

# 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

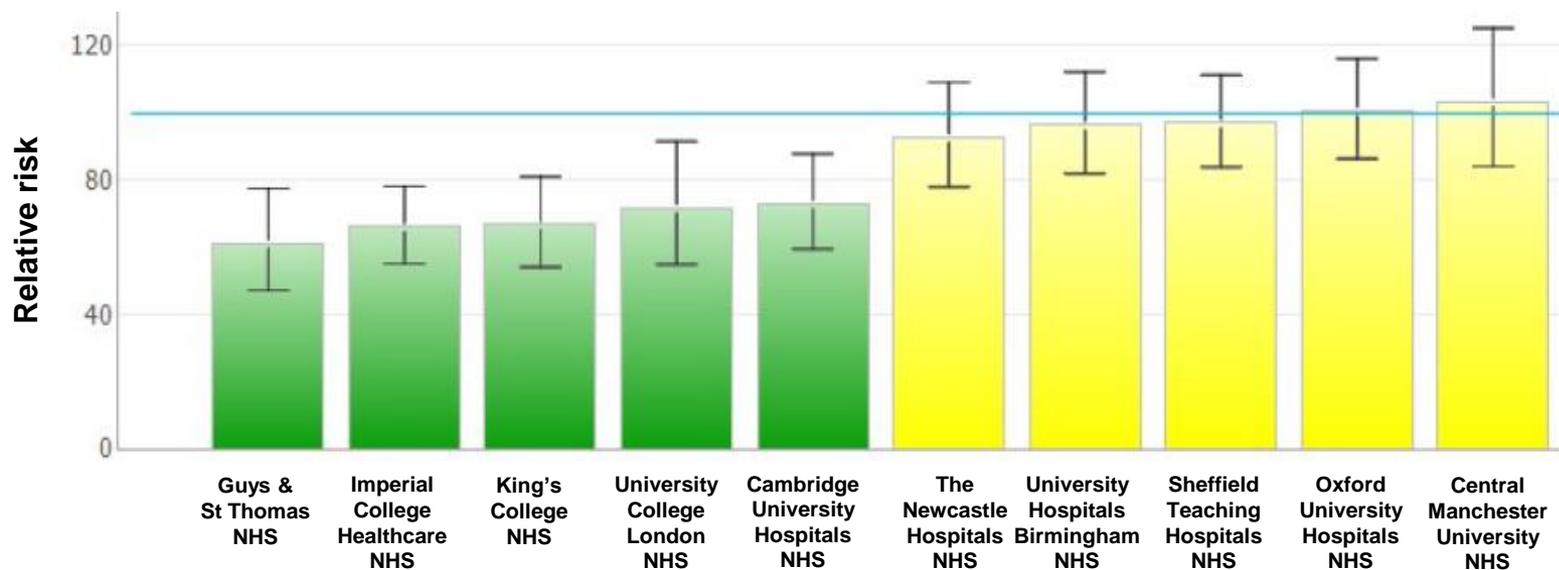
- make our services more accessible
- continuously improve safety and clinical outcomes
- tailor care, support and treatment
- have modern, technology-enabled facilities and infrastructure
- work in a more collaborative way

# 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

# Hospital standardised mortality ratio

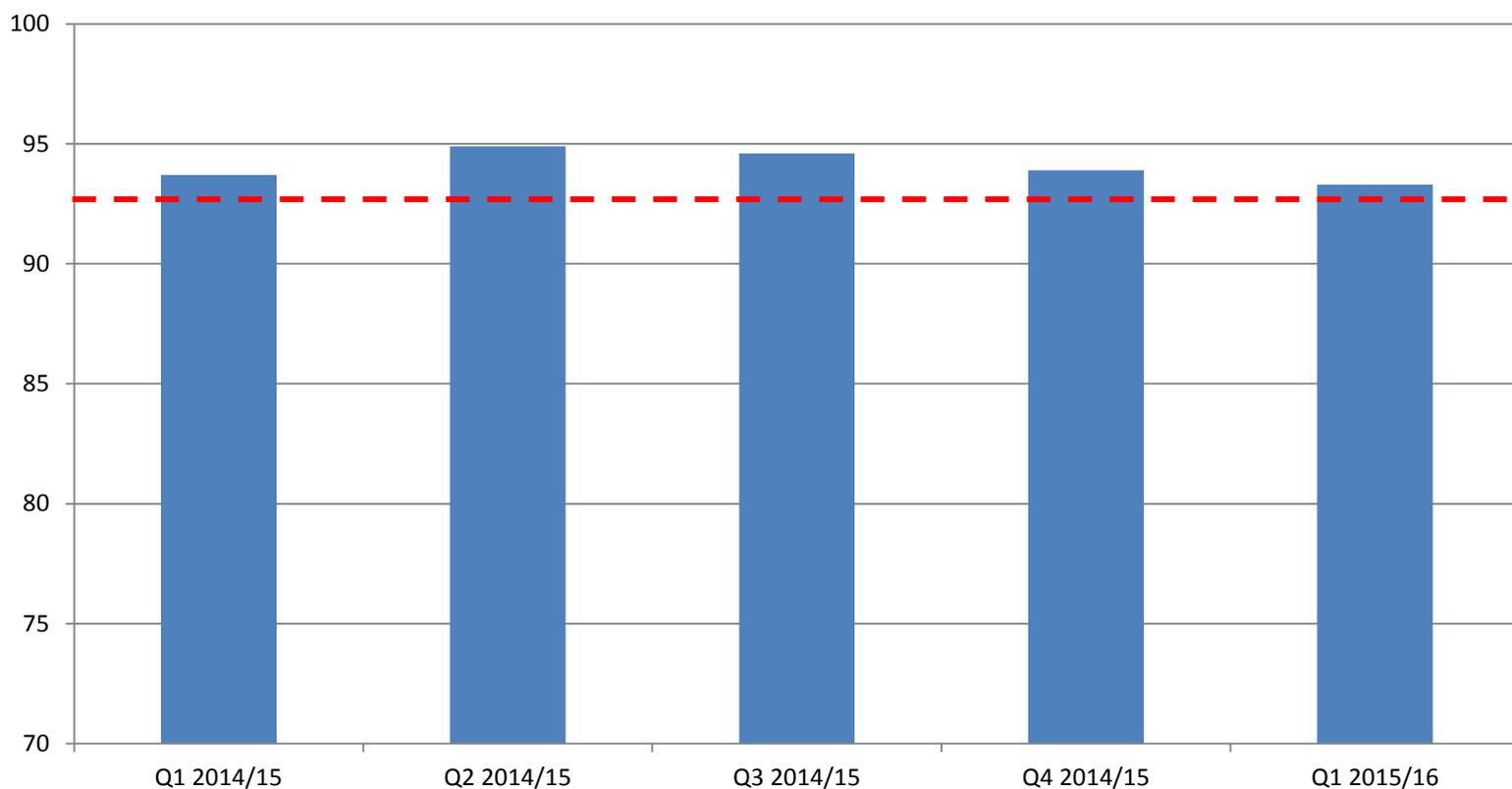
In April 2015 we had the second lowest HSMR in the Shelford Group.



# Cancer care 2-week wait standard

Percentage of patients urgently referred seen in under two weeks

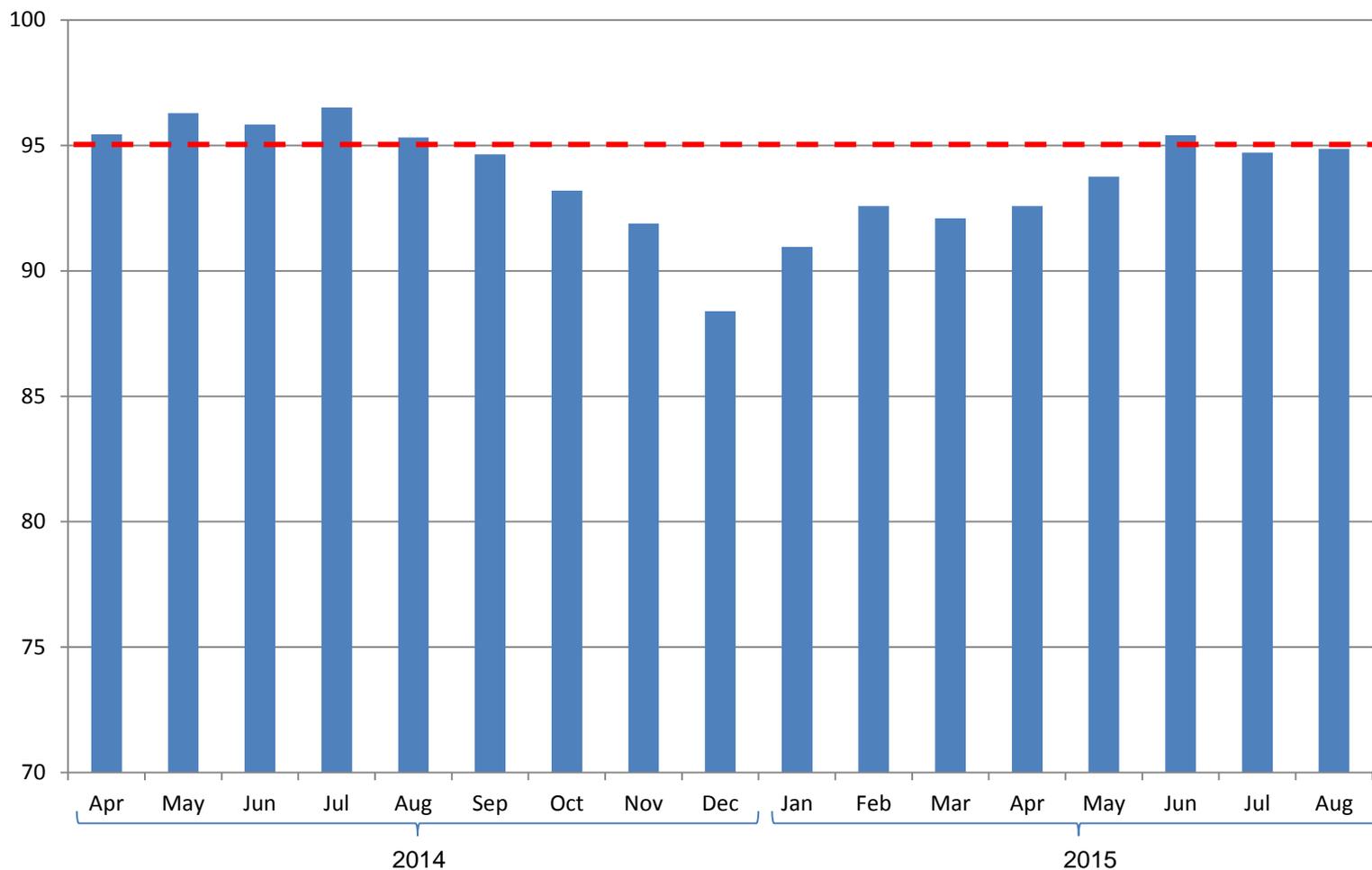
--- national standard (92 per cent)



