

Clinical Research Network

R&D – realising the vision

Professor Stephen Smye, Theme Director, NIHR CRN & R&I Director, Leeds Teaching Hospitals NHS Trust

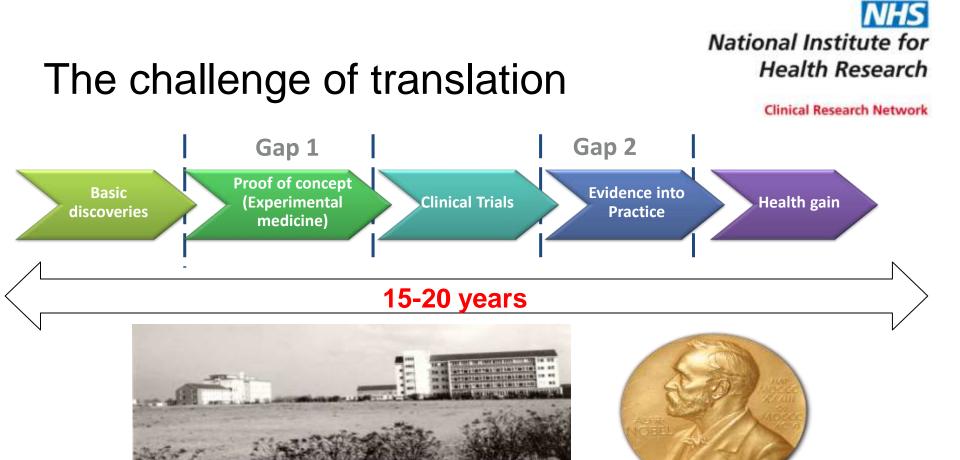


R&D

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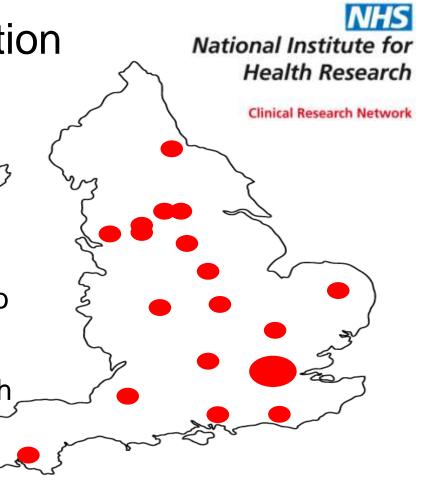


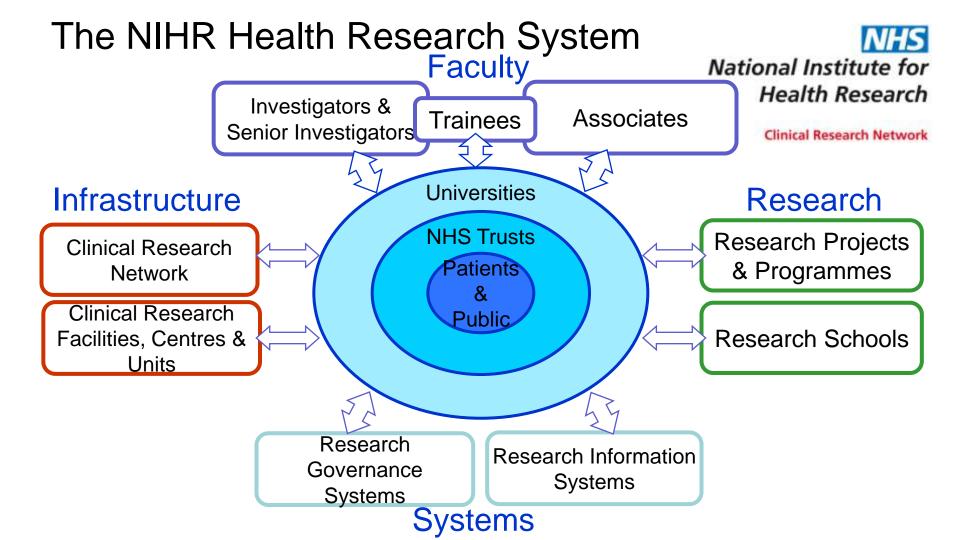




The challenge of participation

- Research mainly centred on acute teaching hospitals
- Culyer funding
- Academic medicine fragile
- "Discovery" science strong
- Loss of global market share
- Limited opportunity for patients to participate in clinical studies
- Funders lacked nationwide infrastructure to conduct research_









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Taking stock of achievements...

