Welcome to our AGM 2014/15

- Please help yourself to refreshments
- If you have any questions please speak to a member of staff
Please take a seat, the AGM is about to begin
Welcome
Chairman, Sir Richard Sykes
2014/15 review and a look ahead
Chief executive, 
Dr Tracey Batten
We want to

• make our services more accessible
• continuously improve safety and clinical outcomes
• tailor care, support and treatment
• have modern, technology-enabled facilities and infrastructure
• work in a more collaborative way
Key milestones in 2014/15

- improved staff engagement
- began the move to digital patient records
- became lead health provider for community independence service
- expanded community-based specialty services
- made planned changes to emergency and urgent care services
- innovation and translational research
- Care Quality Commission inspection
In April 2015 we had the second lowest HSMR in the Shelford Group.
Cancer care 2-week wait standard

Percentage of patients urgently referred seen in under two weeks

- national standard (92 per cent)
A&E 4-hour wait standard

Percentage of patients assessed, treated, admitted or discharged within four hours

- national standard (95 per cent)
Referral to treatment – under 18 wks

Percentage of patients on our waiting lists who have waited less than 18 weeks

national standard (92 per cent)
Looking ahead

- new quality strategy
- implementation of our core strategies – clinical, quality and financial – supported by refreshed organisational values and behaviours
- increased involvement of our patients, GPs and other stakeholders
Format

• headlines for the year
• statement of comprehensive income
• where does the income come from?
• how do we spend it?
• a look ahead
Headlines for the year

• Year-end surplus: £15.4m
• Underlying picture more challenging as includes:
  o £24.4m for additional costs of providing specialist care
• Cash balance: £43.3m
• Capital expenditure: £32.9m
• Savings programme: £39.7m of efficiencies
Maintaining our recovery

Plan vs actual 2012/13 to 2014/15
## Statement of comprehensive income

<table>
<thead>
<tr>
<th></th>
<th>2012/13 £m</th>
<th>2013/14 £m</th>
<th>2014/15 £m</th>
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<tbody>
<tr>
<td>Revenue from patient care activities</td>
<td>752.7</td>
<td>774.4</td>
<td>795.7</td>
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<tr>
<td>Other operating revenue</td>
<td>218.5</td>
<td>204.9</td>
<td>204.9</td>
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<tr>
<td><strong>Total revenue</strong></td>
<td>971.2</td>
<td>979.3</td>
<td>1000.6</td>
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<tr>
<td>Employee benefits</td>
<td>-522.5</td>
<td>-526.2</td>
<td>-553.4</td>
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<tr>
<td>Other costs*</td>
<td>-417.7</td>
<td>-419.0</td>
<td>-418.0</td>
</tr>
<tr>
<td><strong>Operating surplus</strong></td>
<td>31</td>
<td>34.2</td>
<td>29.3</td>
</tr>
<tr>
<td>Net financing costs</td>
<td>-1.5</td>
<td>-0.8</td>
<td>-0.4</td>
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<tr>
<td><strong>Surplus for the financial year</strong></td>
<td>29.5</td>
<td>33.3</td>
<td>28.9</td>
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<tr>
<td>Public dividend capital payable</td>
<td>-21.1</td>
<td>-18.8</td>
<td>-14.4</td>
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<tr>
<td>Adjustment for donated assets</td>
<td>0.6</td>
<td>0.6</td>
<td>0.9</td>
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<tr>
<td><strong>Retained surplus/(deficit) for the year</strong></td>
<td>9</td>
<td>15.1</td>
<td>15.4</td>
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* Excluding impairments
Where does our £1 billion income come from?

2014/15

- NHS Patient Care: 73%
- Non-NHS Patient Care: 6%
- Education, training and research: 13%
- Other revenue: 4%
- Rental revenue from operating leases: 1%
- Non-patient care services to other bodies: 3%
- Income generation: 0%
How do we spend our income?

1 Operating expenses – substantive staff
How do we spend our income?

2 Operating expenses – non pay

<table>
<thead>
<tr>
<th>Category</th>
<th>2012-13</th>
<th>2013-14</th>
<th>2014-15</th>
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<tbody>
<tr>
<td>Services from NHS Bodies</td>
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<td>Purchase of healthcare</td>
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<td>Supplies and services - clinical</td>
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<td>Supplies and services - drugs</td>
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<td>Consultancy</td>
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<td>Establishment</td>
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<td>Transport</td>
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<td>Premises</td>
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<td>Depreciation</td>
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<td>Bad debt provision</td>
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<td>Clinical negligence</td>
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<td>R&amp;D (excl staff costs)</td>
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<tr>
<td>Education and Training</td>
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<tr>
<td>Other</td>
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</table>
## Looking ahead: 2015/16 plan