# A&E 4-hour wait standard

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

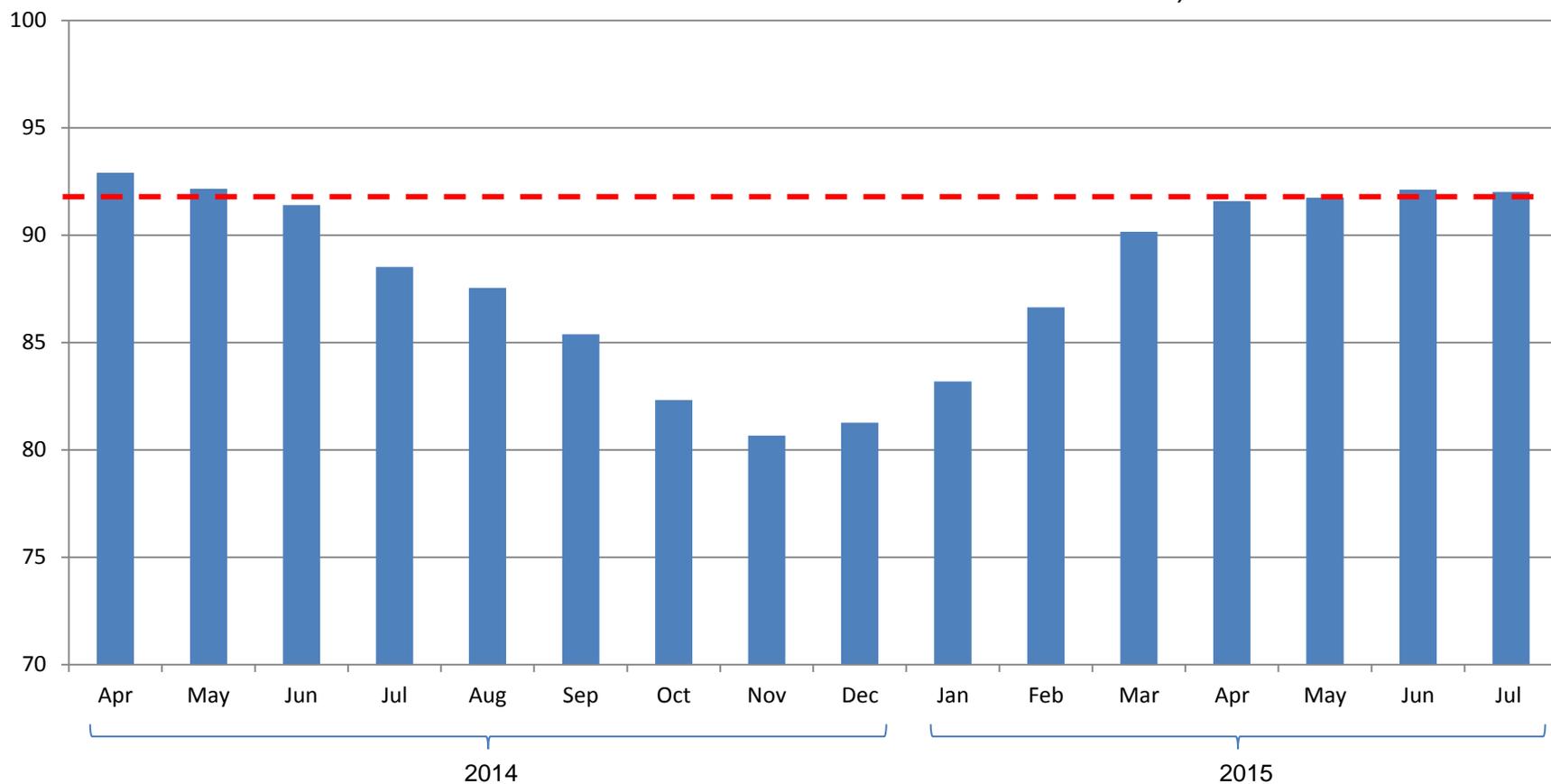
--- national standard (95 per cent)



# 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

# Financial accounts

## 2014/15

Chief financial officer,

Richard Alexander

# Format

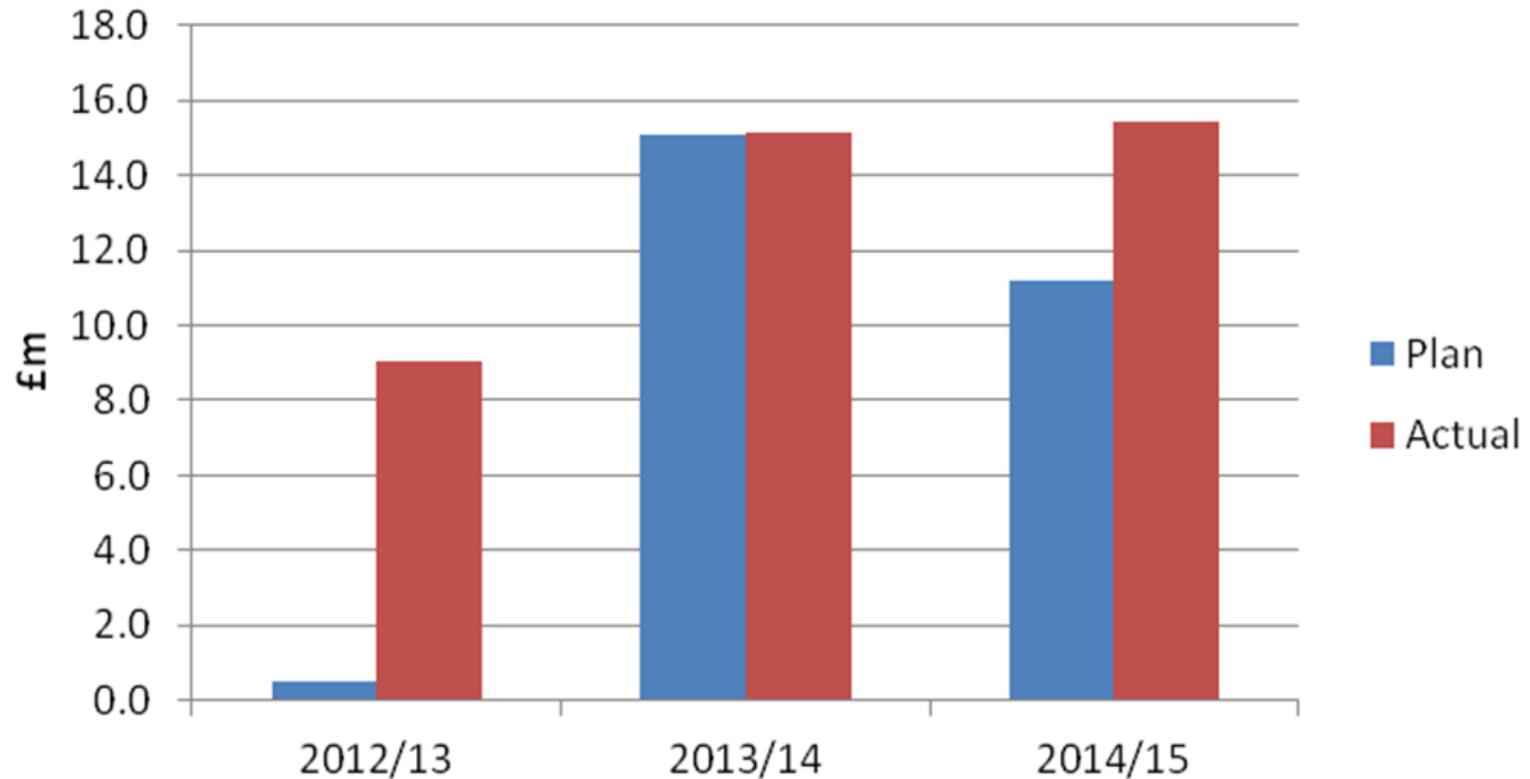
- headlines for the year
- statement of comprehensive income
- where does the income come from?
- how do we spend it?
- a look ahead

# Headlines for the year

- Year-end surplus: £15.4m
- Underlying picture more challenging as includes:
  - £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



