https://data.unicef.org/topic/nutrition/malnutrition/


https://www.adb.org/countries/timor-leste/poverty
Background: Evidence from the National Hospital

Lower Respiratory Tract Infection

2542/5909 (43%) admissions
92/327 (28%) deaths

J Paediatr Child Health 2013; 49(12): 1004-9

Malnutrition

280/880 (32%) admitted children malnourished.

WHZ available 233/280
HAZ available 227/280

62% (144/233) had severe malnutrition and
60.4% (137/227) were stunted

J Paediatr Child Health 2006; 42(1-2): 28-32
NITAG-TL PCV recommendation
NITAG-TL Technical Sub-committee on Pneumococcal Disease

• The Timor-Leste NITAG PCV-Subcommittee was established on 30 May 2019
• Dr Celia dos Santos as Pneumococcal Subcommittee Chair – continued with Nevio Sarmento since April 2021
• Major role of this Subcommittee is to provide recommendations to the Ministry of Health on PCV introduction
• Three Subcommittee meetings held
  • Discuss and formulate the PCV recommendations
• Evidence-based decision-making workshop with NITAG members also undertook substantial work on PCV recommendations
• Recommendations drafted by Subcommittee with support from the National Centre for Immunisation Research and Surveillance (NCIRS), Menzies School of Health Research, UNICEF and WHO Timor-Leste Country Office
Vaccine schedule for Timor-Leste

• The WHO recommends the 2p+1 or 3p+0 schedule

• However, considering:
  • the higher vaccine coverage achieved at 6, 10 and 14 week
  • likely higher burden of disease in the 1st year of life compared to >1 year of age

• NITAG-TL recommends a 3p+0 schedule for Timor-Leste (changes may happen adjusted to any research output).
Vaccine schedule – Cont.....

• **Protection**
  - mixed evidence about if 3p+0 schedule provides better protection in first year of life compared to 2p+1
  - 2p+1 schedule may provide better longer-term protection due to higher antibody levels in the second year of life

• **Currently 2 injections at 14 weeks of age (Penta3 & IPV)**
  - Introducing PCV either as 3p+0 or 2p+1 into the routine immunization will mean a third injection at 14 weeks of age
  - 2p+1 schedule at 6 and 10 weeks and 9 months of age, to avoid a third injection at 14 weeks of age, not recommended because of lower antibody responses compared to when given at 6 and 14 weeks

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1 WHO position paper 2019; 2 Hamaluba et al. 2015 Lancet Infect Dis; 3 Kandasamy et al. Lancet Infect Dis 2019
Vaccine schedule – Cont....

• Coverage highest for vaccines recommended at 6, 10 and 14 weeks of age

• Coverage is lower for measles-rubella vaccine, recommended at 9 months of age
Target population

• NITAG Timor-Leste recommends the target population for the routine PCV program to be all infants

• NITAG Timor-Leste recommends, if MoH or donor resources permits, to have catch-up vaccination at the time of introduction of PCV to accelerate its impact on disease in children aged 1–<5 years as recommended by WHO, with one dose of PCV vaccine
Pneumococcal carriage study

Hospital carriage study or PULSA “Healthy lung Study” (2019 – 2021) – completed
PULSA Study Patient recruitment from one of the wards in the Ped. Dept. HNGV
Hospital pneumococcal carriage laboratory work
## Hospital serotyping for *S. pneumoniae*

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<tr>
<th>Serotype identified from the study</th>
<th>6B</th>
<th>6C</th>
<th>9V</th>
<th>13</th>
<th>14</th>
<th>10A</th>
<th>11A</th>
<th>15A</th>
<th>15B</th>
<th>16B</th>
<th>16F</th>
<th>17F</th>
<th>18C</th>
<th>19A</th>
<th>19F</th>
<th>22F</th>
<th>23A</th>
<th>23B</th>
<th>23F</th>
<th>35B</th>
<th>35F</th>
<th>NT</th>
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<tbody>
<tr>
<td>Total identified</td>
<td>10</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>8</td>
<td>3</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>19</td>
<td>19F</td>
<td>22F</td>
<td>23A</td>
<td>23B</td>
<td>23F</td>
<td>35B</td>
<td>35F</td>
</tr>
<tr>
<td>Serotypes matching Pneumosil (PCV10)</td>
<td>6B</td>
<td>14</td>
<td>19A</td>
<td>19F</td>
<td>23F</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>34</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Total *Streptococcus pneumoniae*** 121/580 (21%)  
Vaccine type  46/121 (38%)  
Non vaccine type  41/121 (34%)  
Non typeable  34/121 (28%)
Pneumococcal carriage study

- Community carriage study – (2023) - ongoing
Rationale – current research project

• Lower carriage in hospitalised children

• Antibiotic exposure

• Thus, there is an identified need to understand baseline (pre-PCV) pneumococcal carriage rates in children without recent antibiotic use.
Serotyping of Pneumococcus at Microbiology Laboratory, Timor-Leste
• Preliminary findings – Community carriage

• Carriage 40% (222/555)
• About 100 (45%) *Streptococcus pneumoniae* isolates has been serotyped
• Majority serogroups 6 no 14 which are covered in our PCV-10 (Pneumosil)
• Interestingly, we have identified serogroup 15 almost 25% (24/100) which is not covered in our Pneumosil vaccine type.
• This is preliminary findings. Once this study is concluded, will discuss with the stakeholders for the vaccine strategy or further studies.

