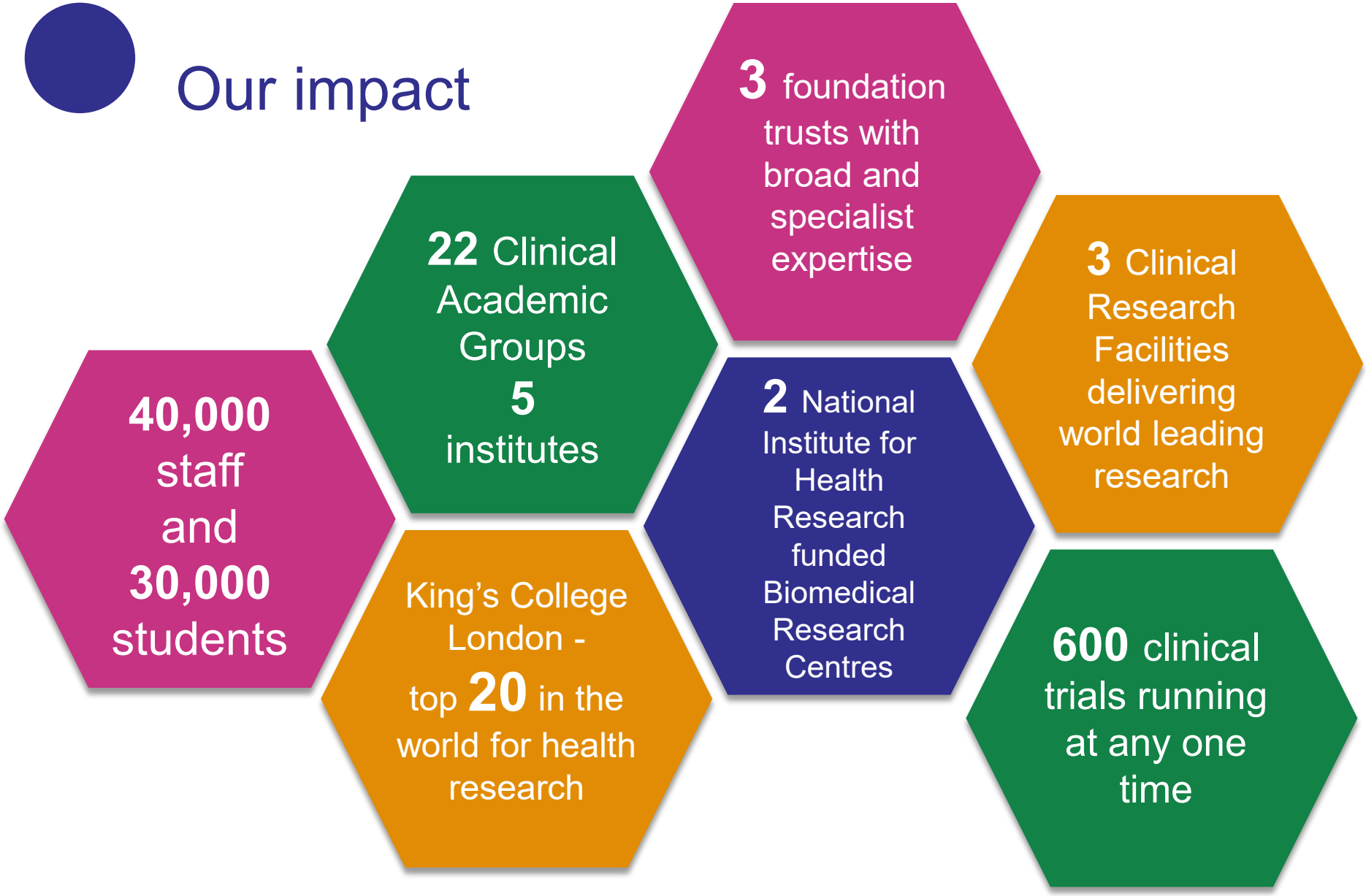
King's Health Partners at 10

Prof Sir Robert Lechler

2019 King's Health Partners annual conference

Our impact


3 foundation trusts with broad and specialist expertise
22 Clinical Academic Groups 5 institutes
3 Clinical Research Facilities delivering world leading research
40,000 staff and 30,000 students
2 National Institute for Health Research funded Biomedical Research Centres
King's College London - top 20 in the world for health research
600 clinical trials running at any one time