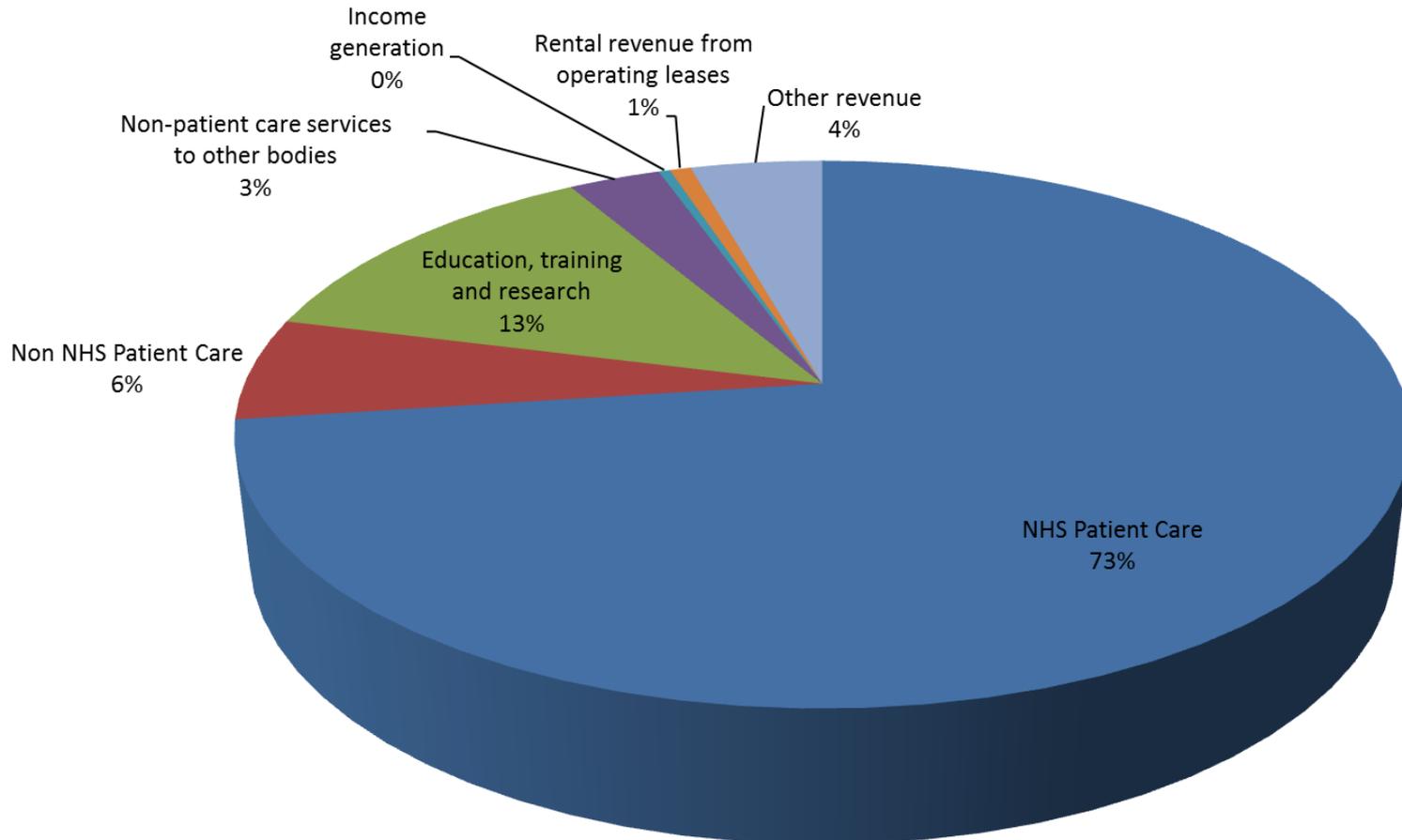
# Statement of comprehensive income

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

\* Excluding impairments

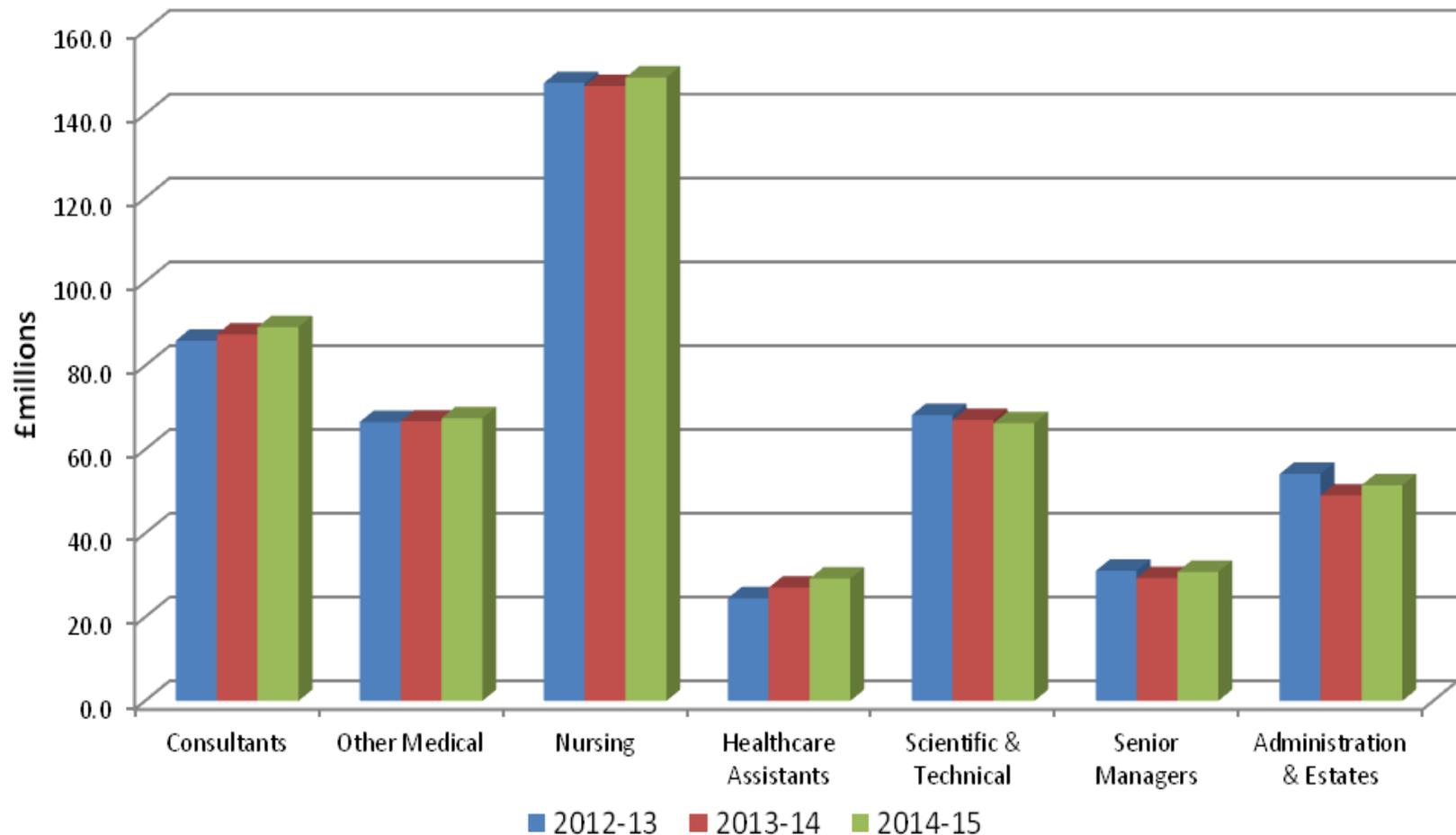
# Where does our £1 billion income come from?

## 2014/15



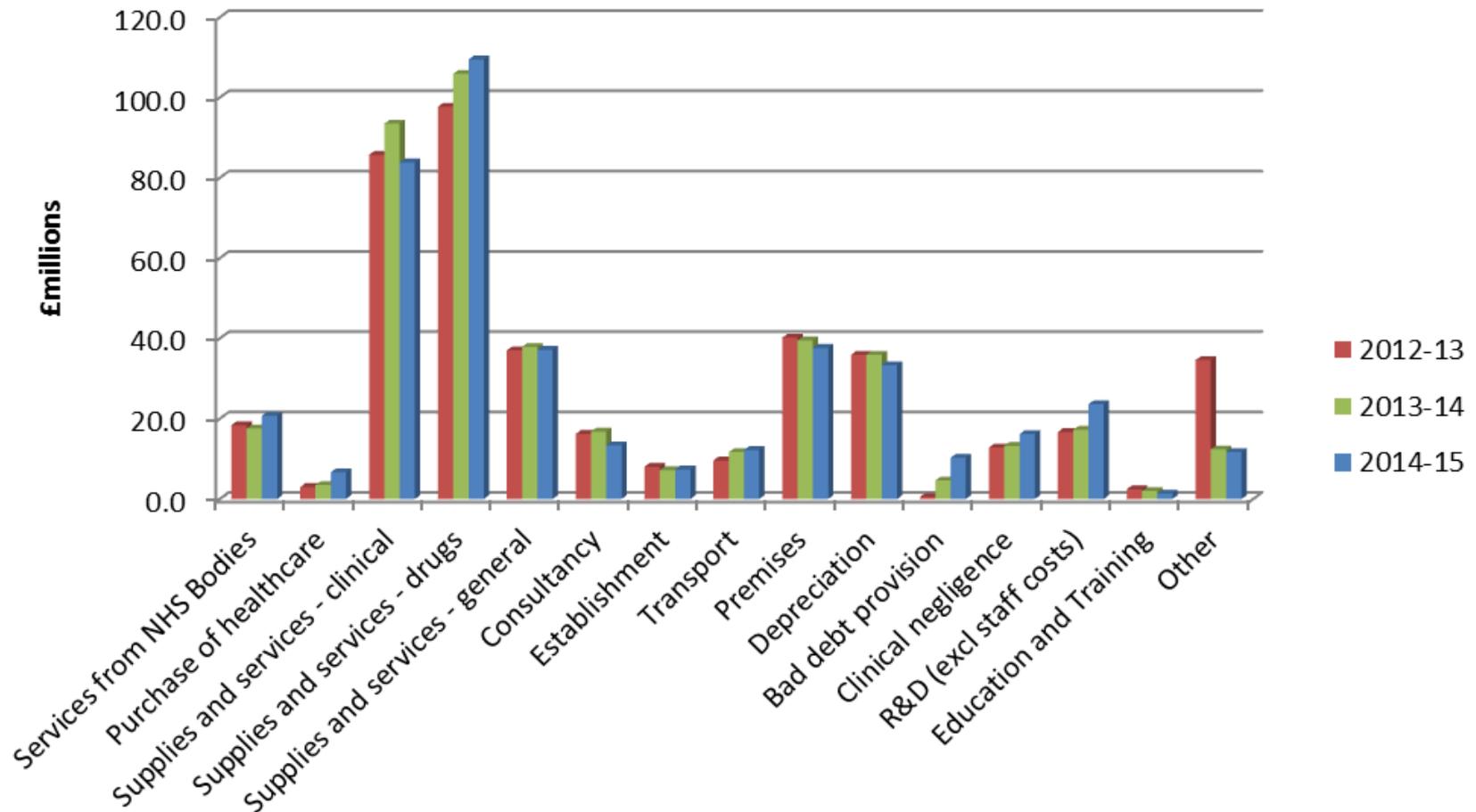
# How do we spend our income?

## 1 Operating expenses – substantive staff



# How do we spend our income?

## 2 Operating expenses – non pay



# Looking ahead: 2015/16 plan

Financial plan 2015/16	2014/15 actual £m	2015/16 plan	Movement between years £m
Income*	1,001.1	1,027.5	↑26.4
Expenditure	985.7	1,046.0	↑60.3
Surplus / (Deficit)**	15.4	(18.5)	↓33.9
CIP	39.7	36.1	↓3.6
Capex	32.9	38.0	↑5.1
Cash	43.3	36.1	↓7.2

\*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

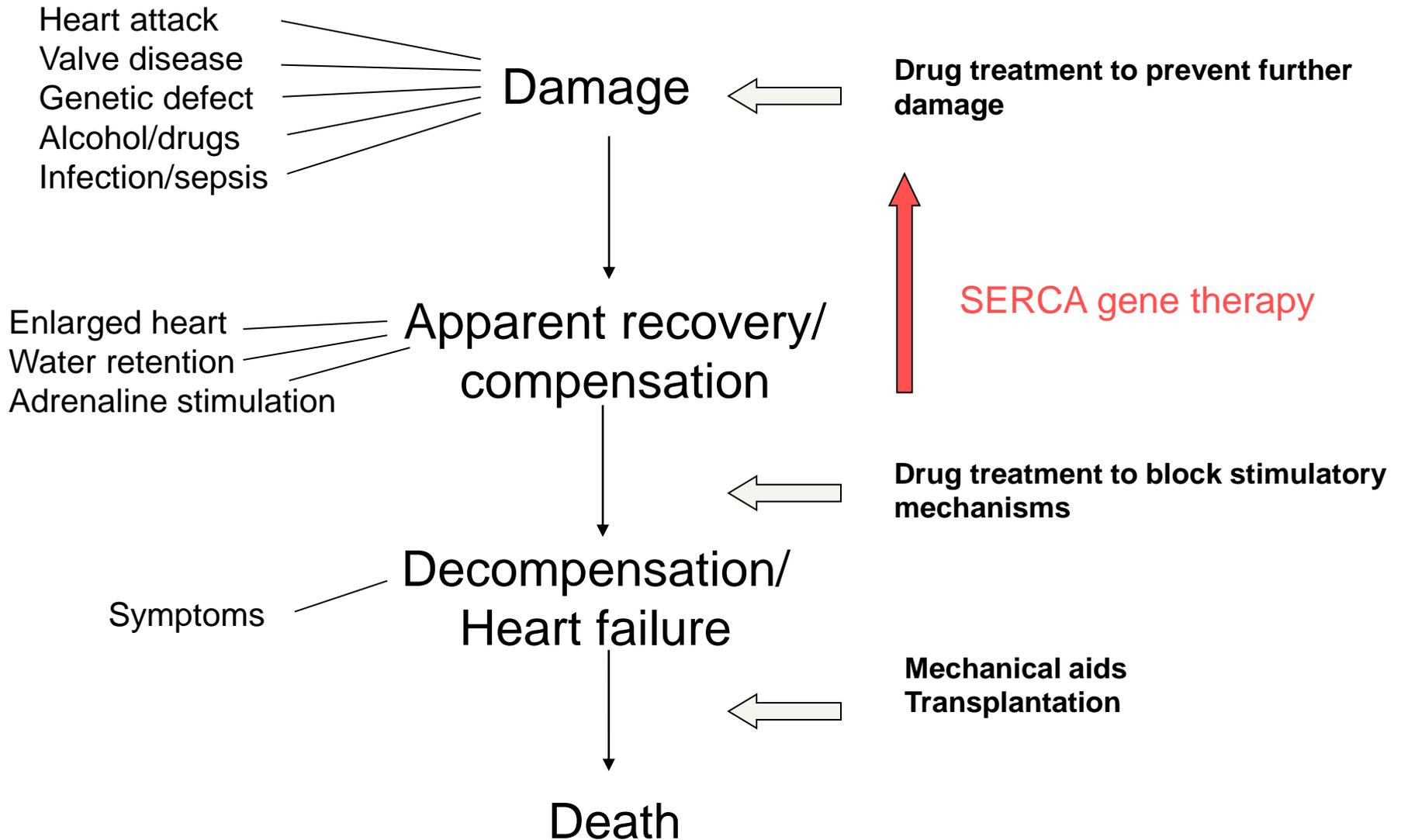
Deputy medical director, Dr Julian Redhead