<table>
<thead>
<tr>
<th>Serotypes/serogroup identified</th>
<th>Serotype 4</th>
<th>Serogroup 6</th>
<th>Serogroup 7</th>
<th>Serogroup 9</th>
<th>Serogroup 10</th>
<th>Serogroup 11</th>
<th>Serotype 14</th>
<th>Serogroup 15</th>
<th>Serogroup 18</th>
<th>Serogroup 19</th>
<th>Serotype 20</th>
<th>Serogroup 23</th>
<th>Non-vaccine serotypes (NVS)</th>
<th>Non-Typeable (NT)</th>
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<tbody>
<tr>
<td>Total identified</td>
<td>3</td>
<td>50</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>6</td>
<td>14</td>
<td>21</td>
<td>1</td>
<td>32</td>
<td>2</td>
<td>19</td>
<td>33</td>
<td>11</td>
</tr>
<tr>
<td>Serotypes covered by Pneumosil (PCV-10)</td>
<td>1, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F, 23F</td>
<td>6A/6B</td>
<td>9V</td>
<td>14</td>
<td>14</td>
<td>19A/19F</td>
<td>23F</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
Pneumosil Introduction
2018

Participatory active discussion lead by NITAG-TL

In collaboration with EPI-MoH TL, WHO-TLS, UNICEF, Menzies School of Health Research, Religious groups, pediatrics, vaccinators, community leaders, religion leaders and parents

2019

GAVI proposal development and submission

NITAG-TL, WHO-TLS, EPI-MoH TL, NCIRS, Menzies School of Health Research, UNICEF

2021

Approval

Progress HALTED

Procurement (UNICEF)

2022

- Vaccine arrived in Timor-Leste (Sept. 2022)
- Health promotion and information dissemination (Sept. 22 - Dec. 22)
- Training of vaccinators (Dec. 2022)

Pneumosil vaccination start 12 January 2023

2020 - COVID-19 pandemic
**Product overview**

**Type:** Pneumococcal (conjugate)

**Commercial Name:** PNEUMOSIL®

**Manufacturer:** Serum Institute of India Pvt. Ltd.

**Country:** India

**URL:** [http://www.seruminstitute.com/](http://www.seruminstitute.com/)

**Responsible NRA:** Central Drugs Standard Control Organization

**Country:** India

**URL:** [www.cdsco.nic.in](http://www.cdsco.nic.in)

**Bulk Supplier:** Not applicable
PCV STATUS in ASEAN COUNTRIES

- Brunei: NOT YET
- Cambodia: 2015 – PCV-13
- East Timor: 2023 – PCV-10
- Indonesia: 2021 – PCV-13
- Malaysia: 2011 – PCV-10. STOPPED for review
- Burma: 2016 – PCV-10
- Philippines: 2015 – PCV-13
- Singapore: 2013 – PCV-10
- Thailand: 2007 – 2011 Introduced and Optional as of 2020
- Vietnam: SOON
LANSAMANTU KAMPAÑA NASIONAL INTEGRADU