99%+ of Trusts engaged in Portfolio studies: including hardto-reach Trusts We recruited more than 630,000 patients in 2012/13 The number of studies achieving NHS Permission within 40 days has improved five-fold in 2 years

Global recognition

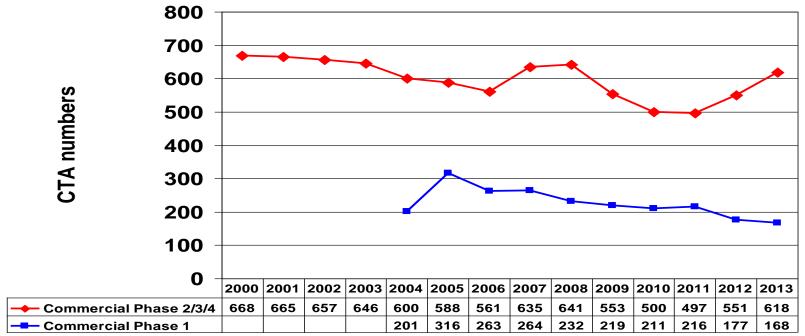
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The number of commercial contract studies rose to 685 in 2012/13 - ourhighest ever The number of commercial contract studies delivering to time and target doubled

UK Commercial applications received



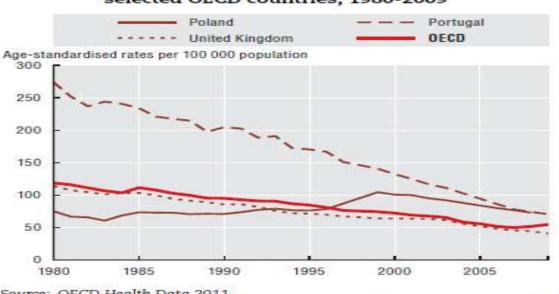




Improving outcomes



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1.3.4 Trends in stroke mortality rates, selected OECD countries, 1980-2009

> OECD (2011), Health at a Glance 2011: OECD Indicators, OECD Publishing. http://dx.doi.org/10 .1787/health_glan ce-2011-en

Source: OECD Health Data 2011.

StatLink and http://dx.doi.org/10.1787/888932523405

R&D

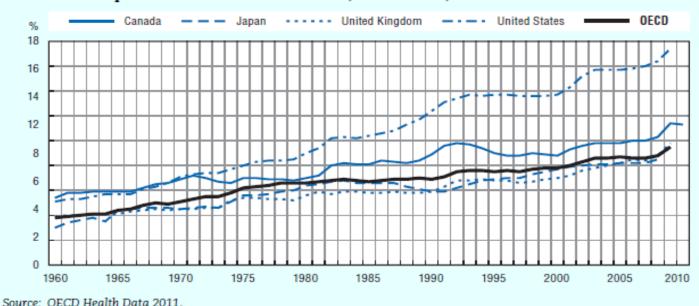




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Health challenges

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Health expenditure as a share of GDP, 1960-2009, selected OECD countries

StatLink and http://dx.doi.org/10.1787/888932523215

OECD (2011), Health at a Glance 2011: OECD Indicators, OECD Publishing. http://dx.doi.org/1 0.1787/health_gl ance-2011-en

Life expectancy – years gained since 1960 (2009)

Italy Spain Australia Israel Iceland Sweden France Norway New Zealand Canada Luxembourg Netherlands Austria United Kingdom Germany Greece Korea Belgium Finland Ireland Portugal OECD Denmark Slovenia Chile United States Czech Republic Poland Mexico Estonia Slovak Republic Hungary Turkey

Japan

Switzerland

Years gained, 1960-2009

			15.2		
		10.9			
-	-	12.0			
		12.0			
_		10.7			
_		9.9			
-	8				
-	8.				
-		10.7			
-	7.2				
-		9.7			
-		9.4			
-		11.3			
-	7.1	- 11.5			
-		11.7			
-		9.6			
-		11.2			
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-		10.4			27.9
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-		10.0			
-		10.0	15.6		
-		11.2	13.0		
-	6.6				
-	0.0	10.5			
-		10.5		21.4	
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-	6.7	P			
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)	5 1	0 1	5 2	20 2	25 3