Director of nursing, Janice Sigsworth

# **Regenerating the failing heart: pushing the boundaries of health and health care**

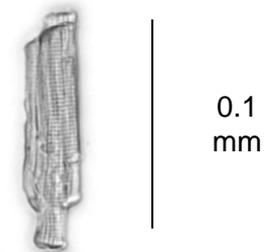
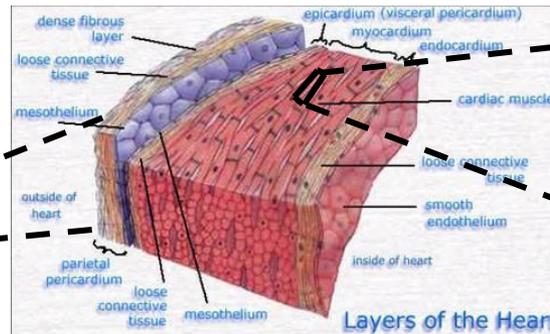
**Professor Sian Harding**  
**Imperial College**  
**London**

# Natural history of heart failure

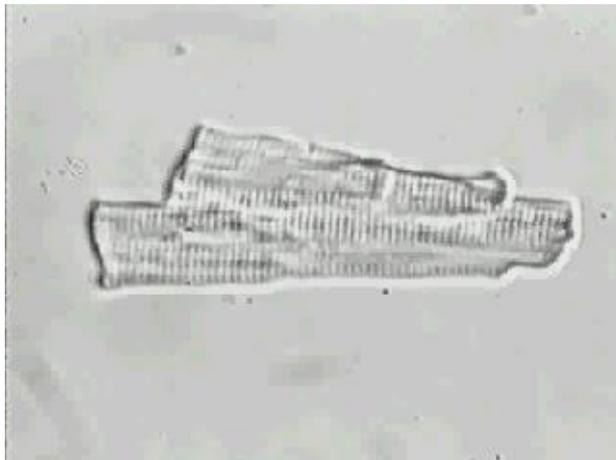


*0.75-1 M people with heart failure*

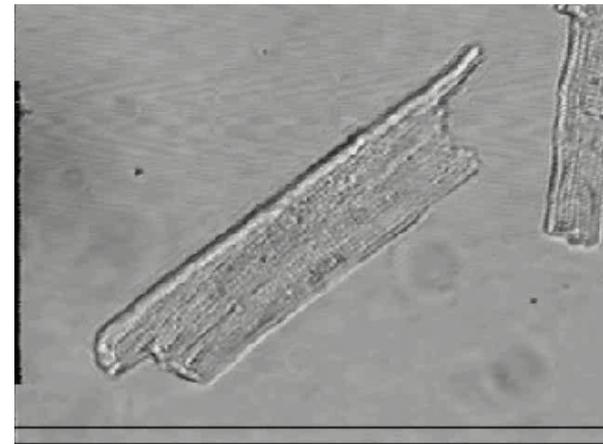
# Why is there a progressive deterioration in contraction of the failing heart? Can we stimulate the remaining muscle safely?



Myocyte (muscle cell)

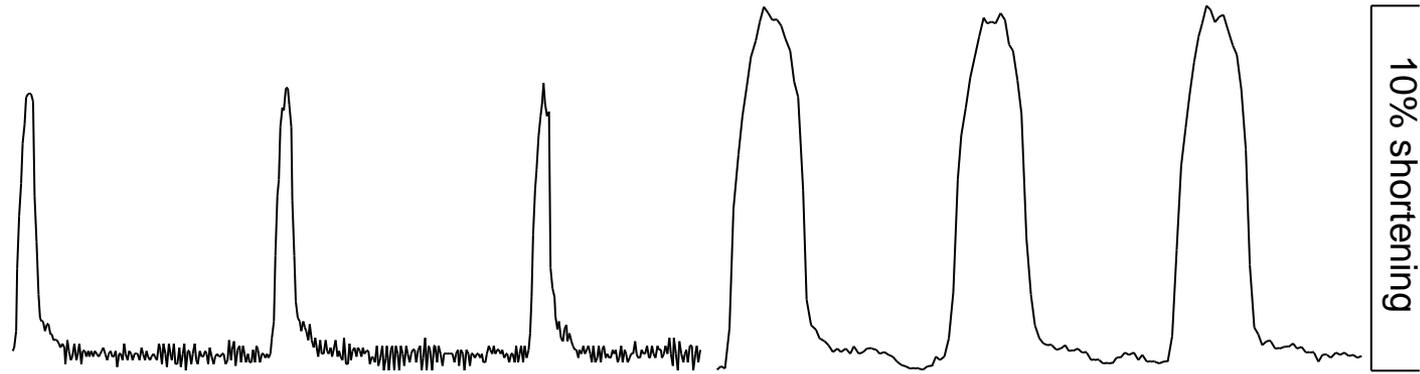
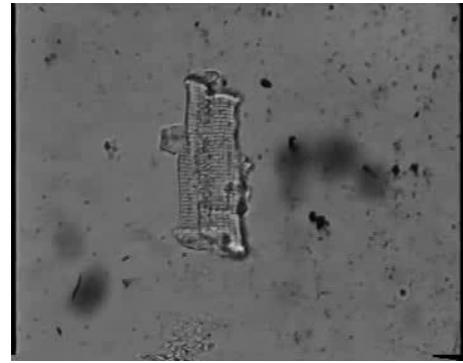


Normal myocyte



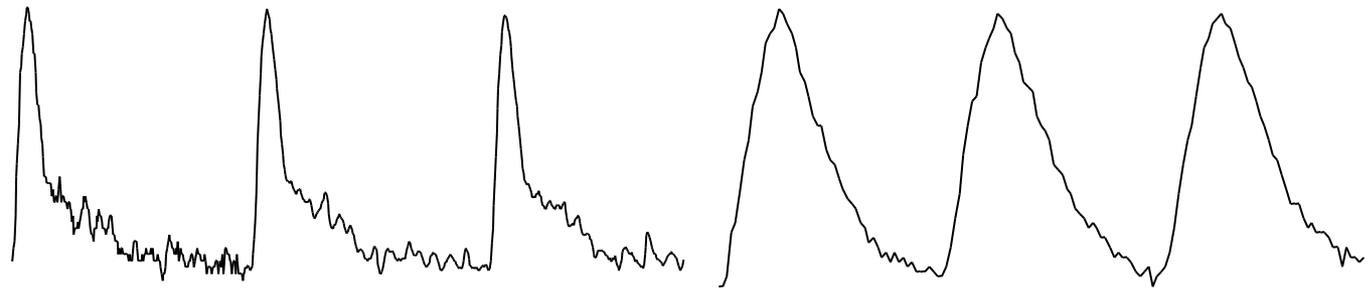
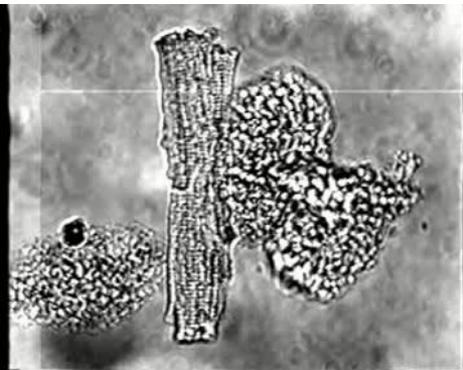
Dying myocyte

