How has the evidence for stroke care progressed over the past decade?

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10th Anniversary UKSF

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Huge increase over the decade
in knowledge of stroke and its
treatment

Epidemiology
Acute treatment
Rehabilitation
Prevention
Global burden of stroke: mortality

[Map showing stroke mortality rates worldwide, with varying color intensity representing different mortality rates per 100,000.]
10 treatment headlines for the decade

2005 Early supported discharge services
2007 Hemicraniectomy for malignant MCA stroke
2008 Time window for iv rt-PA extends to 4.5 hours
2009 Novel anticoagulants for stroke prevention in AF
2010 GCS ineffective for post-stroke DVT prevention
2012 Statins for prevention stroke & MI
2013 Organised inpatient care (Stroke Unit) update
2014 iv rt-PA for acute ischaemic stroke – who benefits?
2014 IPC for DVT prevention
2015 Mechanical clot retrieval for acute ischaemic stroke
2015 Effects of Very Early Rehabilitation
10 treatment headlines for the decade

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Evidence: past problems

• ‘Breakthrough science’ often not replicated\(^1\)
• 85% of research is wasted,\(^2\) usually because it was
  – Not published or poorly reported
  – Asked the wrong questions
  – Badly designed
  – Failed to review existing research systematically before starting new work
• Huge information overload for us all.

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Number of reports of trials

Cumulative Number of Reports of Trials in the Cochrane Stroke Group Specialised Register

2005-15: Doubling in number of reports of trials 12,000 → 24,000
Have research METHODS improved?

• EQUATOR guidelines for how to report research
• Better at asking the right research questions
  – James Lind Alliance: Research priority setting
  – Measuring the right core outcomes (COMET)
  – Stakeholder involvement
• Help to increase research value & reduce waste
  – REWARD Alliance researchwaste.net
  – Trial Forge; gathering evidence on how to make trials more efficient www.trialforge.org
• Cochrane Collaboration making continual efforts to improve quality and relevance of its systematic reviews with greater focus on priority topics
Number of Cochrane stroke systematic review topics

Cumulative Number of Reviews Published by the Cochrane Stroke Group

= 100 new topics reviewed and many important reviews of priority topics updated
Evidence is cumulative: effect of stroke unit care on being ‘dead or needing institutional care’

- The question has been answered
- There is ‘proof beyond reasonable doubt’ of the benefits
- The next question is ‘can this be translated to low and middle income countries?’
Stroke Unit care in low- and middle-income countries reduces case-fatality

<table>
<thead>
<tr>
<th>Region</th>
<th>Stroke Unit</th>
<th>Control</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>China</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beijing, China</td>
<td>12</td>
<td>195</td>
<td>19</td>
<td>197</td>
</tr>
<tr>
<td>Huaihua, China</td>
<td>10</td>
<td>134</td>
<td>10</td>
<td>73</td>
</tr>
<tr>
<td>Meta-analysis (8 sites)</td>
<td>27</td>
<td>862</td>
<td>71</td>
<td>804</td>
</tr>
<tr>
<td>India and SE Asia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ludhiana, India</td>
<td>24</td>
<td>201</td>
<td>95</td>
<td>202</td>
</tr>
<tr>
<td>Bangkok, Thailand</td>
<td>6</td>
<td>301</td>
<td>9</td>
<td>106</td>
</tr>
<tr>
<td>South America</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Joinville, Brazil</td>
<td>9</td>
<td>35</td>
<td>12</td>
<td>39</td>
</tr>
<tr>
<td>Africa</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cape Town, South Africa</td>
<td>16</td>
<td>101</td>
<td>33</td>
<td>94</td>
</tr>
<tr>
<td>Nouakchott, Mauritania</td>
<td>5</td>
<td>42</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>East Europe/Middle East</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Istanbul, Turkey</td>
<td>37</td>
<td>352</td>
<td>69</td>
<td>352</td>
</tr>
<tr>
<td>Zagreb, Croatia</td>
<td>698</td>
<td>5450</td>
<td>1095</td>
<td>5451</td>
</tr>
</tbody>
</table>

Langhorne and Pandian Lancet Neurol 2012
Benefit of stroke unit care

• Independent of parent specialty\(^1\)
• Demonstrated in all regions studied, including low-and middle income countries\(^1\)
• Not dependent on ‘technology’ or CT scan
• Result from reduction in stroke complications\(^2\)
• Global impact -> WHO
2015 WHO meeting on managing stroke and heart disease