Our impact

1st in world mental health research at IoPPN

65,000 patients screened for signs of anxiety or depression alongside their physical health needs

13.5% of all UK hospital research published by our partner trusts

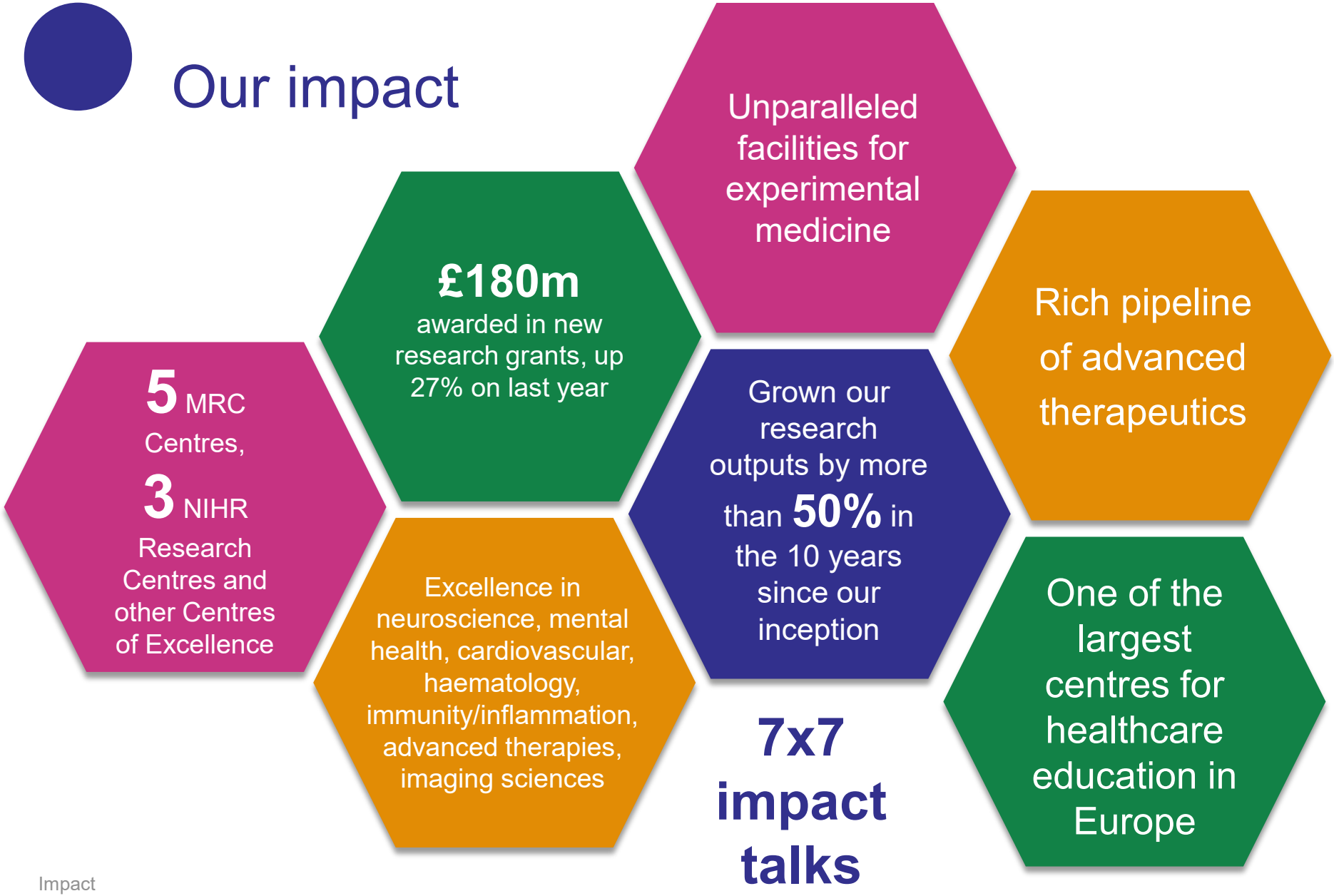
38,000 patients in clinical trials last year