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OECD (2011), Health at a Glance 2011: OECD Indicators, OECD Publishing. http://dx.doi.org/10.1787/h ealth_glance-2011-en

Limitations in daily activities, population aged 75 and over, 2009

		Limited to se	ome extent		Limited s	trongly	
Sweden	16.9	17.1					
Norway	19:1	14.0					
Denmark	28.5		16.0				
Iceland	8.6	24.2					
United Kingdom	23.0		23.9				
Switzerland	32.2		13.2				
Ireland	34.8		18.2				
Luxembourg	33.9		15.1				
Belgium	34.3		20.0	1			
Netherlands	41.9			14.9			
Czech Republic	40.4			22.1			
Slovenia	26.5		29.2				
France	33.8			32.2			
Finland	39.2			27.6			
OECD	34.0		26	.1			
Austria	34.0		and the second second	33.6			
Spain	42.6			21.6			
Poland	37.0			29.2			
Italy	44.1			29.	8		
Greece	35.5			39	.0		
Germany	44.5			30	0.8		
Hungary	42.3			3	3.2		
Estonia	46.6				32.5		
Portugal	38.9				37.9		
Slovak Republic	37.7			_	49.9		
	0	20	40	6	0	80	
			% 0	f populatio	in aged 75	years and o	over

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OECD (2011), Health at a Glance 2011: OECD Indicators, OECD Publishing. http://dx.doi.org/10.1787/health_ glance-2011-en



Alistair Burns, National Clinical

overview of dementia research

Focus on Dementia

Message from the CMO



This site provides a snapshot of the work of the National Institute for Health Research is doing in the area of dementia. Dame Sally Davies, Chief Medical Officer. introduces this new resource. Read more >>

About dementia



Dementia is a common condition that affects about 800,000 people in the UK. It is estimated that by 2021, this number will have increased to around 1 million. Read more >>



About dementia research

NIHR in action



Hear from some of our researchers

today.

Read more >>

Dementia research case studies



Living with dementia



Ken Clasper (left) is living with dementia and actively involved in dementia research. Ken and his wife and carer Janice explain how dementia affects their daily life and how research has helped them to cope. Read more >>

Getting involved



We encourage members of the public to become actively involved in clinical research, forming a partnership with researchers to improve the relevance and design of studies. Read more >>



Research and Growth: Strategy for UK Life Sciences



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"Life science - and the UK's role in it - is at a crossroads.

Behind us lies a great history of discovery, from the unravelling of DNA to MRI scanning and genetic sequencing.

We can be proud of our past, but this government is acutely aware that we cannot be complacent about the future." *David Cameron, December 2011*

R&D



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It is not in the stars to hold our destiny but in ourselves



• Science

• Industry

• Patients









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• Science

• Industry

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- NHS



Science

Industry

• Patients

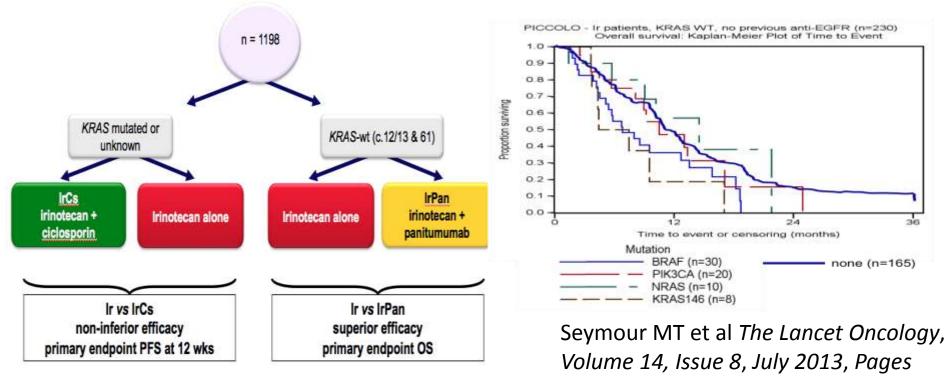


• 100,000 whole genomes by 2017

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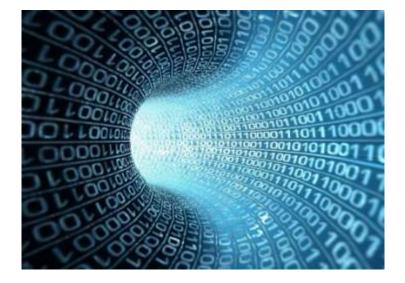
Advanced disease – Piccolo multiple mutation testing



749-759



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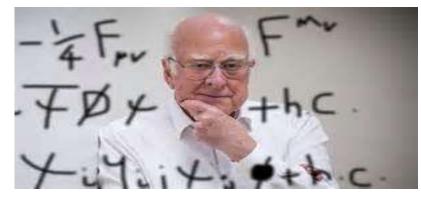
"When you can measure what you are speaking about, and express it in numbers, you know something about it, when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind; it may be the beginning of knowledge, but you have scarcely, in your thoughts, advanced to the stage of science."