• Previous WHO focus for reducing burden of non-communicable disease was *prevention*, but…

• Systems of care for people with stroke and heart disease patchy and inadequate

• In low and middle income countries, WHO considering new initiative to get health systems to
  – ‘Do the simple things well’
  – Ensure equitable access to basic acute stroke care facilities for all
Advances in rehabilitation research

New research designs
• Multicentre Trials
• Methods to develop trials of complex interventions

Discipline-specific
• Speech therapy
• Occupational therapy
• Physiotherapy

New technology
• CIMT
• Transcranial stimulation
  – Electrical
  – Magnetic
• Robotics
Robots for arm therapy: effect on ADL

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment N</th>
<th>Treatment Mean(SD)</th>
<th>Control N</th>
<th>Control Mean(SD)</th>
<th>Std. Mean Difference IV, Random, 95% CI</th>
<th>Weight</th>
<th>Std. Mean Difference IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burgar 2011</td>
<td>36</td>
<td>19.6 (8.47)</td>
<td>18</td>
<td>15.9 (6.36)</td>
<td></td>
<td>6.5%</td>
<td>0.46 [-0.11, 1.04]</td>
</tr>
<tr>
<td>Conroy 2011</td>
<td>41</td>
<td>3.98 (11.94)</td>
<td>21</td>
<td>-3.19 (10.72)</td>
<td></td>
<td>6.8%</td>
<td>0.61 [0.08, 1.15]</td>
</tr>
<tr>
<td>Fazekas 2007</td>
<td>15</td>
<td>12.07 (9.26)</td>
<td>15</td>
<td>25.53 (14.32)</td>
<td></td>
<td>5.2%</td>
<td>-1.09 [-1.86, -0.31]</td>
</tr>
<tr>
<td>Hesse 2005</td>
<td>22</td>
<td>22.45 (15.14)</td>
<td>22</td>
<td>17.27 (13.95)</td>
<td></td>
<td>6.4%</td>
<td>0.35 [-0.25, 0.95]</td>
</tr>
<tr>
<td>Hesse 2014</td>
<td>25</td>
<td>25.2 (11)</td>
<td>25</td>
<td>16 (15.7)</td>
<td></td>
<td>6.5%</td>
<td>0.67 [0.10, 1.24]</td>
</tr>
<tr>
<td>Housman 2009</td>
<td>17</td>
<td>0.2 (0.4)</td>
<td>17</td>
<td>0.1 (0.3)</td>
<td></td>
<td>5.8%</td>
<td>0.28 [-0.40, 0.95]</td>
</tr>
<tr>
<td>Hsieh 2011</td>
<td>12</td>
<td>0.13 (0.19)</td>
<td>6</td>
<td>0.06 (0.32)</td>
<td></td>
<td>4.0%</td>
<td>0.28 [-0.71, 1.27]</td>
</tr>
<tr>
<td>Kutner 2010</td>
<td>11</td>
<td>6.89 (9.995)</td>
<td>10</td>
<td>8.49 (11.33)</td>
<td></td>
<td>4.7%</td>
<td>-0.14 [-1.00, 0.71]</td>
</tr>
<tr>
<td>Liao 2011</td>
<td>10</td>
<td>0.25 (0.17)</td>
<td>10</td>
<td>0.03 (0.28)</td>
<td></td>
<td>4.3%</td>
<td>0.91 [-0.02, 1.84]</td>
</tr>
<tr>
<td>Lo 2010</td>
<td>49</td>
<td>6.31 (11.76)</td>
<td>78</td>
<td>1.37 (12.1)</td>
<td></td>
<td>8.1%</td>
<td>0.41 [0.05, 0.77]</td>
</tr>
<tr>
<td>Lum 2006</td>
<td>24</td>
<td>2.85 (1.21)</td>
<td>6</td>
<td>3.2 (1.4)</td>
<td></td>
<td>4.5%</td>
<td>-0.27 [-1.17, 0.62]</td>
</tr>
<tr>
<td>Masiero 2007</td>
<td>17</td>
<td>32.6 (7.2)</td>
<td>18</td>
<td>25.5 (10.5)</td>
<td></td>
<td>5.7%</td>
<td>0.77 [0.08, 1.46]</td>
</tr>
<tr>
<td>Masiero 2011</td>
<td>11</td>
<td>1.83 (1.4)</td>
<td>10</td>
<td>1 (0.7)</td>
<td></td>
<td>4.5%</td>
<td>0.71 [-0.18, 1.60]</td>
</tr>
<tr>
<td>Rabadi 2008</td>
<td>10</td>
<td>25.49 (7.23)</td>
<td>20</td>
<td>28.29 (6.72)</td>
<td></td>
<td>5.2%</td>
<td>-0.40 [-1.16, 0.37]</td>
</tr>
<tr>
<td>Volpe 2000</td>
<td>30</td>
<td>9.1 (3.3)</td>
<td>26</td>
<td>4.4 (2)</td>
<td></td>
<td>6.2%</td>
<td>1.67 [1.05, 2.29]</td>
</tr>
<tr>
<td>Volpe 2008</td>
<td>11</td>
<td>67.1 (7.96)</td>
<td>10</td>
<td>65.5 (7.59)</td>
<td></td>
<td>4.7%</td>
<td>0.20 [-0.66, 1.06]</td>
</tr>
<tr>
<td>Wu 2012</td>
<td>14</td>
<td>3.26 (7.16)</td>
<td>28</td>
<td>-2.88 (9.56)</td>
<td></td>
<td>5.9%</td>
<td>0.68 [0.02, 1.34]</td>
</tr>
<tr>
<td>Yoo 2013</td>
<td>11</td>
<td>0.4 (6.1)</td>
<td>11</td>
<td>0.1 (3.2)</td>
<td></td>
<td>4.8%</td>
<td>0.06 [-0.78, 0.90]</td>
</tr>
</tbody>
</table>