# Ventricular myocytes from failing and non-failing human heart



Non-failing, 0.2 Hz

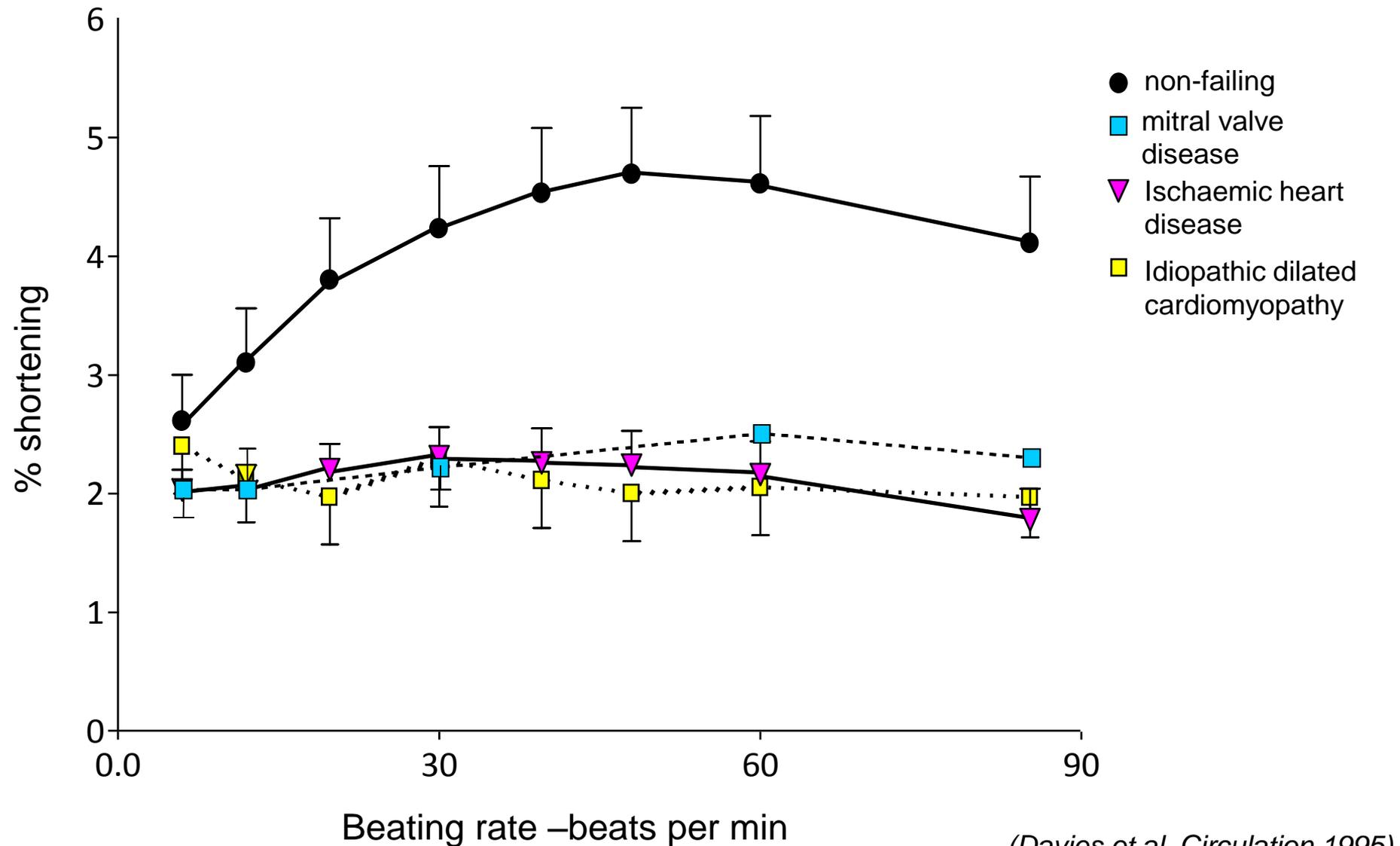
Non-failing, 1 Hz



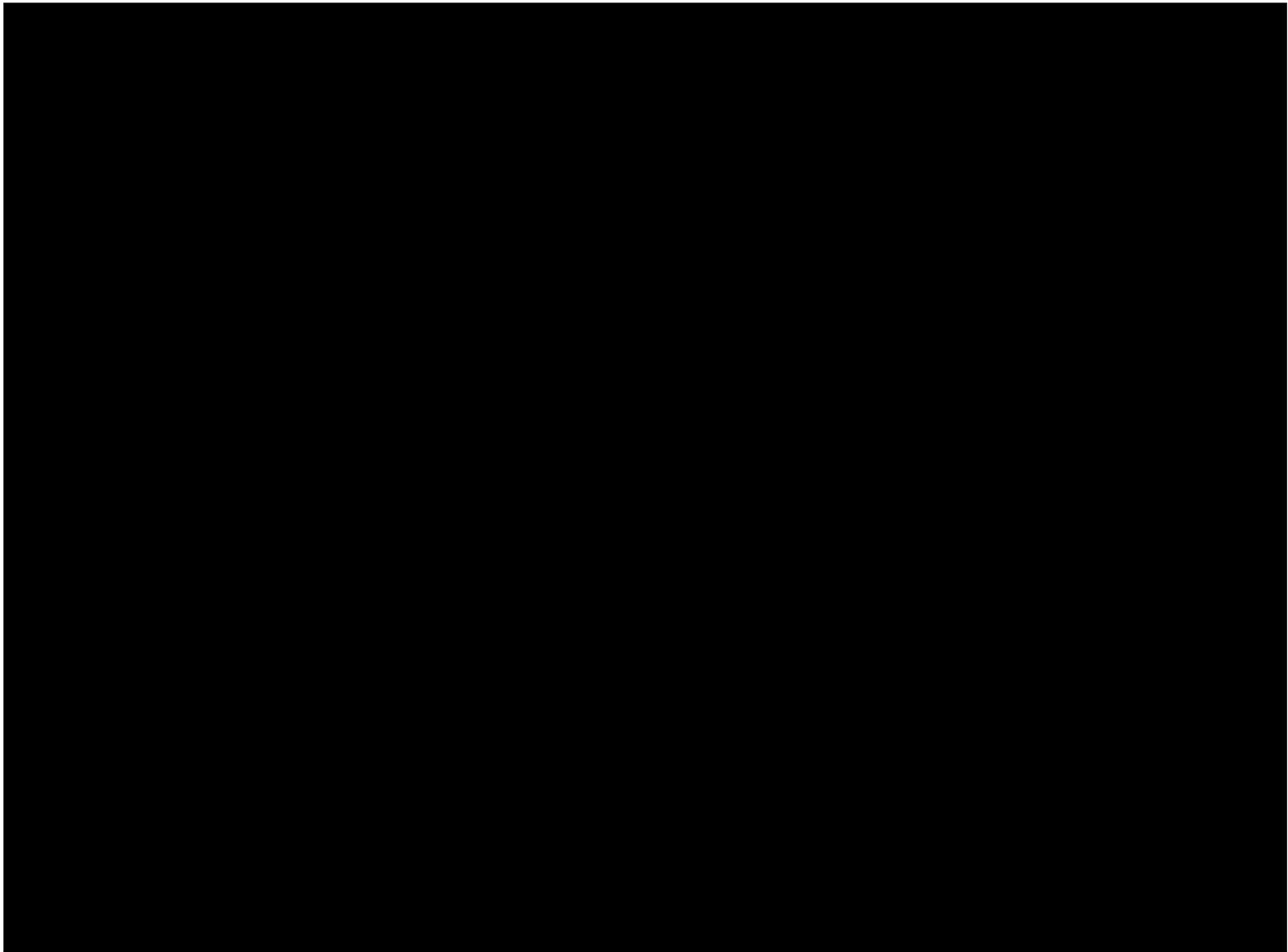
Failing, 0.2 Hz

Failing, 1 Hz

# Change in myocyte contraction is seen in all causes of heart failure – acquired defect

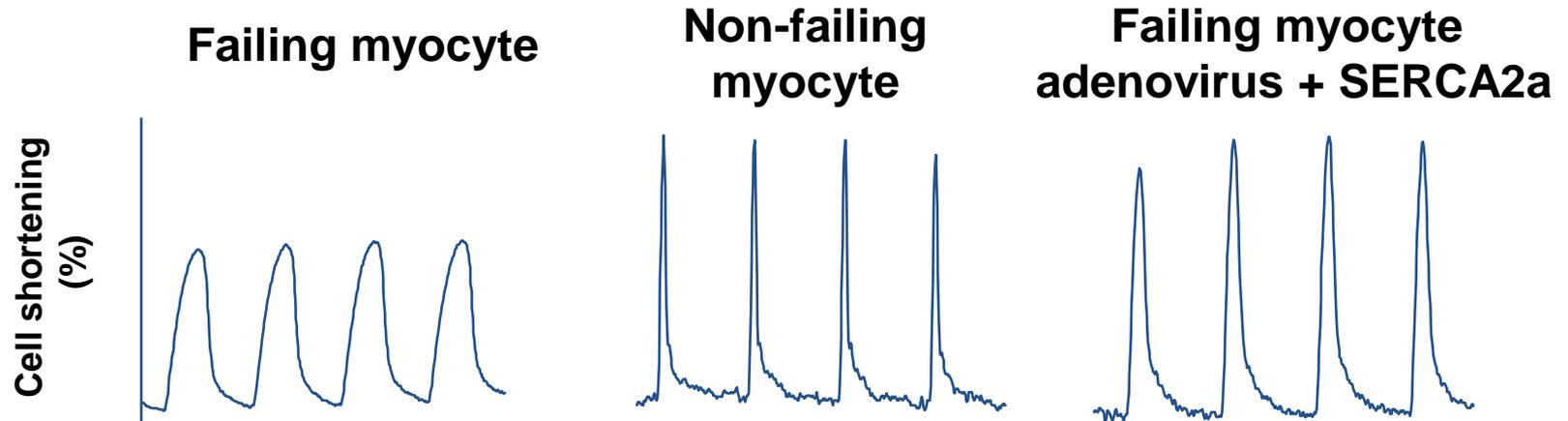


(Davies et al, Circulation 1995)



SERCA2a

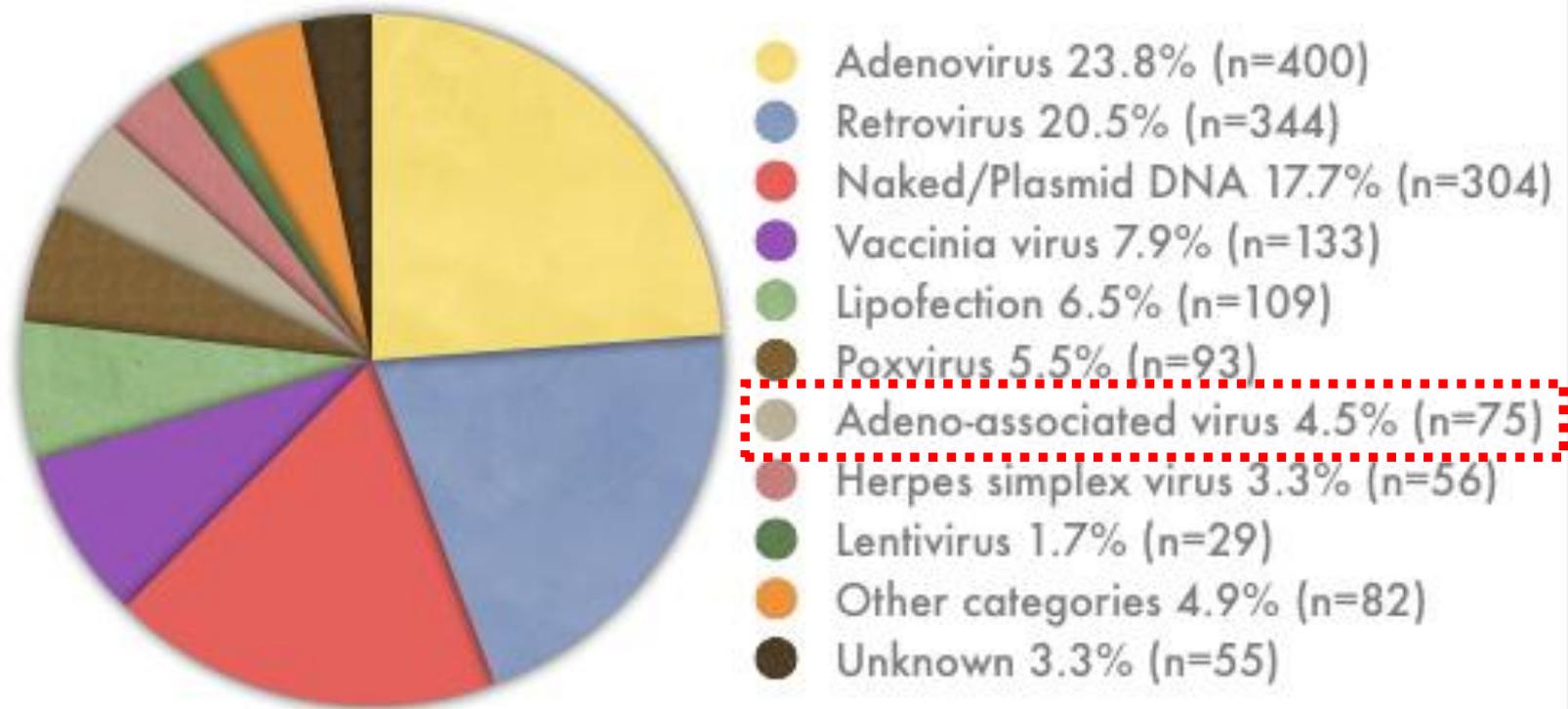
# Restoration of SERCA2a speeds contraction and relaxation in human myocytes



*It has not been possible to develop a drug to stimulate SERCA  
Strategy – use SERCA gene therapy to improve cardiac contraction*

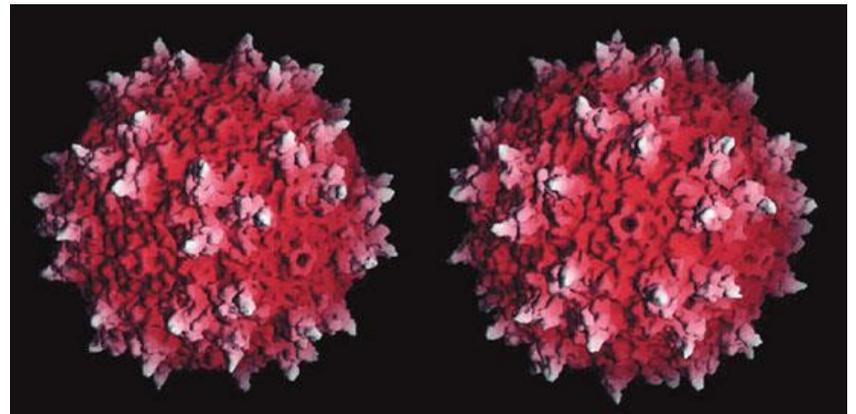
# Viral vectors in registered clinical gene therapy trials

Vectors Used in Gene Therapy Clinical 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