William Thomson, 1st Baron Kelvin



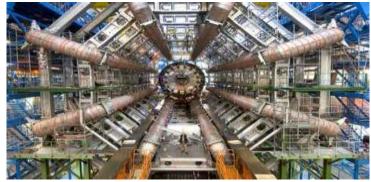
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http://www.crick.ac.uk/

AN ATLAS OF EXPRESSION

The first draft of the complete human proteome has been more than a decade in the making in the process, the effort has also delivered kosons about technology and hiology.



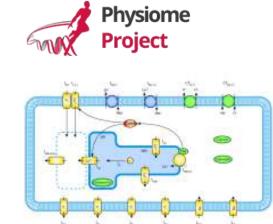
29 MAY 2014 | VOL 509 | NATURE | 649

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http://www.cambridgecancer.org.uk/

http://physiomeproject.org/

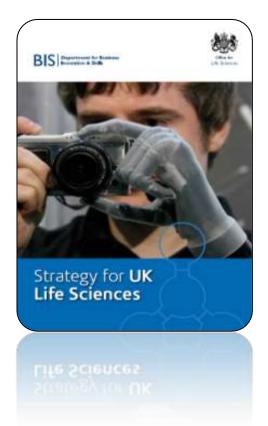
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UK Life Sciences Industry



- 4,500 firms, 165,000 staff, R&D spend £5bn - 8% of UK total manufacturing.
- > 300 pharmaceutical companies,78,000 people, turnover £31bn pa.
- Medical technology and medical biotechnology sectors employ 87,000 people, turnover £18.4bn pa.
- third biggest "industry" in the UK







Data collected outside the controlled constraints of

conventional clinical trials to evaluate what is happening in

normal clinical practice.



Bringing medicines to *life*

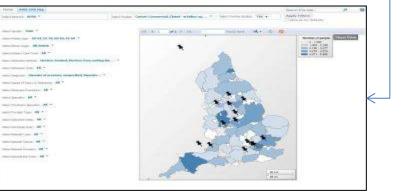




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BIG data





Shaping the future..... Salford Lung Study



- First major pre-licence pragmatic real-world effectiveness study
- GSK selected NHS total population coverage, e records in primary care and GP prescribing, full hospital EPR & integrated e-records with primary care)
- COPD and asthma studies both on-track (COPD c2000 patients out of target of 2800

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Health Research

- 70 separate pharmacies engaged in the project & > 60 GP practices
- Study expanded outside Salford to help speed recruitment which includes getting data from a different CCG area and a different hospital site - technology is capable of scaling across the NHS
- > 150 jobs created
- unique electronic near-real-time safety monitoring system and e systems also record all health-related events linked to the study outcomes - the number of study visits is kept to a minimum (2)
 Prof M Gibson



Novel Disease Indications for Science AstraZeneca Clinical Compounds

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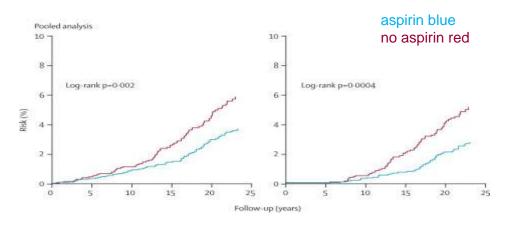
- AWARD: \$15,000 USD | DEADLINE: 5/31/14 | ACTIVE SOLVERS: 638 | POSTED: 3/24/14
- Industry
 SOLVERS: 638 | POSTED: 3/24/14 AstraZeneca is seeking novel clinical indications for a select set of compounds previously in clinical development. These "patient-ready" compounds, with evidence of human target coverage and manageable tolerability, are available for novel clinical indications- preferably in diseases with significant unmet medical need.
- NHS Source: InnoCentive

https://www.innocentive.com/ar/challenge/9933012?cc=Nature9933012&utm_source=nature&utm_medium=pa vilion&utm_campaign=challenges