<table>
<thead>
<tr>
<th>Financial plan 2015/16</th>
<th>2014/15 actual £m</th>
<th>2015/16 plan £m</th>
<th>Movement between years £m</th>
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<tbody>
<tr>
<td>Income*</td>
<td>1,001.1</td>
<td>1,027.5</td>
<td>↑26.4</td>
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<tr>
<td>Expenditure</td>
<td>985.7</td>
<td>1,046.0</td>
<td>↑60.3</td>
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<tr>
<td>Surplus / (Deficit)**</td>
<td>15.4</td>
<td>(18.5)</td>
<td>↓33.9</td>
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<tr>
<td>CIP</td>
<td>39.7</td>
<td>36.1</td>
<td>↓3.6</td>
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<tr>
<td>Capex</td>
<td>32.9</td>
<td>38.0</td>
<td>↑5.1</td>
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<tr>
<td>Cash</td>
<td>43.3</td>
<td>36.1</td>
<td>↓7.2</td>
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*Including investment revenue
**Excluding technical adjustments
Looking ahead: 2015/16 and beyond

• Challenging financial position in 2015/16 and into the future
  ○ No further funding for additional costs of specialist care
• In 2015/16 we plan to double the investment in repairs and improvements to our aging estate
• Maintaining investment in IT
• Supporting implementation of the clinical strategy
Question time

Chaired by:
Chairman, Sir Richard Sykes

Panel:
Chairman, Sir Richard Sykes
Chief executive, Dr Tracey Batten
Chief financial officer, Richard Alexander
Chief operating officer and deputy chief executive, Steve McManus
Deputy medical director, Dr Julian Redhead
Director of nursing, Janice Sigsworth
Regenerating the failing heart: pushing the boundaries of health and health care

Professor Sian Harding
Imperial College
London
Natural history of heart failure

- Heart attack
- Valve disease
- Genetic defect
- Alcohol/drugs
- Infection/sepsis

Damage

- Enlarged heart
- Water retention
- Adrenaline stimulation

Apparent recovery/compensation

- Symptoms

Decompensation/Heart failure

- Drug treatment to prevent further damage
- Drug treatment to block stimulatory mechanisms
- Mechanical aids
- Transplantation

Death

0.75-1 M people with heart failure
Why is there a progressive deterioration in contraction of the failing heart? Can we stimulate the remaining muscle safely?
Ventricular myocytes from failing and non-failing human heart
Change in myocyte contraction is seen in all causes of heart failure – acquired defect

% shortening

Beating rate – beats per min

(Davies et al, Circulation 1995)
Restoration of SERCA2a speeds contraction and relaxation in human myocytes

It has not been possible to develop a drug to stimulate SERCA
Strategy – use SERCA gene therapy to improve cardiac contraction
Viral vectors in registered clinical gene therapy trials
Cardiac gene therapy adeno-associated viral vectors

- No disease associated with infection
- Safety in humans has been shown
  - haemophilia gene therapy trials
- Long lasting gene expression – 9 years from a single injection
- Can target the heart
- Safe with immunosuppression – good for future transplants
SERCA2a gene therapy clinical trials

Patients with moderate to severe heart failure have one injection of adeno-associated virus with SERCA2a into blood vessels of the heart, with an overnight stay in hospital.

- **CUPID**
  Pilot study, 39 patients, 3 years – safety and some evidence of efficacy.

- **SERCA-LVAD**
  Imperial-sponsored study, 24 patients, to provide information on the amount of gene delivery to tissue, as well as effect of pre-existing immunity.

- **Agent-HF**
  French trial to look at effects on heart size.

- **CUPID2**
  International Multicentre trial, 240 patients, recruitment. Imperial researcher was UK Lead.
CUPID phase 2 SERCA2a gene therapy trial

First 9 patients reported Jaski, J Card Fail. 2009
Full 39 patients, Jessup, Circulation, 2011
Three year follow-up Zsebo, Circ Res 2013

First 9 patients reported Jaski, J Card Fail. 2009
Full 39 patients, Jessup, Circulation, 2011
Three year follow-up Zsebo, Circ Res 2013

All patients through 18 months in long term follow up

* p<0.05 vs placebo

WHF • MI • LVAD • Transplant • Chronic Inotrope • Death • NAb+
SERCA2a gene therapy clinical trials

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- **CUPID2**
  International Multicentre trial, 240 patients, recruitment. **Safe but no effect, too little virus.**
What is the next step?