Months 6 12 18

Placebo

All patients through 18 months in long term follow up

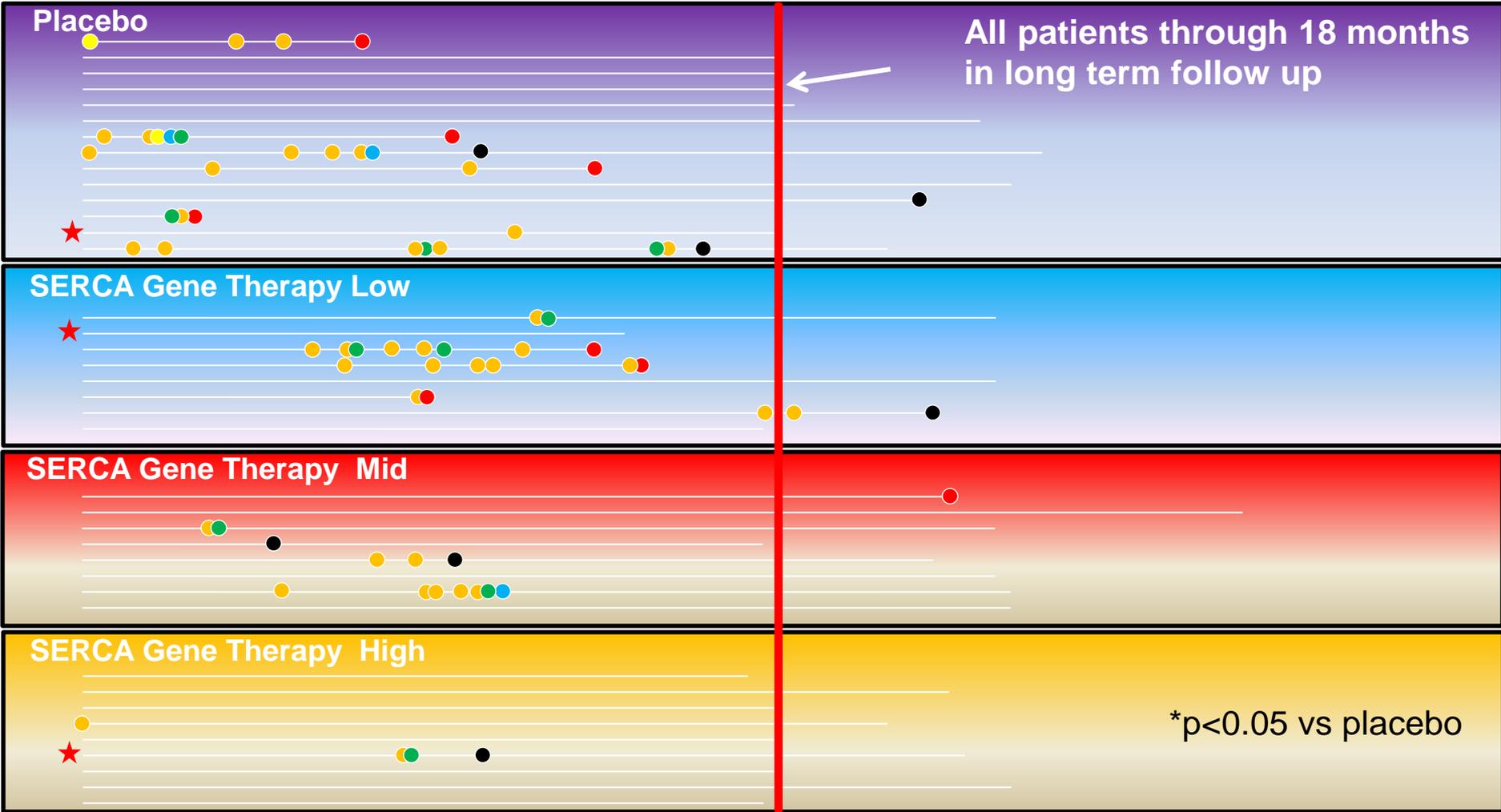
SERCA Gene Therapy Low

SERCA Gene Therapy Mid

SERCA Gene Therapy High

\*p<0.05 vs placebo

WHF ● MI ● LVAD ● Transplant ● Chronic Inotrope ● Death ● NAb+ ★



# SERCA2a gene therapy clinical trials

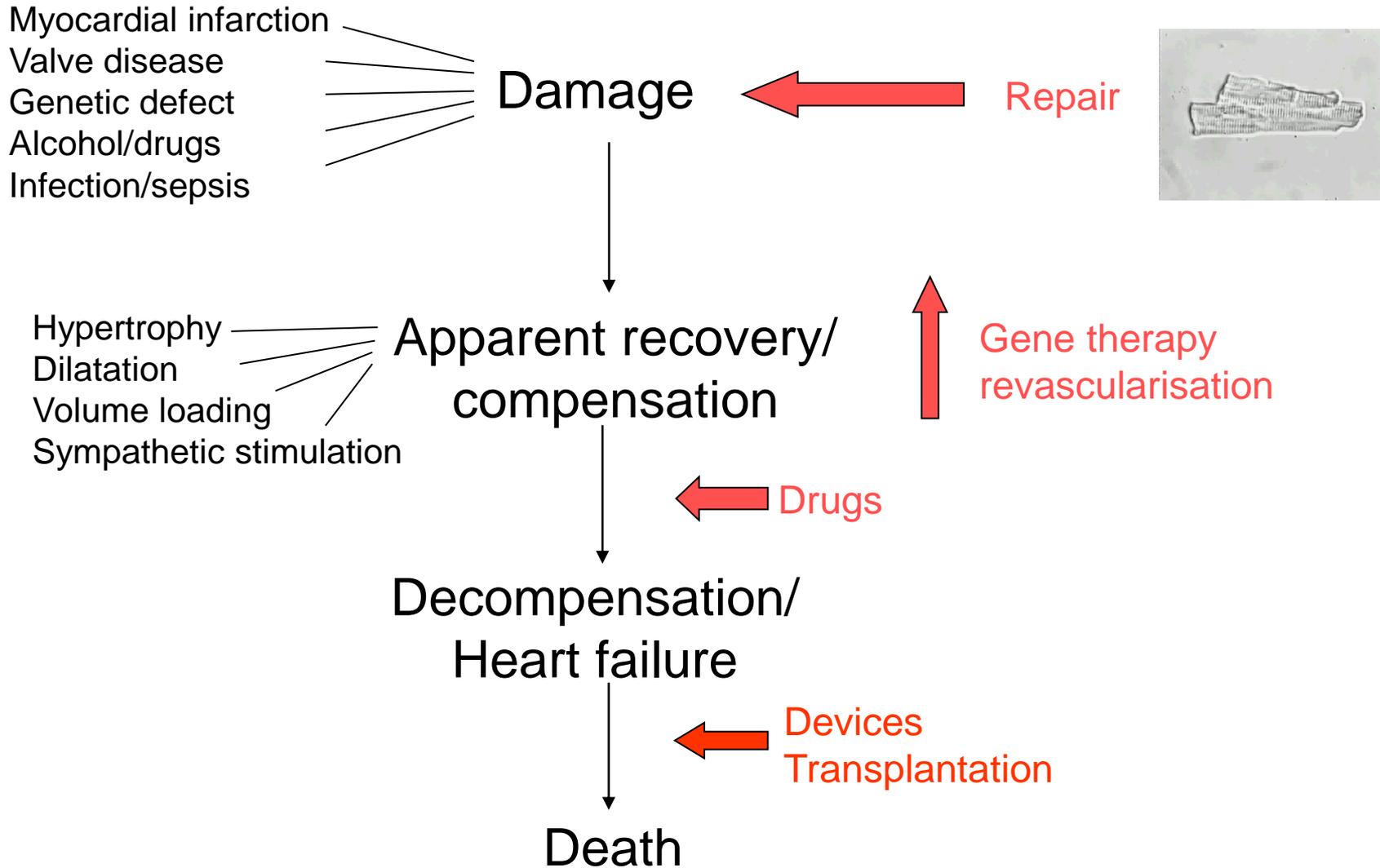
Patients with moderate to severe heart failure have one injection of adeno-associated virus with SERCA2a into blood vessels of the heart, with an overnight stay in hospital.

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

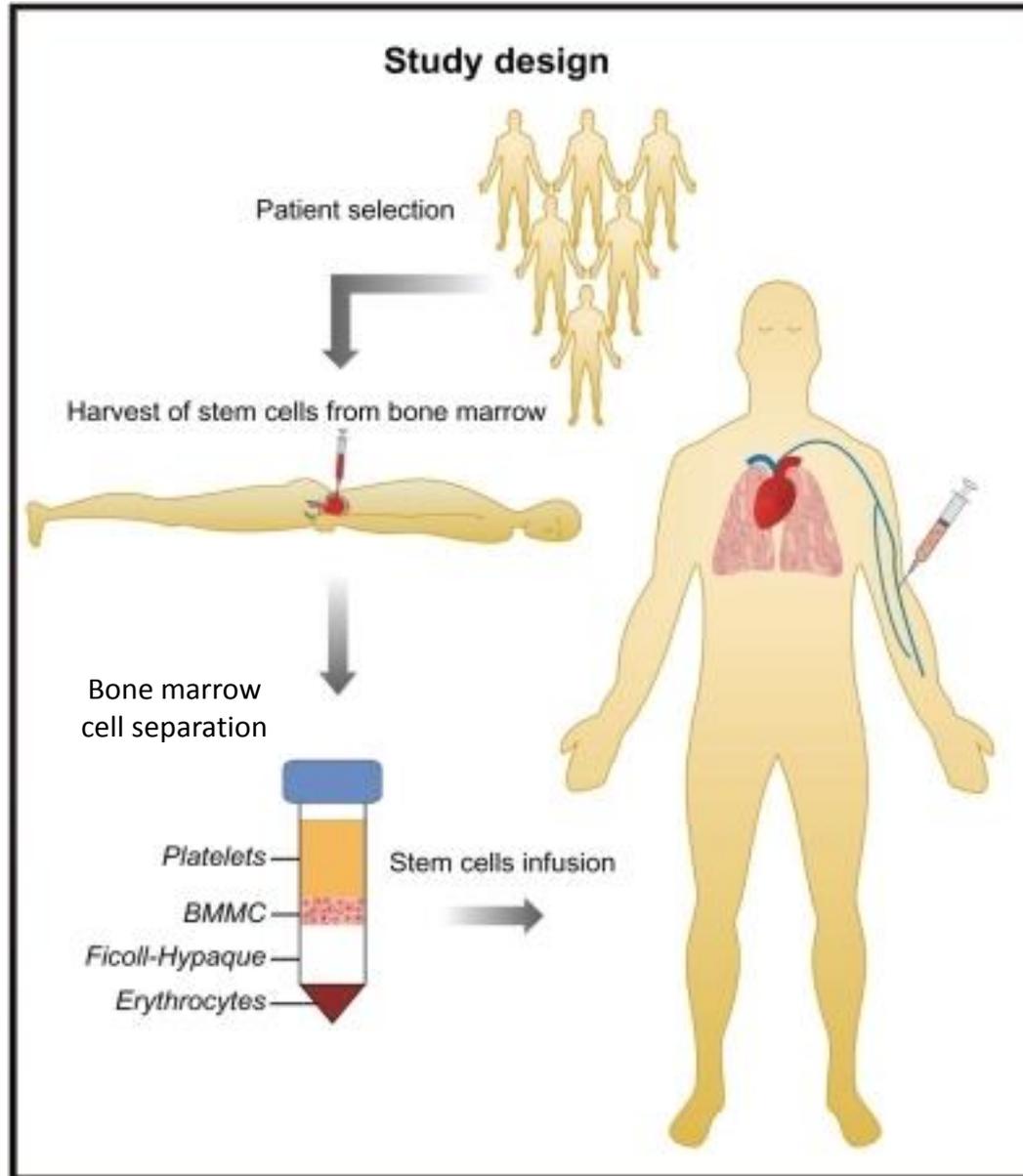
# Natural history of heart failure



# Which stem cells for cardiac repair?

		<b>Skeletal myoblasts</b>	<b>Bone marrow-derived stem cells</b>	<b>Tissue-derived MSCs</b>	<b>Endogenous cardiac progenitors</b>	<b>Embryonic stem cells</b>	<b>Induced pluripotent cells</b>
<b>Immune matching</b>							
<b>Forms true cardiomyocytes</b>							
<b>Large scale proliferation</b>							
<b>Clinical safety</b>							
<b>Ethically neutral</b>							

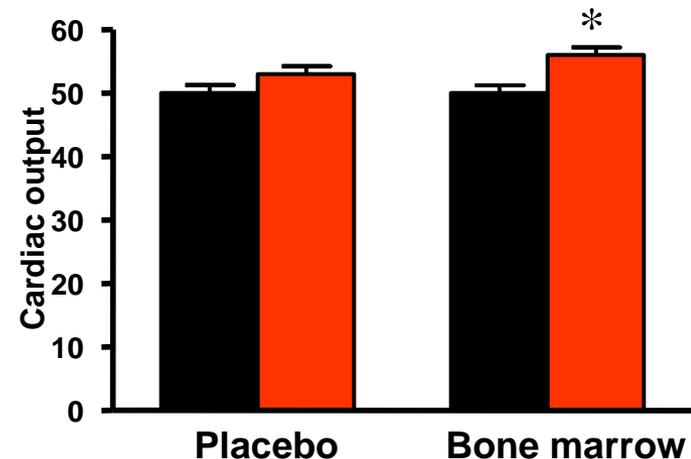
# Bone marrow cells implanted into heart