6.8% per year growth in overall research activity at King's Health Partners, the highest of any AHSC

Excellence in neuroscience, mental health, cardiovascular, haematology, immunity/inflammation, advanced therapies, imaging sciences

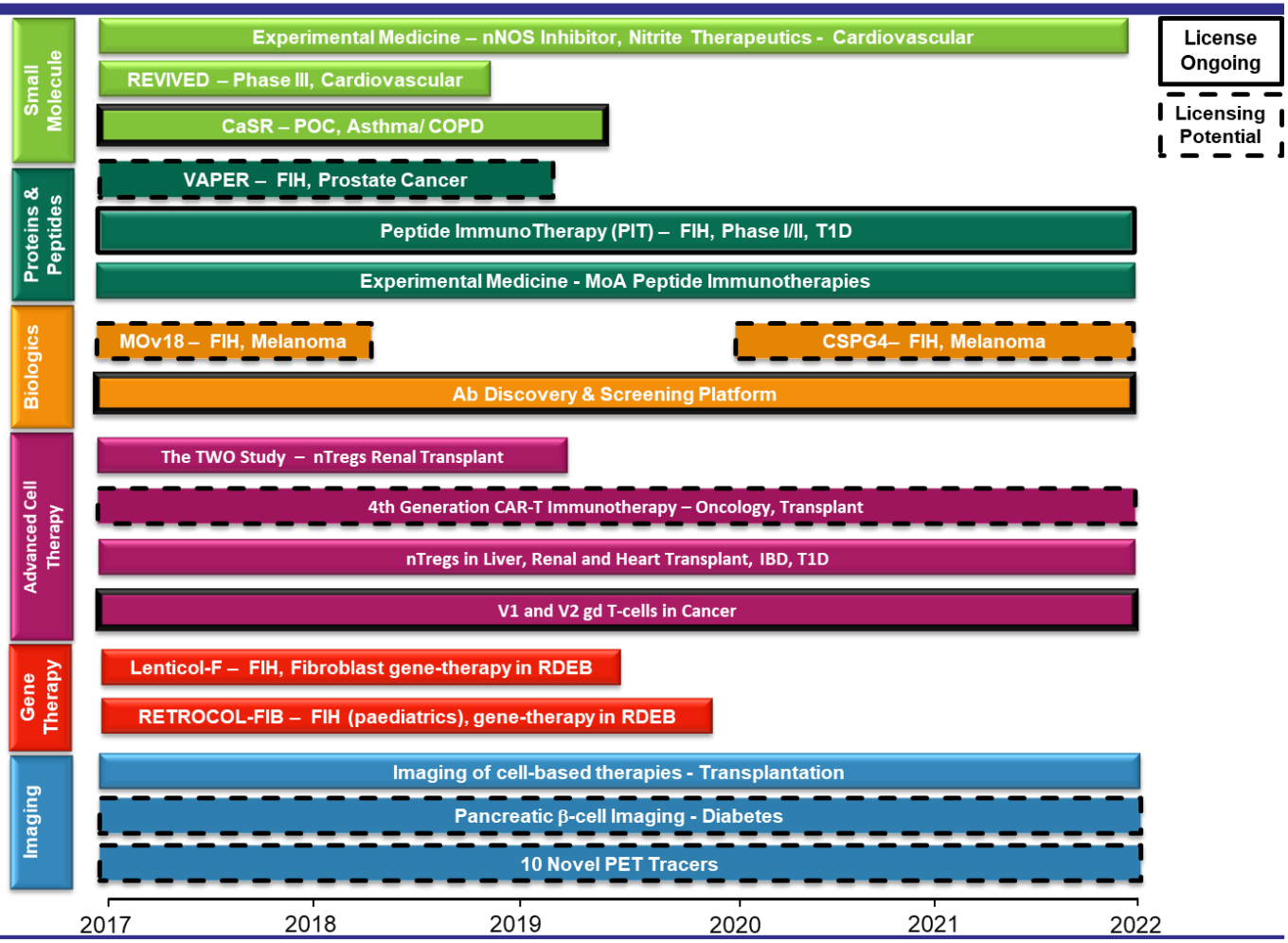
Expanding portfolio of industry partnerships