- Increase the concentration of virus
  - Liver trials use 50x more

- Use an indirect way to stimulate SERCA through an interacting protein
  - To overcome the bodies response to reduce SERCA

- Engineer a new type of virus to overcome problems with antibodies
  - Up to 70% of people already have antibodies
Natural history of heart failure

Damage

Apparent recovery/compensation

Decompensation/Heart failure

Death

Repair

Gene therapy
evvascularisation

Myocardial infarction
Valve disease
Genetic defect
Alcohol/drugs
Infection/sepsis

Hypertrophy
Dilatation
Volume loading
Sympathetic stimulation

Drugs

Devices
Transplantation
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<tr>
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<th>Bone marrow-derived stem cells</th>
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<td>Immune matching</td>
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Bone marrow cells implanted into heart

Study design

Patient selection

Harvest of stem cells from bone marrow

Bone marrow cell separation

Platelets

BMMCC

Ficoll-Hypaque

Erythrocytes

Stem cells infusion
Results of bone marrow stem cell implantation for heart disease

- Started almost 10 years ago with small safety trials
- Now around 1000 treated and 1000 control patients in many small double-blind randomised placebo-controlled trials
- Procedure is safe in the short and medium term
- Some benefit, but not very large
- They don’t make myocytes

Large trials underway to decide if therapy is useful
Adult stem cells from the heart, expanded and re-injected

Do heart patients want their own stem cells back?

• One important benefit of receiving your own cells is immune matching

• But – bone marrow stem cells from heart patients are less active

• These risk factors reduce your bone marrow stem cell activity
  
  - Age
  - Smoking
  - Diabetes
  - High lipids
  - Hypertension
  - Lack of exercise
  - Male gender

• In fact, poor stem cell activity is another risk factor

Are heart patients there because their own stem cells haven't worked?

Vasa Circ Res 2001 89: e1 - e7
Schmidt-Lucke C. Circulation. 2005 111:2981-7
Which stem cells for cardiac repair?

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<td>Forms true cardiomyocytes</td>
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<td>Blue</td>
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Embryonic stem cells in vitro
Differentiation of embryonic stem cells

Undifferentiated ES cell colonies

-LIF/feeders fibroblasts

+ Growth factors

Embryoid bodies

Neuronal

Epithelial

Cardiac
induced pluripotent stem cells

patient-specific genotype

adult human cells

drugs in clinical trials

genetic and pharmaceutical screen

in vitro disease modelling

cardiovascular cells
Calcium transient – optical mapping
iPSC-CM

Membrane potential – multielectrode array
hESC-CM cluster
Which stem cells for cardiac repair?

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Stem cell therapy for heart failure: first implant of cardiac cells derived from human embryonic stem cells

16.01.2015 – COMMUNIQUÉ

On the 21 October 2014, Professor Philippe Menasché and his team from the cardiovascular surgery service of the Georges Pompidou European Hospital, AP-HP, carried out a transplant of cardiac cells derived from human embryonic stem cells*, according to a method developed by the Department of Cell and Tissue Biotherapies of the Saint-Louis hospital, directed by Professor Jérôme Larghero and through research led by this group within Inserm.

The surgery, coupled with a coronary bypass*, was carried out on a woman of 68 years suffering from severe heart failure. Ten weeks after the intervention, the patient is feeling well, her condition has improved markedly, with no complications having been observed. This promising advance was presented this Friday, 16 January 2015 at the XXV European Days Conference of the French Society of Cardiology.
A patch for stem cell delivery to the heart

- Applies cells directly to infarcted area
  - Can be prepared in advance

- Maintains cells in position

- Supports scar to prevent expansion
  - Specialised biomaterials being developed in Imperial

London's research quarter
Imperial's White City Campus and the Hammersmith Hospital Campus are two poles of a new research quarter for London. The co-location of research, business and healthcare will be a first in the capital, reinforcing its position as a catalyst for scientific development and economic growth.

Imperial's White City Campus will create a culture of research and innovation, electric with ideas. The campus will buzz with exchanges between students, researchers and entrepreneurs; a place where questions are posed and solutions found.

One of the first buildings, the £200 million Research and Translation Hub, will be Imperial West’s centrepiece. With space for 1,000 researchers alongside 50 spin-out companies, the Hub will support innovation on an unprecedented scale in London.
Imperial College, NHLI

- Alex Lyon
- Nick Banner
- Andy Morley-Smith
- Gabor Foldes
- Nicola Hellen
- Nazanin Dolatshad
- Thusharika Kodagoda
- Maxime Mioulane
- Mirna Chahine
- Ljudmila Kolker (and UKSCB)
- Nadire Ali
- Cesare Terracciano
- Peter O’Gara

Roger Hajjar – Mt Sinai NY

Chris Denning – Univ. Nottingham

Stephan Amisten – KCL

Thomas Eschenhagen, UKE Hamburg

Rosetree’s Trust

SC4SM

Stem Cells for Safer Medicines

British Heart Foundation

Mending Broken Hearts

National Centre for the Replacement, Refinement and Reduction of Animals in Research
Any questions?
Thank you
Chairman, Sir Richard Sykes