Aspirin



- Observational and RCT evidence that aspirin
 - prevents colorectal adenoma and CRC
 - alters natural history of established CRC (inhibition of metastasis)
- Uncertainty about
 - Mechanism(s)
 - Optimum dose ('low' 75 mg vs 'high' 300 mg) for chemoprevention versus adverse events (GI bleeding and haemorrhagic stroke)
 - Appropriate target population (age, family history)



10-14 yrs after randomisation HR 0.26 (0.12-0.56) if aspirin \geq 5 yrs

Lancet 2007;**369**:1603



The seAFOod (Systematic Evaluation of Aspirin and Fish Oil) polyp prevention trial



Double-blind randomised placebocontrolled trial

2 x 2 factorial design; EPA free fatty acid (FFA) entericcoated 2 g daily aspirin EC 300 mg daily

CI Professor Mark Hull *Trials* 2013;**14**:237

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'... it is quite hard to find out about research - there aren't the notices in surgeries and very few in hospitals. It is only if the clinician or GP is directly involved or has been asked to find volunteers that the information is given..' - Patient



Public appetite, patient demand

- 82 per cent of people believe it is important for the NHS to offer opportunities to take part in healthcare research.
- Less than 7% said they would never take part in a clinical research study.
 NIHR Clinical Research Networks Survey May 2012
- 69% of women with ovarian cancer say they would travel to another hospital to be on a trial *Target Ovarian Cancer, Pathfinder Study Report 2013*
- Over 70% of patients look for information about clinical trials ecancer 5 235 2011 'Information needs of cancer patients'

What we do already



Mystery shopper



UK Clinical Trials Gateway www.ukctg.nihr.ac.uk National Institute for Health Research

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International Clinical Trials Day 20th May

This marks the day in which James Lind began his study on scurvy.



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Shaping the future...

Science

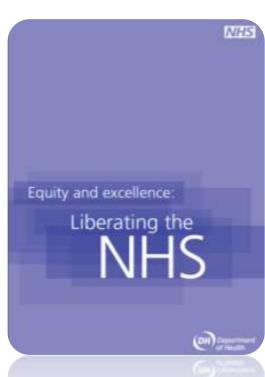
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• Patients

• NHS







Shaping the future.....

• Science

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Shaping the future.....



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Science

Objective

To assess the impact of electronic health record (EHR) implementation on primary care diabetes care.

Principal Findings

- Industry patients exposed to the EHR were significantly more likely to receive "optimal care" when compared with unexposed patients (p < .001), with an estimated difference of 9.20 percent (95% CI: 6.08, 12.33) in the final year between exposed patients and patients never exposed.
- Patients Conclusion

Implementation of a commercially available EHR in primary care practice may improve diabetes care and clinical outcomes.

Herrin, J., da Graca, B., Nicewander, D., Fullerton, C., Aponte, P., Stanek, G., Cowling, T., Collinsworth, A., Fleming, N. S. and Ballard, D. J. (2012), The Effectiveness of Implementing an Electronic Health Record on Diabetes Care and Outcomes. Health Services Research, 47: 1522– 1540.

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Comparative Effectiveness of Revascularization Strategies

William S. Wainthuah, M.D., Maria V. Grau-Sepulawda, M.D., M.P.H., Josehn M. Weitz, Ph.D., M.P.H., Soan M. O'Beien, Ph.D., Eric D. Peterson, M.D., M.P.H., Paul Kohn, Ph.D., Zugui Zhang, Ph.D., Lloyd W. Blain, M.D., Rickard E. Shawi, Ph.D., Charles McKay, M.D., Laura L. Riczenfisker, M.B.A., Jeffrey J. Popma, M.D., John C. Metsengey, M.D., Onvid M. Shahian, M.D., Frederick L. Girover, M.D., John E. Mayer, M.D., Cymbia M. Shawom, Ph.D., Kirk H. Garrutt, M.D., Issam D. Moussa, M.D., George D. Dangiat, M.D., and Froid H. Edwards, M.D.

ABSTRACT

• Patients

Ouestions per

Questions persist concerning the comparative effectiveness of percutaneous coronary intervention (PCI) and coronary-array bypass grafting (CABG), the American College of Cardiology Foundation (ACCF) and the Society of Thoracic Surgeons (STS) collaborated to compare the rates of long-term survival after PCI and CABG.