Our impact


Unparalleled facilities for experimental medicine
£180m awarded in new research grants, up 27% on last year
Rich pipeline of advanced therapeutics
5 MRC Centres, 3 NIHR Research Centres and other Centres of Excellence
Grown our research outputs by more than 50% in the 10 years since our inception
Excellence in neuroscience, mental health, cardiovascular, haematology, immunity/inflammation, advanced therapies, imaging sciences
7x7 impact talks
One of the largest centres for healthcare education in Europe

Discovery science – feeding the translational pipeline

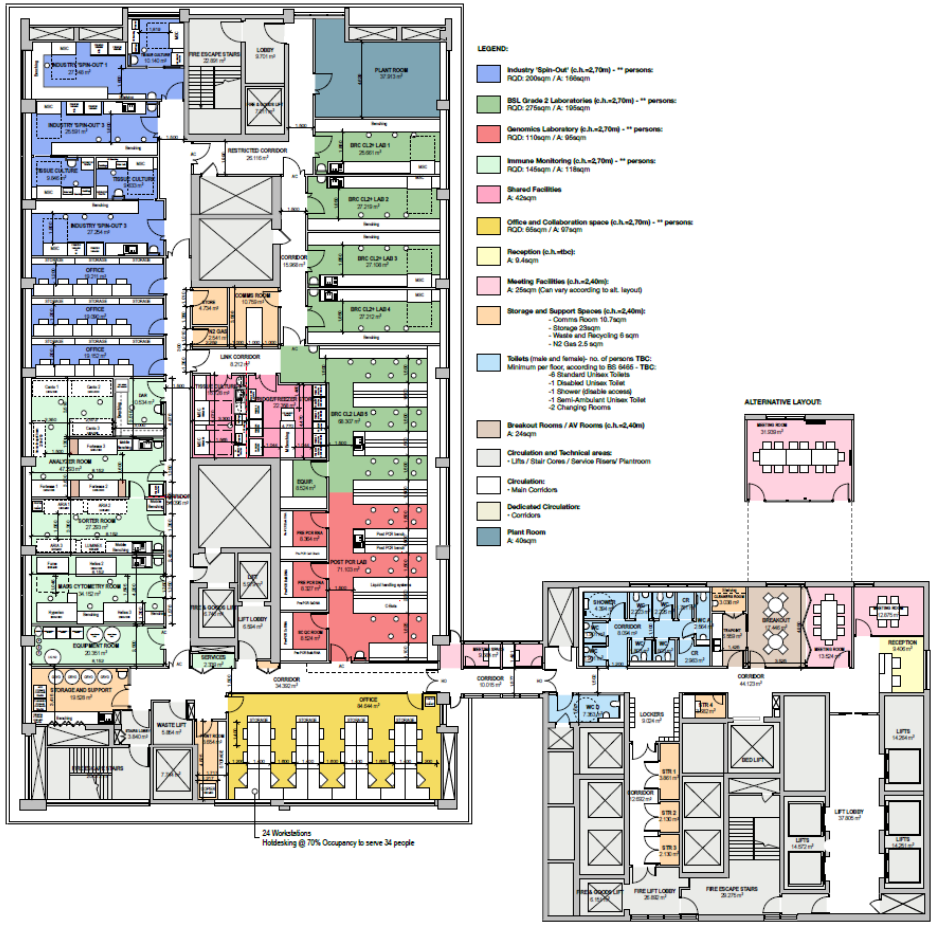
- Our distinct contribution as an **engine room of high impact innovation**
- At the forefront of innovation and **exploiting new technologies** including advanced therapies, biomedical engineering, imaging & digital health



