Clinical Research in England

Franco-British Symposium, October 2012
Clinical research: what can we learn from each other?

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Director, NIHR Evaluation, Trials and Studies
Analysis of spend by public funder:

Research spend 2004/2005
UKCRC analysis

Insufficient spend on applied & clinical research
### Treatment works vs. Treatment is worse

<table>
<thead>
<tr>
<th>Study</th>
<th>Corticosteroid</th>
<th>Adjusted control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alexander 1972</td>
<td>16/55</td>
<td>22/55</td>
</tr>
<tr>
<td>Ransohoff 1972</td>
<td>9/17</td>
<td>13/18</td>
</tr>
<tr>
<td>Faupel 1976</td>
<td>16/67</td>
<td>(16/28)×2</td>
</tr>
<tr>
<td>Cooper 1979</td>
<td>26/49</td>
<td>(13/27)×2</td>
</tr>
<tr>
<td>Hernesniemi 1979</td>
<td>35/81</td>
<td>36/83</td>
</tr>
<tr>
<td>Pitts 1980</td>
<td>114/201</td>
<td>(38/74)×3</td>
</tr>
<tr>
<td>Saul 1981</td>
<td>8/50</td>
<td>9/50</td>
</tr>
<tr>
<td>Braakman 1983</td>
<td>44/81</td>
<td>47/80</td>
</tr>
<tr>
<td>Giannotta 1984</td>
<td>34/72</td>
<td>(7/16)×4</td>
</tr>
<tr>
<td>Dearden 1986</td>
<td>33/68</td>
<td>21/62</td>
</tr>
<tr>
<td>Chacon 1987</td>
<td>1/5</td>
<td>0/5</td>
</tr>
<tr>
<td>Zagara 1987</td>
<td>4/12</td>
<td>4/12</td>
</tr>
<tr>
<td>Stubbs 1989</td>
<td>13/98</td>
<td>(5/54)×2</td>
</tr>
<tr>
<td>Gaab 1994</td>
<td>19/133</td>
<td>21/136</td>
</tr>
<tr>
<td>Grumme 1995</td>
<td>38/175</td>
<td>49/195</td>
</tr>
<tr>
<td>Zarate 1995</td>
<td>0/30</td>
<td>0/30</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td>410/1194</td>
<td>432/1230</td>
</tr>
</tbody>
</table>

**Heterogeneity**
- $\chi^2$ 18.11, 34.3%
- $P < 0.2$

**Effect of steroids on death in head injury**

Research in the NHS

- NHS as a customer for research
- NHS as a top class environment for the conduct of research

- NHS as a driver of health and wealth
  - Decrease lost productivity
  - Research as a driver of wealth creation via life sciences industries

- Research as a core activity in the NHS, not an optional extra
• NHS R&D Strategy 2006

• To transform research in the NHS
• To create a health research system in which the NHS supports outstanding individuals, working in world-class facilities, conducting leading-edge research, focused on the needs of patients and the public
National Institute for Health Research

Infrastructure
- Clinical Research Networks
- Clinical Research Facilities & Centres

Faculty
- Investigators & Senior Investigators
- Trainees
- Associates

Universities
- NHS Trusts
- Patients & Public

Research
- Research Projects & Programmes
- Research Units & Schools

Systems
- Research Governance Systems
- Research Information Systems
Programmes

- Health Technology Assessment
- EME, joint funded by MRC/NIHR
- Public Health Research
- Health Services and Delivery Research
- Systematic Reviews
  - Open to all UK

- Research for Patient Benefit
- Programme Grants for Applied Research
- Invention for Innovation
  - England only
Examples of HTA commissioned Primary Research

• Published in Lancet
  – SANAD
  – NACHBID
  – FOOD
  – PAC-MAN
  – CESAR

• Published in NEJM
  – C3PO
  – BELL’S trial
  – EVAR
  – Price et al
Examples of HTA responsive mode

• Themed calls
  – M4C, trauma & emergency care, healthcare acquired infections,
  – Diagnostics, dementia, surgical interventions, obesity

• IVAN – bevacizumab v ranibizumab
  – Inhibit VEGF in Age-related choroidal Neovascularisation.

• Persephone - comparing six months Trastuzumab treatment with twelve months, in women with early stage breast cancer
The Number of RCTs Funded by NIHR* Opening to Recruitment by Financial Year

<table>
<thead>
<tr>
<th>Financial Year</th>
<th>Number of Studies Opening to Recruitment</th>
</tr>
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<tbody>
<tr>
<td>2008/09</td>
<td>50</td>
</tr>
<tr>
<td>2009/10</td>
<td>70</td>
</tr>
<tr>
<td>2010/11</td>
<td>95</td>
</tr>
<tr>
<td>2011/12</td>
<td>148</td>
</tr>
</tbody>
</table>
Facilities & Centres

- Biomedical Research Centres x 11
- Biomedical Research Units x 20
- Based within the most outstanding NHS and University partnerships in the country, are leaders in scientific translation...to translate fundamental biomedical research into clinical research that benefits patients and they are early adopters of new insights in technologies, techniques and treatments for improving health.