METHODS

We linked the ACCI National Cardiovascular Data Registry and the STS Adult Cardiac Surgery Database to claims data from the Centura for Medicare and Medicaid Services for the years 2004 through 2008. Outcomes were compared with the use of propensity scores and Inverse-probability-weighting adjustment to reduce treatment-

From the Christians Cure Hauth System. Neurals, DJ, WS SW, HL, Z.S.: Dube Classical Betweeth Initiatis, Buchars, NC (MAVG 4, S. MO, C. E.D.R.), Une American Catage of Candidragy, Washington, DC (MAW, L.L.R.), Advocume Mission Materials (MAW, C.L.R.), Advocume Mission Materials (MAW, C.L.R.), Advocume Mission Materials (Chrough, Catherina Backfin Material Materials (Chrough, Catherina Backfin Material Materials San, Francisco (BLS)), Harbor-USCA Medical Center, Turasco, C. (S. M.), Biel Manacharother, Turasco, C. (S. M.), Steh Manacharother, General Hospital (DM SJ), Al-

• NHS

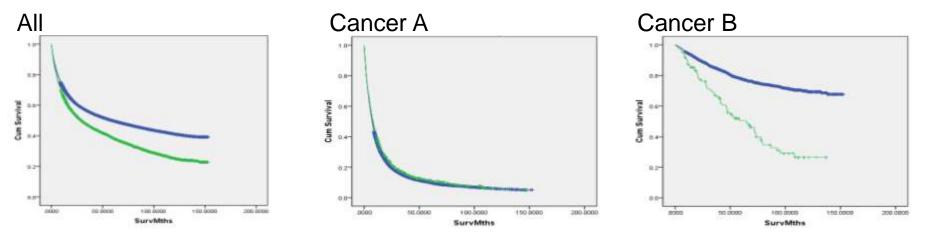
"We linked the ACCF National Cardiovascular Data registry & the STS Adult Cardiac Surgery database to claims data from the Centers for Medicare and Medicaid Services for the year 2004-2008..."

Analysis of linked data

- University of Leeds and Leeds Teaching Hospitals with N&Y Cancer Registry and Information Service and NHS IC - Cancer registration and HES data
- Impact of co-morbidity at diagnosis on
 - Overall survival and recurrence-free survival



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Courtesy of G Hall, University of Leeds

Shaping the future...



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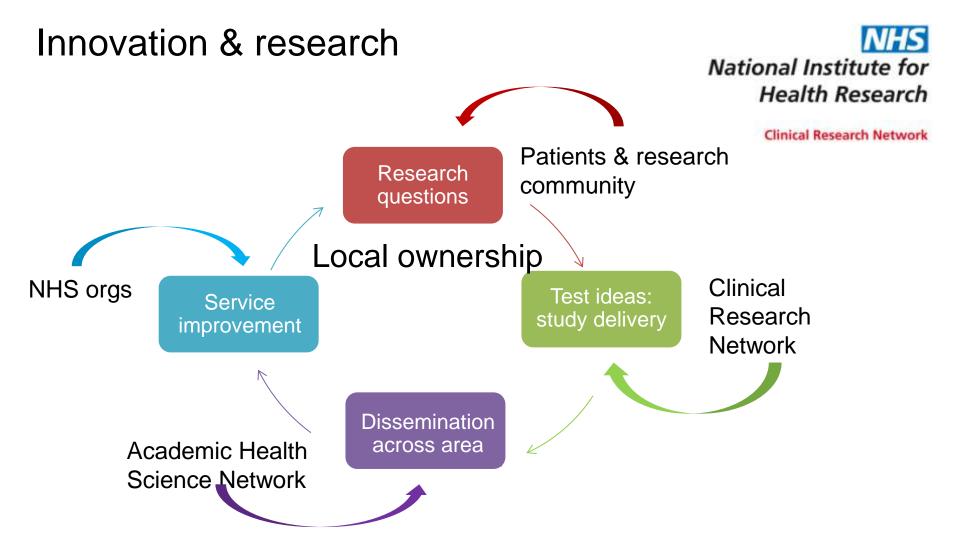
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R&D management