Impact - advanced therapies and experimental medicine snapshot

- £10m Advanced Therapies Centre opening 2019
- Planned expansion of gene therapy manufacturing (Denmark Hill) and cell therapy manufacturing (Guy's)
- British Heart Foundation Centre of Research Excellence
- Cancer Research UK Centre
- City of London Cancer Centre
- Experimental Cancer Medicine Centre, and
- Founding partner of The Francis Crick Institute

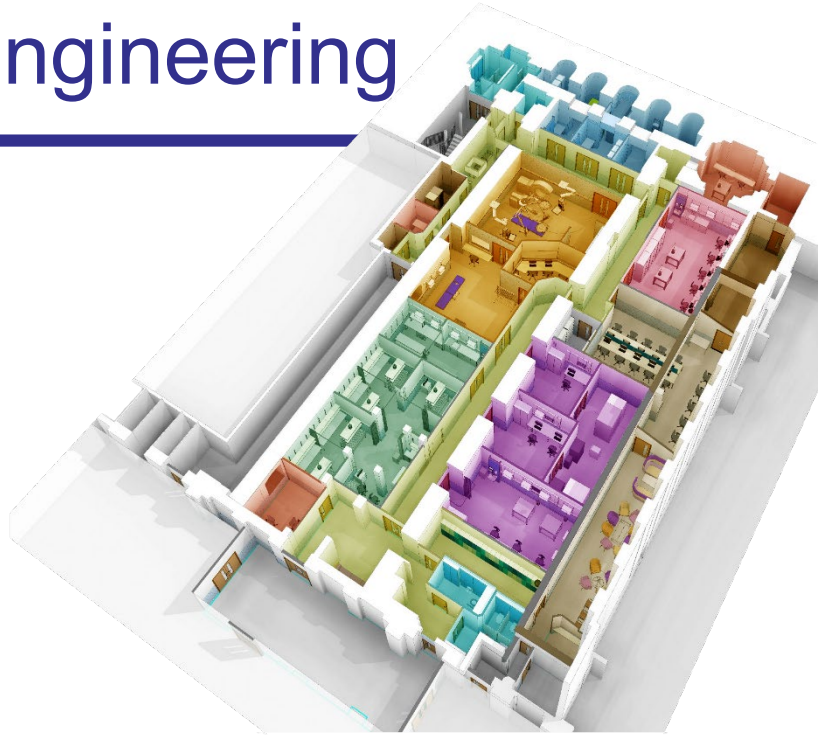
The London Medical Imaging & Artificial Intelligence Centre for Value-Based Healthcare



Impact - healthcare engineering

Institute for Healthcare Engineering

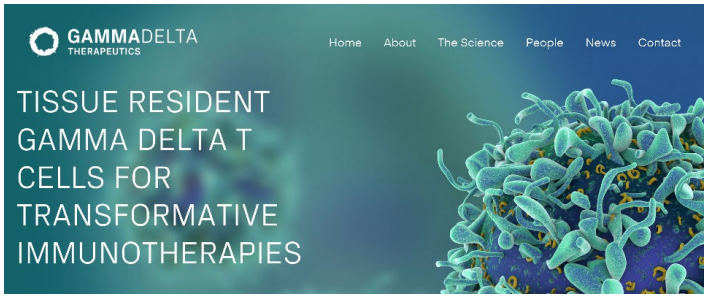
(£16m UKRPIF pending)



Department of Surgical & Interventional Engineering

£1m Wolfson & £5m Wellcome Medical Devices Manufacturing Facility

Impact - clinical academic spinouts



GammaDelta Therapeutics Ltd was founded on pioneering research into gamma delta (γδ) T cells led by **Professor Adrian Hayday** and **Dr Oliver Nussbaumer**