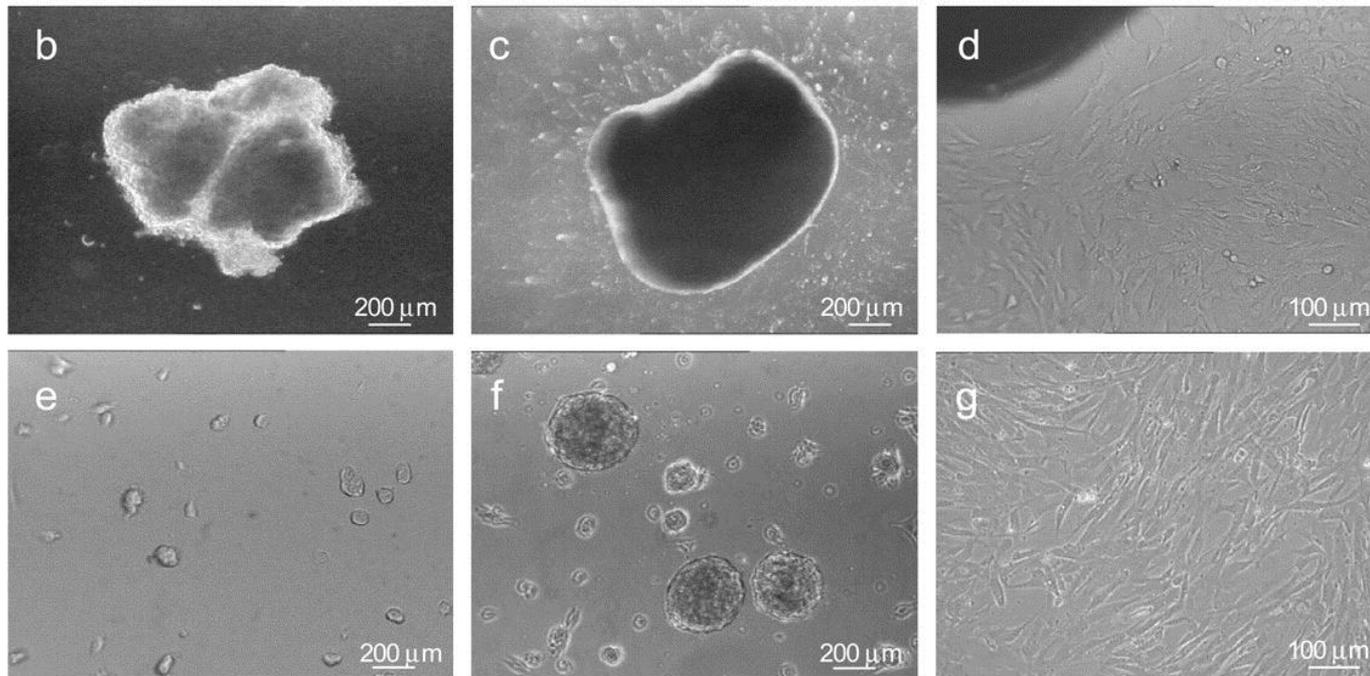
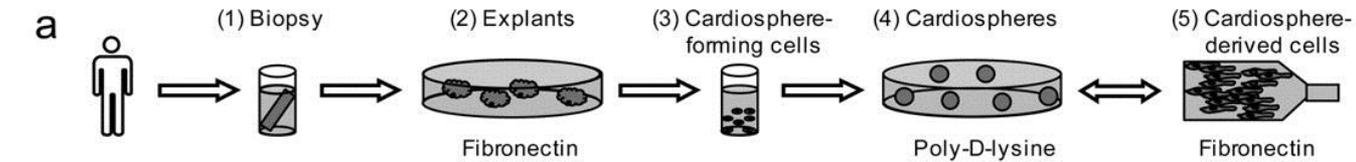
# Results of bone marrow stem cell implantation for heart disease

- 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



Smith, R. R. et al. *Circulation* 2007;115:896-908

# 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

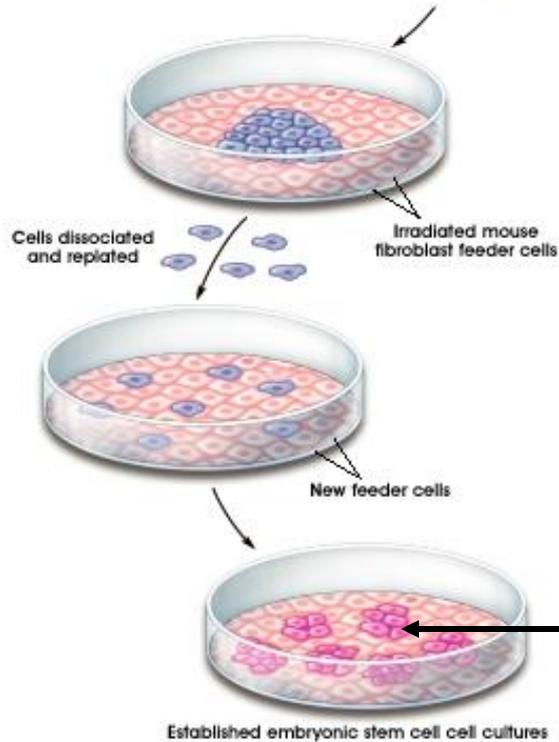
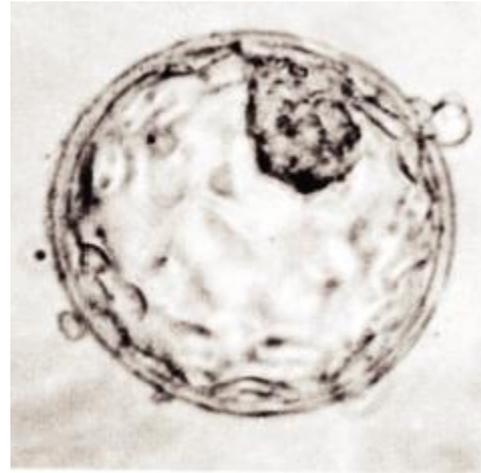
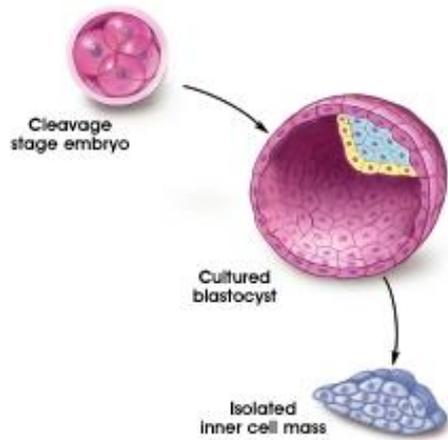
**Are heart patients there because their own stem cells haven't worked?**

*Vasa Circ Res 2001 89: e1 - e7*

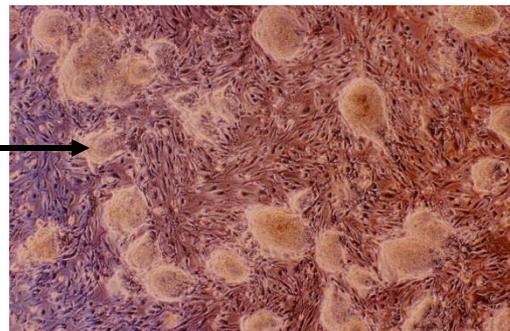
*Schmidt-Lucke C. Circulation. 2005 111:2981-7*

# Which stem cells for cardiac repair?

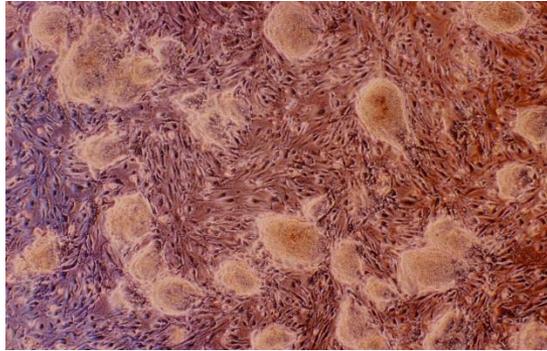
		Skeletal myoblasts	Bone marrow-derived stem cells	Tissue-derived MSCs	Endogenous cardiac progenitors	Embryonic stem cells	Induced pluripotent cells
Immune matching		Green	Green	Olive	Green	White	White
Forms true cardiomyocytes		Red	Red	Blue/Red	Blue/Red	White	White
Large scale proliferation		Green	Green	Green	Green	White	White
Clinical safety		Red	Green	Green	Green	White	White
Ethically neutral		Green	Green	Green	Green	White	White



# Embryonic stem cells *in vitro*

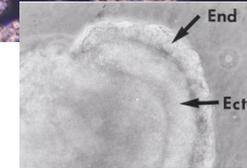
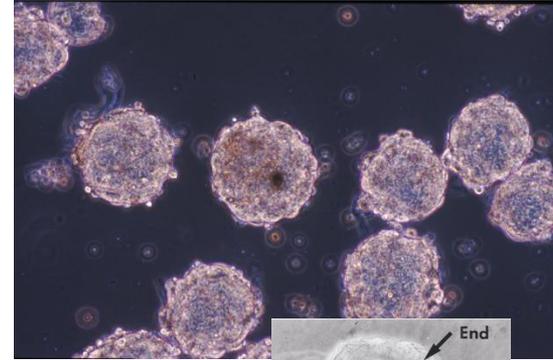