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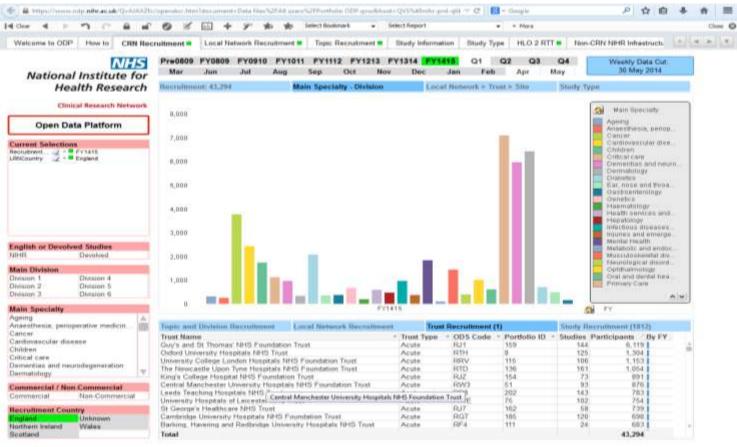
R&D management

service

• patient-facing

 known for leading-edge use of data in the NHS

R&D management – data informed



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R&D management



- use of information to integrate services
- access and support to use information
 - Including access to people's own health and care records
- Empower service users
- Improve efficiency of research





NHS R&D management – efficient research National Institute for Health Research twork Questions relevant Unbiased Appropriate Accessible to clinicians & design and and usable full patients? methods? publication? report? >30% of trial >50% of studies Low priority questions >50% of studies interventions not well never published in designed without described full Important outcomes reference to SRs of

Clinicians and patients not involved in setting

>50% of study **Biased under**not assessed evidence outcomes not reporting of reported studies with > 50% of studies Most research not disappointing insufficiently interpreted with research agendas results reduce biases reference to other relevant evidence **Research waste**

Avoidable waste in the production and reporting of research evidence, lain Chalmers, Paul Glasziou Lancet 2009; 374: 86–89

R&D management



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 secondments to industry, academia & clinic

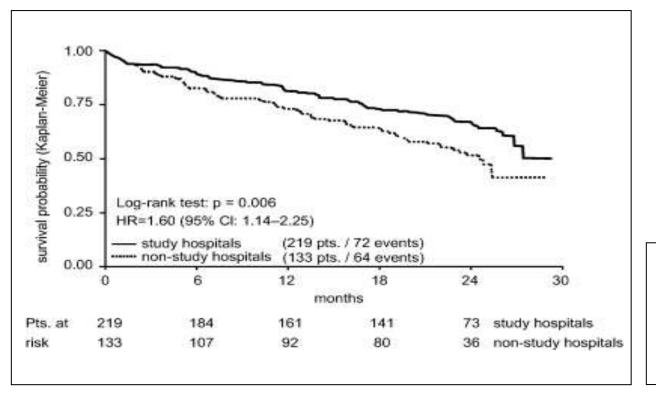
 element in general manager training Research to improve the quality, accessibility and organisation of health services

Health Services and Delivery Research (HS&DR) Programme

managers and researchers

http://www.nets.nihr.ac.uk/programmes/hsdr

R&D management





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Pattern of care and impact of participation in clinical studies on the outcome in ovarian cancer Du Bois et al, *Int J Gynecol Cancer 2005*, *15*, *183*.

R&D management – system pilots

INVENTION	EVALUATIO	ADOPTION	DIFFUSION
Creation	Assessment	Uptake	Spread
 new things 	 new things 	 new things 	 new things
 new ideas 	 new ideas 	 new ideas 	 new ideas
 new techniques 	new techniques	 new techniques 	 new techniques
 new approaches 	 new approaches 	 new approaches 	new approaches
Basic Research	Applied Research	Commissioning	Patient Care
MRC & Charities	NIHR	NHS Commissioners	Providers of NHS services
AHSC • Better Quality • Better Value AHSN			

R&D management – a community of practice



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networked and networking



"Building research active communities Our Stroke Research Network has shown how long-term focus on involvement and engagement can lead to better participation, having grown the research participation rate in the stroke population from 1% to nearly 10%. The Mental Health Research network has similarly shown how patients and researchers working together can lead to more effective recruitment strategies meaning that studies are four times more likely to recruit to time and to target."

http://www.nihr.ac.uk/files/pdfs/Promoting%20A%20Research%20Active %20Nation_NIHR%20Strategic%20Plan_May%202014.pdf

Research

- for all
- informed by data
- focused on patient outcomes
- delivering economic benefit
- managed





R&D

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Research – the way we provide best care