- Up to $100m investment from Takeda and Abingworth

IGEM Therapeutics

Founded by **Dr Sophia Karagiannis**

- Development of IgE antibody drugs for cancer

Leucid Bio

Founded by **Dr John Maher**

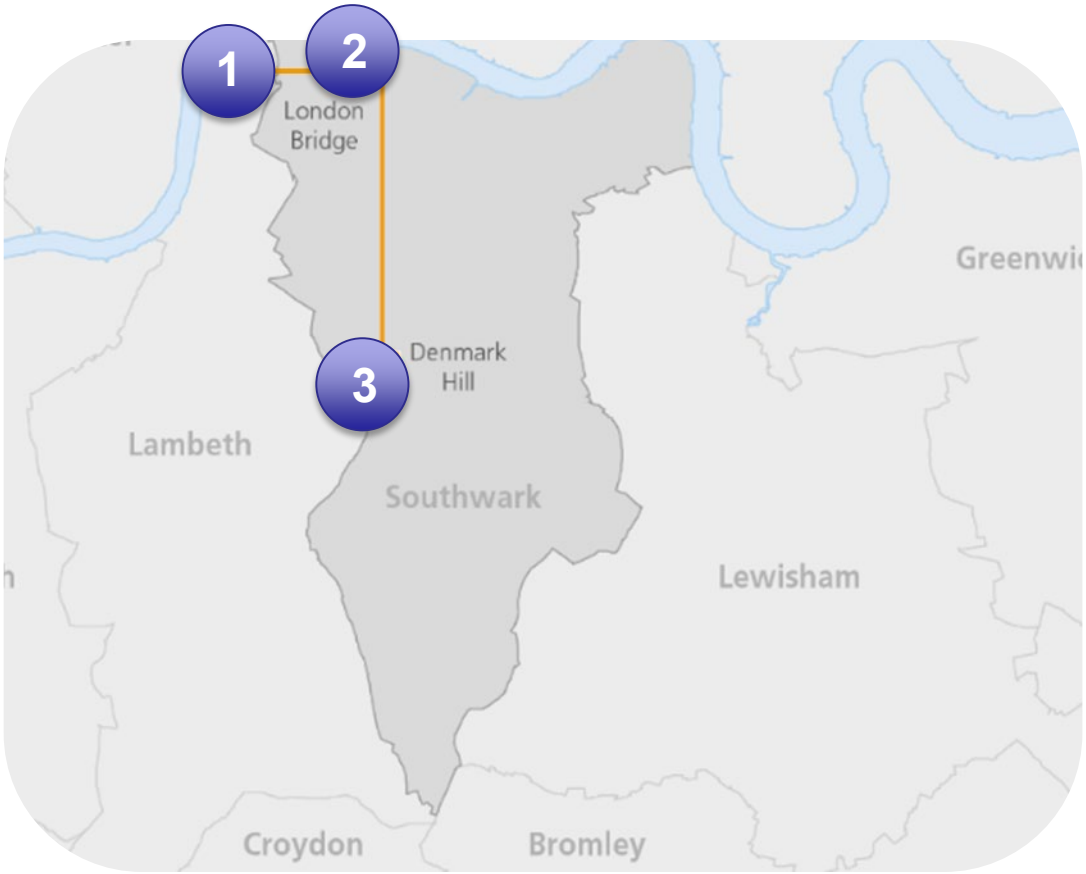
- CAR T cells

Impact - industry partnerships

Major strategic partnerships:

- UCB
- Siemens
- GSK
- Medtronic
- Nvidia
- IBM
- Celgene
- MSD

Impact - partnerships



1. Westminster Bridge	MedTech hub
2. London Bridge	Biomedical hub
3. Denmark Hill	Translational hub

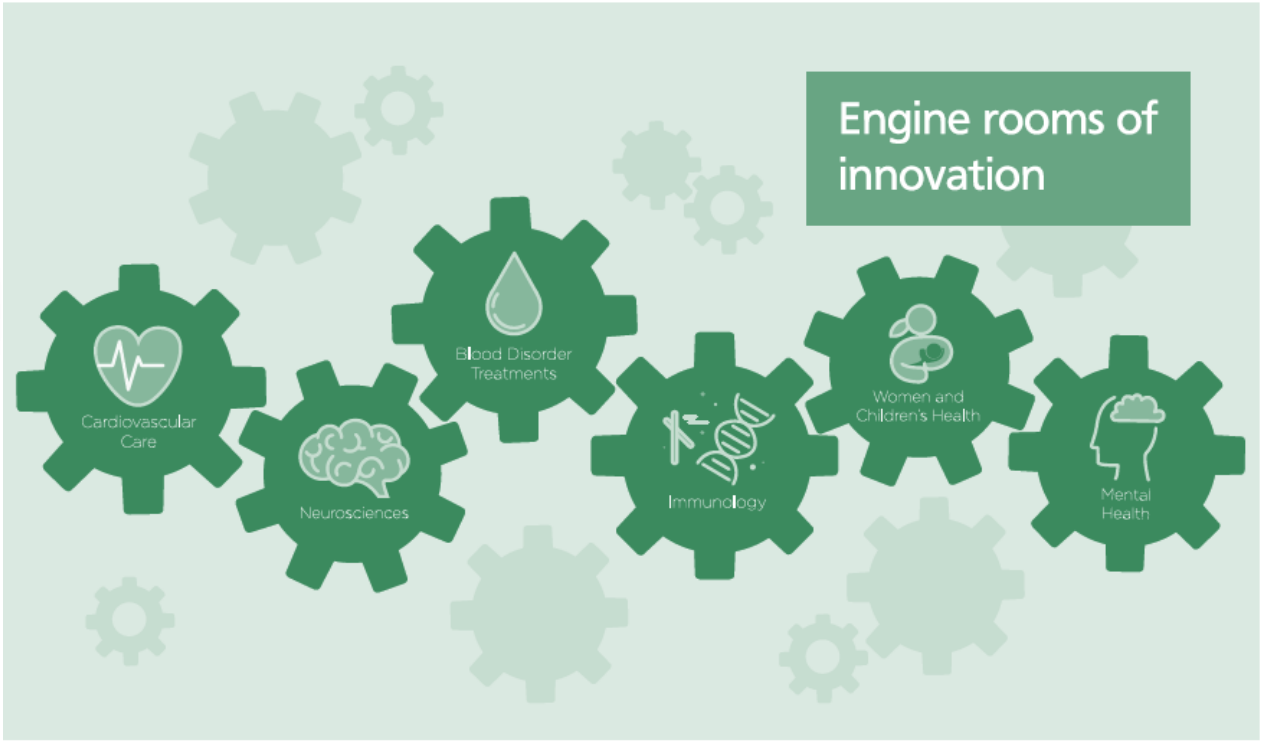
Impact – partnerships in health and science

- Academic Health Sciences Centres
- Academic Health Science Networks – the Health Innovation Network
- Our Healthier South East London Sustainability and Transformation Partnership
- South West London Sustainability and Transformation Partnership
- Collaborations for Leadership in Applied Health Research and Care / ARC
- One London – London as a health data capital of the world
- MedCity | The Crick | Health Catapults
- Cardiovascular partnerships
- Haematology partnerships
- International visitors – Denmark | China | Singapore | Australia | Malaysia

Impact - Clinical Academic Groups and institutes

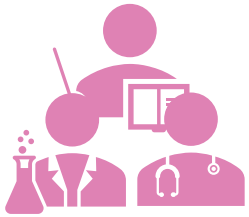
We build on our strengths to bring together our clinicians and academics across clinical practice, research and education to deliver world-class care that achieves better outcomes for our patients and service users.

Where the NHS and University connect



Transforming care for the number one cause of death in the developed world

- Host the largest (£15 million to date) British Heart Foundation (BHF) Centre of Research Excellence
- Developed integrated one team models across our trusts and university to improve outcomes and consistency with joint programmes in
  - valve disease,
  - coronary and cardiac surgery,
  - heart failure,
  - electrophysiology,
  - vascular and,
  - inherited cardiac conditions
- Exploring partnership opportunities with Royal Brompton & Harefield NHS Foundation Trust
- Have the largest vascular surgery network in England and UK's most comprehensive heart valve service
- Merged aortovascular on-call services showcased in a Getting It Right First Time (GIRFT) report
- Integrated mental and physical healthcare in 12 clinics.