# Differentiation of embryonic stem cells



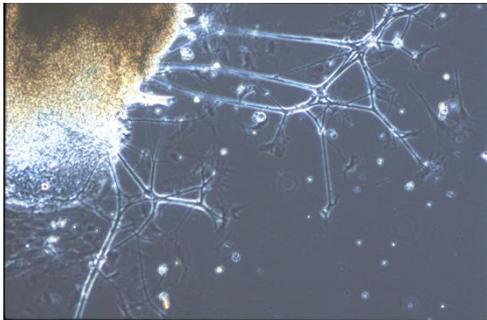
Undifferentiated ES cell colonies

-LIF/feeder fibroblasts

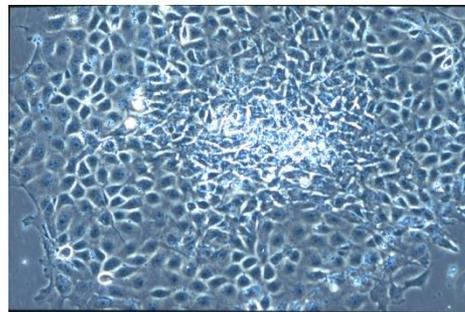


Embryoid bodies

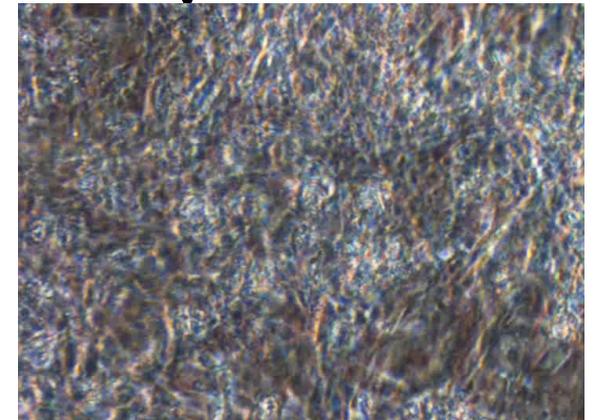
+ Growth factors



Neuronal



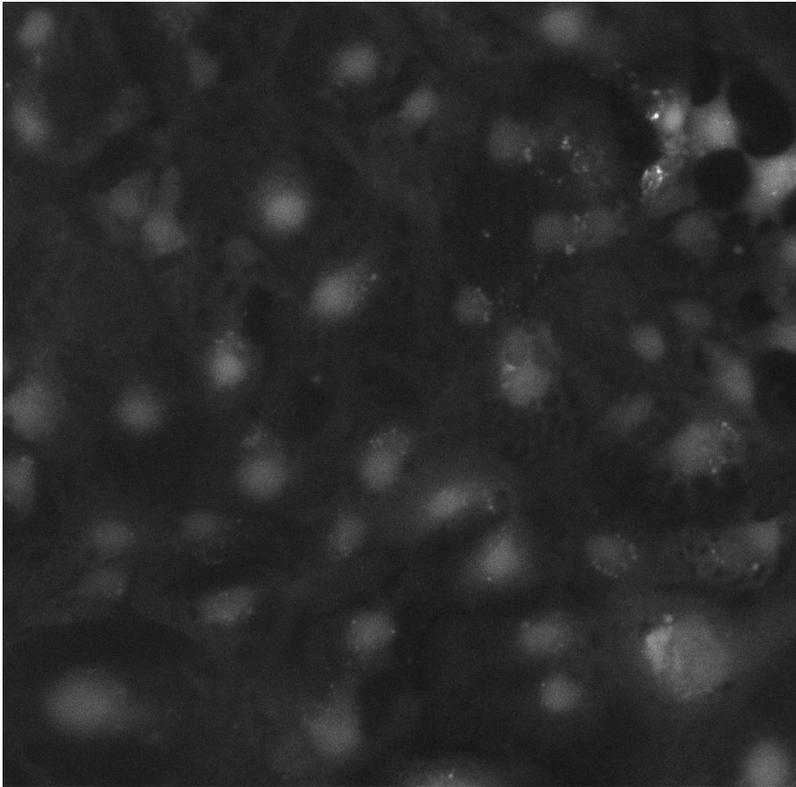
Epithelial



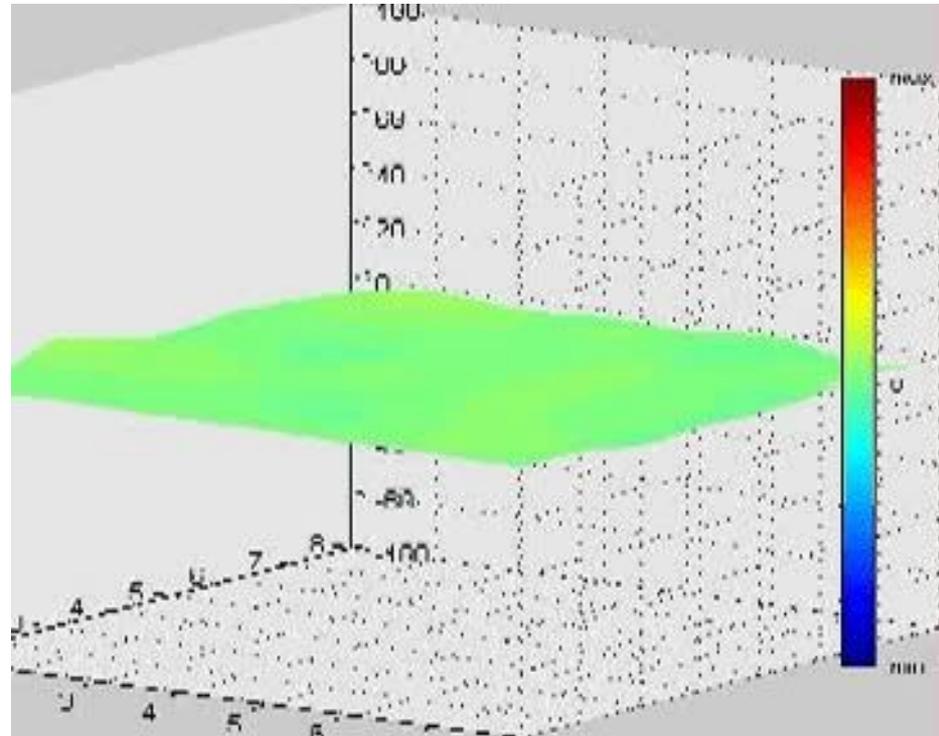
Cardiac



Calcium transient – optical mapping  
iPSC-CM



Membrane potential – multielectrode array  
hESC-CM cluster



# Which stem cells for cardiac repair?

		Skeletal myoblasts	Bone marrow-derived stem cells	Tissue-derived MSCs	Endogenous cardiac progenitors	Embryonic stem cells	Induced pluripotent cells
Immune matching		Green	Green	Olive	Green	Red	Green
Forms true cardiomyocytes		Red	Red	Blue/Red diagonal	Blue/Red diagonal	Green	Green
Large scale proliferation		Green	Green	Green	Green	Green	Green
Clinical safety		Red	Green	Green	Green	Blue/Red diagonal	Blue/Red diagonal
Ethically neutral		Green	Green	Green	Green	Red	Green



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

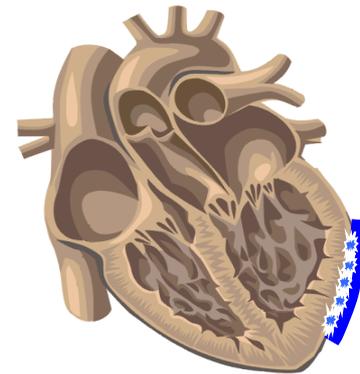
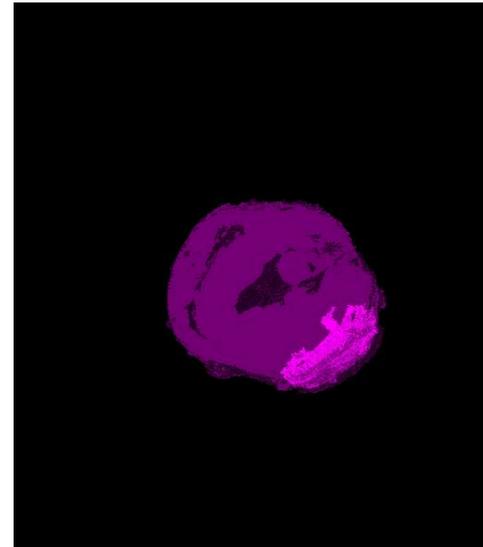
**16.01.2015 – COMMUNIQUÉ**

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.

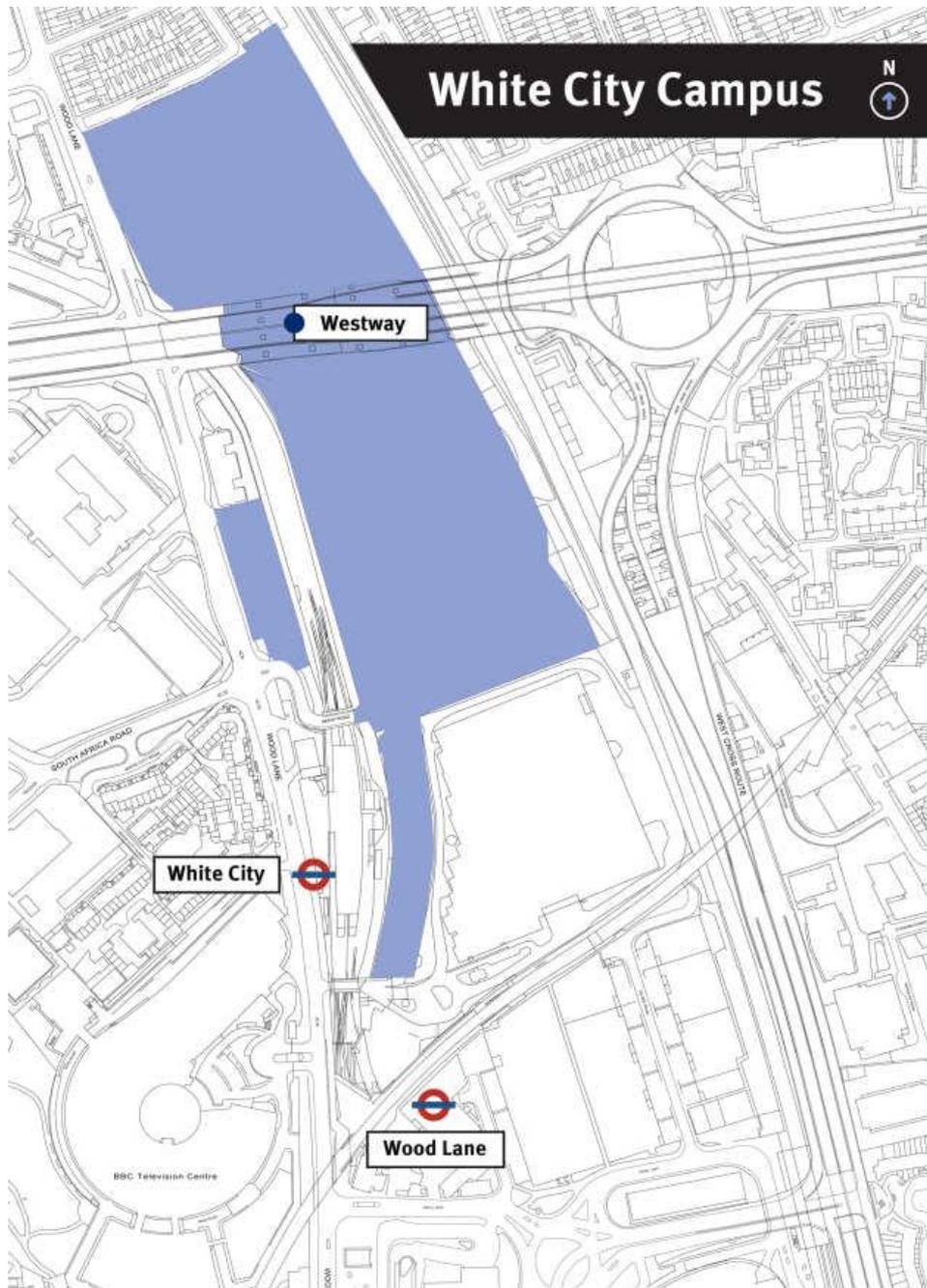
The surgery, coupled with a coronary bypass\*, was carried out on a woman of 68 years suffering from severe heart failure. Ten weeks after the intervention, the patient is feeling well, her condition has improved markedly, with no complications having been observed. This promising advance was presented 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*



Chen QZ, Bismarck A, Hansen U, Harding SE, Ali NN, Boccaccini AR. (2007)  
Characterisation of a soft elastomer poly(glycerol sebacate) mechanically designed  
to match myocardial tissue. Biomaterials, 2007



## 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

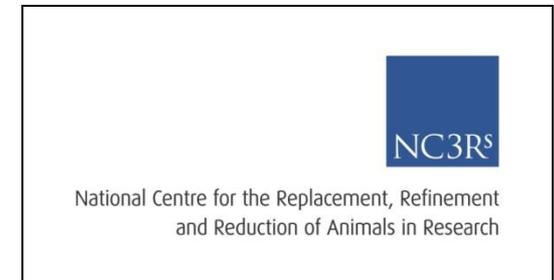
- Alex Lyon
- Nick Banner
- Andy Morley-Smith
- Gabor Foldes
- Nicola Hellen
- Nazanin Dolatshad
- Thusharika Kodagoda
- Maxime Mioulane
- Mirna Chahine
- Ljudmila Kolker (and UKSCB)
- Nadire Ali
- Cesare Terracciano
- Peter O’Gara

Roger Hajjar – Mt Sinai NY

Chris Denning – Univ. Nottingham

Stephan Amisten – KCL

Thomas Eschenhagen, UKE Hamburg



Any questions?

**Thank you**  
Chairman, Sir Richard Sykes