Total (95% CI): 366 - 351
Heterogeneity: Tau² = 0.19; Chi² = 44.26, df = 17 (P = 0.00031); I² = 62%
Test for overall effect: Z = 2.81 (P = 0.0049)
Test for subgroup differences: Not applicable

Mehrholz et al CDSR 2015
Conclusion: robotics for the post-stroke arm & hand

Implications for practice

• electromechanical and robot-assisted arm and hand training after stroke might improve activities of daily living & arm and hand function…

• it is still not clear if the difference… is clinically meaningful

Implications for research

• There is still a need for well-designed, large-scale, multicentre studies to evaluate benefits and harms
Population impact of services in 5 million inhabitants (10,000 strokes per year): number of extra independent survivors per year

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Maximum impact</th>
<th>Proportion eligible for treatment (%)</th>
<th>Actual impact Extra independent survivors per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid secondary prevention</td>
<td>200</td>
<td>All TIA; 15 stroke</td>
<td>100</td>
</tr>
<tr>
<td>Stroke unit (CSU) service</td>
<td>500</td>
<td>80</td>
<td>400</td>
</tr>
<tr>
<td>Rehabilitation (ESD) service</td>
<td>500</td>
<td>25</td>
<td>130</td>
</tr>
<tr>
<td><strong>Service total</strong></td>
<td>-</td>
<td>-</td>
<td><strong>630</strong></td>
</tr>
<tr>
<td>Aspirin</td>
<td>100</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>rtPA within 0-3 hrs</td>
<td>1100</td>
<td>10</td>
<td>160</td>
</tr>
<tr>
<td>rtPA within 3-4.5 hrs</td>
<td>500</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Mechanical thrombectomy</td>
<td>1200</td>
<td>10</td>
<td>120</td>
</tr>
<tr>
<td>Hemicraniectomy</td>
<td>2000</td>
<td>0.5</td>
<td>10</td>
</tr>
<tr>
<td><strong>Acute medical total</strong></td>
<td>-</td>
<td>-</td>
<td><strong>370</strong></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>-</td>
<td>-</td>
<td><strong>1000</strong></td>
</tr>
</tbody>
</table>

Table courtesy of Peter Langhorne and Jeyaraj Pandian
How has the evidence ‘progressed’?

• We understand better what the problems are
• We now know much more reliably
  – which interventions are effective
  – which are definitely not
• We have better methods for research:
  – Design
  – Conduct, analysis and reporting
  – Evidence synthesis
  – Priority-setting for and planning of new research
• Conclusion: the past decade of research has clearly
  – Improved patient care
  – Helped improve future research (and make it less wasteful?)
Thank you

Acknowledgements
Cochrane Stroke Group
Peter Langhorne and Jeyaraj Pandian