12 Januari 2023 to'o 28 Fevereiro 2023

Pul sakënde saktë de Saktë kampañia

Diar 1
Quë 2
Quë-bëwë de idadë

18 de bëwë.
House to house and farm sweeping

Photo credit: Ministry of Health, Timor-Leste and SABEH
<table>
<thead>
<tr>
<th>Municipality</th>
<th>OPV</th>
<th>PCV</th>
<th>MR</th>
<th>Vitamin A</th>
<th>Albendazole</th>
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<tbody>
<tr>
<td></td>
<td>Target</td>
<td>Doses Given</td>
<td>Coverage</td>
<td>Target</td>
<td>Doses Given</td>
</tr>
<tr>
<td>Aluau</td>
<td>6,396</td>
<td>7,205</td>
<td>112.6%</td>
<td>6,321</td>
<td>7,066</td>
</tr>
<tr>
<td>Alinoro</td>
<td>6,807</td>
<td>6,872</td>
<td>99.4%</td>
<td>6,724</td>
<td>6,712</td>
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<tr>
<td>Atebu</td>
<td>1,550</td>
<td>1,127</td>
<td>78.0%</td>
<td>1,524</td>
<td>1,097</td>
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<tr>
<td>Baucau</td>
<td>22,450</td>
<td>16,249</td>
<td>121.2%</td>
<td>13,177</td>
<td>15,774</td>
</tr>
<tr>
<td>Bobonaro</td>
<td>10,199</td>
<td>11,920</td>
<td>116.9%</td>
<td>9,909</td>
<td>11,528</td>
</tr>
<tr>
<td>Covimba</td>
<td>7,982</td>
<td>8,261</td>
<td>103.5%</td>
<td>7,801</td>
<td>8,044</td>
</tr>
<tr>
<td>Dili</td>
<td>54,016</td>
<td>53,946</td>
<td>98.8%</td>
<td>52,105</td>
<td>51,915</td>
</tr>
<tr>
<td>Ermero</td>
<td>20,499</td>
<td>23,036</td>
<td>112.3%</td>
<td>10,269</td>
<td>21,992</td>
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<tr>
<td>Lautem</td>
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<td>8,572</td>
<td>115.0%</td>
<td>7,358</td>
<td>8,418</td>
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<tr>
<td>Liquica</td>
<td>10,620</td>
<td>10,864</td>
<td>100.4%</td>
<td>10,551</td>
<td>10,281</td>
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<tr>
<td>Manufahi</td>
<td>5,518</td>
<td>5,857</td>
<td>106.1%</td>
<td>5,408</td>
<td>5,638</td>
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<tr>
<td>Manufahi</td>
<td>7,796</td>
<td>7,788</td>
<td>99.9%</td>
<td>7,616</td>
<td>7,538</td>
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<tr>
<td>Viqueque</td>
<td>9,499</td>
<td>9,871</td>
<td>103.9%</td>
<td>9,302</td>
<td>9,614</td>
</tr>
<tr>
<td>ZEEMS (Decesso)</td>
<td>6,726</td>
<td>7,169</td>
<td>108.0%</td>
<td>6,573</td>
<td>7,011</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>184,263</strong></td>
<td><strong>178,746</strong></td>
<td><strong>100.2%</strong></td>
<td><strong>163,077</strong></td>
<td><strong>172,648</strong></td>
</tr>
</tbody>
</table>

**Date and time prepared:** 06 March 2023, 02.00 pm

*Source: TLHIS*

*Denominators are based on estimated and enumerated target populations provided by respective municipality directors*
Lesson learned

• Know your own disease burden and act fast
• High burden of lower respiratory tract infection
• Data is important, research is important but saving lives comes first.
• Give children the chance to survive (20% population in TL are under 5)
• Political will and personal commitment
• Open and collaborate with international partners
Next plan

• Expanded Program of Immunization (EPI) Review – October 2023
• GAVI Post-transitional plan proposal 2023 – 2025.
• PCV vaccine impact study – One-year post-introduction carriage survey – Proposal drafted.
• RCT of Pneumosil in malnourished children – Australian NHMRC Grant approved and will be led by Dr Nicholas Fancourt (John Hopkins Bloomberg SPH doctorate graduate)
• Review of Pneumosil schedule. Trial of 1+1 vs 3+0 (immune response) – Looking for funding
• Continue rolling out Pneumosil as routine immunization in health centers including doing house to house sweeping
Acknowledgement
Merci
Beaucoup
(OBRIGADO)
# PCV SIA Coverage

## Age Category (Months)

<table>
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<th>Age Category</th>
<th>Total</th>
<th>PCV Vaccinated in SIA</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td><strong>n</strong></td>
<td><strong>%</strong></td>
</tr>
<tr>
<td>6 weeks-11</td>
<td>166</td>
<td>143</td>
<td>86.1</td>
</tr>
<tr>
<td>12-23</td>
<td>205</td>
<td>151</td>
<td>73.7</td>
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<tr>
<td>24-35</td>
<td>260</td>
<td>188</td>
<td>72.3</td>
</tr>
<tr>
<td>36-47</td>
<td>265</td>
<td>178</td>
<td>67.2</td>
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<tr>
<td>48-60</td>
<td>302</td>
<td>226</td>
<td>74.8</td>
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<tr>
<td>Total</td>
<td>1198</td>
<td>886</td>
<td>74.0</td>
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</table>

## Sex

<table>
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<th>Total</th>
<th>PCV Vaccinated in SIA</th>
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</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td><strong>n</strong></td>
<td><strong>%</strong></td>
</tr>
<tr>
<td>Female</td>
<td>580</td>
<td>434</td>
<td>74.8</td>
</tr>
<tr>
<td>Male</td>
<td>618</td>
<td>452</td>
<td>73.1</td>
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<td>1198</td>
<td>886</td>
<td>74.0</td>
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## Municipality

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<th>Total</th>
<th>PCV coverage in SIA</th>
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<td>51</td>
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<td>Ainaro</td>
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<td>44</td>
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<td>11</td>
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<td>Bobonaro</td>
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<td>84</td>
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<td>62</td>
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<tr>
<td>Dili</td>
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<td>172</td>
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<tr>
<td>Ermera</td>
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<td>60</td>
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<tr>
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</tr>
</tbody>
</table>