- Clinical Research Facilities
NIHR Clinical Research Networks

6 TCRNs
Stroke, Cancer, Diabetes, Mental Health, Medicines for Children, Dementias and neurodegenerative diseases

CCRN
25 Comprehensive Local Research Networks

PCRN
NIHR Clinical Research Network Coordinating Centre
Impact of Research Networks

Recruitment to LRNs, Non-LRN areas and Devolved Nations

Boost-II UK and ADEPT recruitment in LRN and Non-LRN sites

Stroke

Medicines for Children
The Number of Commercial and Non-Commercial Studies Opening to Recruitment by Financial Year

- **Commercial Studies**
  - 2008/09: 58
  - 2009/10: 157
  - 2010/11: 241
  - 2011/12: 302

- **Non-Commercial Studies**
  - 2008/09: 647
  - 2009/10: 726
  - 2010/11: 909
  - 2011/12: 1164
The Number of Commercial and Non-Commercial RCTs Opening to Recruitment by Financial Year

- **Financial Year 2008/09**: 180 Commercial RCTs, 52 Non-Commercial RCTs
- **Financial Year 2009/10**: 231 Commercial RCTs, 114 Non-Commercial RCTs
- **Financial Year 2010/11**: 251 Commercial RCTs, 171 Non-Commercial RCTs
- **Financial Year 2011/12**: 352 Commercial RCTs, 214 Non-Commercial RCTs

Legend:
- Red: Number of Commercial RCTs
- Light Gray: Number of Non-Commercial RCTs
Responding quickly to ‘swine flu’

• June 4\textsuperscript{th} 2009 – first discussions.

1. rapid commissioning against DH priorities
   • 5 projects funded

2. rapid launch of a Themed Call in flu:
   • June 19\textsuperscript{th} open call - 170 expressions of interest received
   • August 6\textsuperscript{th} further 9 projects funded

• Active monitoring of projects to ensure start and deliver rapidly
  NIHR portfolio of 14 flu projects (£2.3M), across all NETS programmes (even HSR)
Responding quickly to ‘swine flu’
NIHR as a system

- Pollard et al. Expediting Clinical Trials in a Pandemic
  BMJ 14th Nov 2009
  - Ethics – 18 days, Research governance 19 days, MHRA 11 days
  - Recruitment to vaccine study closed with 1000 children

- SWIFT study
  - ITUs – 100 hospitals approved within 5 days

- Seroprevalance study
  - Complete by end of October
  - Paper fast tracked in Lancet published Jan 21, 2010
Lessons from Research funding in a pandemic

• NIHR can respond to urgent priorities
• Its health-research system can function rapidly and effectively.
• “...The success of NIHR in this particular case shows how it has transformed clinical research in the NHS...The NIHR is achieving its promise of delivering research that matters to patients”.
• *Walley & Davidson Lancet 21st January 2010*
Not all perfect...

- Governance
  - Health Research Agency
    - The HRA will co-operate with others to combine and streamline the current approval system and promote consistent, proportionate standards for compliance and inspection. In doing so it will reduce the regulatory burden on research-active businesses, universities and the NHS...

- Excess treatment costs
  - Becoming the responsibility of the Commissioning Board

- Academic rewards
  - REF next year

- Changing the culture in the NHS
Clinical research in England

• Thriving!

• NIHR a health research system

• Not all smooth but actively getting better

• Keen to have even greater engagement with industry

• And with international collaborators
Increased CSR funding for health research through NIHR and MRC

<table>
<thead>
<tr>
<th>Year</th>
<th>MRC</th>
<th>NIHR</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008/09</td>
<td>20.4</td>
<td>25</td>
<td>45.4</td>
</tr>
<tr>
<td>2009/10</td>
<td>44</td>
<td>70</td>
<td>114</td>
</tr>
<tr>
<td>2010/11</td>
<td>63</td>
<td>132.6</td>
<td>195.6</td>
</tr>
</tbody>
</table>
Academy of Medical Sciences Review
A new regulation and governance pathway

Health Research Agency

Integrated Research Application System
Triage and single point of contact

National Research Ethics Service
- UK-wide single ethics opinion
- Streamlined process for specialist approvals and licences

National Research Governance Service
- NHS R&D permissions
- Undertake all study-wide governance checks
- Co-ordinate local NHS feasibility assessments

Medicines and Healthcare Regulatory Agency
- Clinical Trial Authorisation

Other approvals
- Ministry of Justice and Ministry of Defence

Response

Co-ordination

Functions of HRA

Application pathway:
- Approvals: all studies
- Authorisation: if required
- Permissions: if required
- Co-ordination: if required
The Managed Translational Pathway
The Managed Translational Pathway

Successful development?

MRC Managed Schemes

Translational stem cell research programme

Developmental pathway funding scheme (DPFS)

Prototype discovery and design

Pre-clinical development

Early clinical trials

Late clinical trials

NIHR Managed Programmes

Developmental clinical studies (DCS)

EME Efficacy and Mechanism Evaluation

HTA Health Technology Assessment

“Pull through”
The Managed Translational Pathway

Promising, non commercial
Fail in testing, no longer promising, or commercial partner