Finding cures for leukaemia, sickle cell, and driving insights in precision medicine

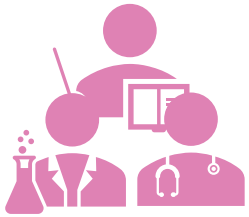
- A leading centre in Europe for research, with a large, high-quality clinical service providing care for more than 20,000 individual patients every year and serving a regional network of more than eight million people

- Developed integrated one team models across our trusts and university to improve outcomes and consistency with joint programmes in
  - blood transfusion,
  - sickle cell services,
  - haem oncology,
  - integrated mental and physical healthcare – Mind & Body
  - diagnostics and precision medicine, and
  - CAR-T unit development

- Research output and impact in haematology among the top 10 in the world, currently conducting nearly 200 clinical trials across all aspects of haematology, in all trial phases

- One of the largest sickle cell practices and one of the largest stem cell transplantation programmes in the UK

- We are one of the first centres globally to use chimeric antigen receptors (CAR-T) cells to treat lymphoma, leukaemia and myeloma.

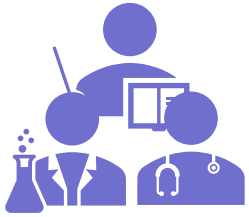


Providing one of the largest, most comprehensive clinical neurosciences services in the country

- Leading research, ranked 2nd in the UK for research power
- Established and operating one team working in:
  - Neuroradiology
  - Neuropsychiatry
  - Neurophysiology
  - Neuropathology
  - Paediatric neurosurgery
  - Neurorehabilitation
  - Neuro-oncology

- Highly regarded clinical services including, neurosurgery services rated as national exemplar by the Getting It Right First Time (GIRFT) review, accredited international Centres of Excellence for Parkinson's disease and neuromuscular disease, and a multi-award winning motor neuron disease clinic, a nationally commissioned neurofibromatosis service

- Dedicated Clinical Research Facility (CRF) for neurosciences and mental health patients, allowing us to deliver numerous phase I trials including stem cell therapies to repair stroke damage, and genetic testing for motor neurone disease
- Established integrated mental and physical healthcare services in stroke, neurorehabilitation and traumatic brain injury.

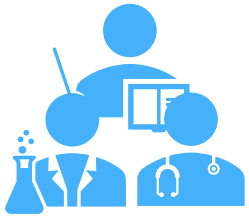


Innovative solutions to the treatment, prevention and better self-management of diabetes care

- Delivering an NHS England funded pilot service for people with type 1 diabetes disordered eating (T1DE), providing integrated diabetes and mental health care

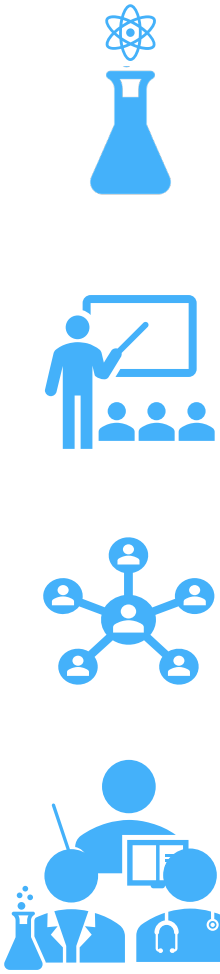
- Developing an MSc in Advanced Diabetes and Obesity, due to launch in October 2020
- Working with partners across the system, conducting a strategic refresh and redesign of the obesity pathway in south London to increase access to preventative and surgical options, and reduce stigma towards obesity

- One of the few teams to have world leading clinical and academic leadership in the mind-body approach to diabetes care, encompassing:
  - psychiatry,
  - immunology,
  - education,
  - therapies, and
  - the use of data and informatics to improve patient care.



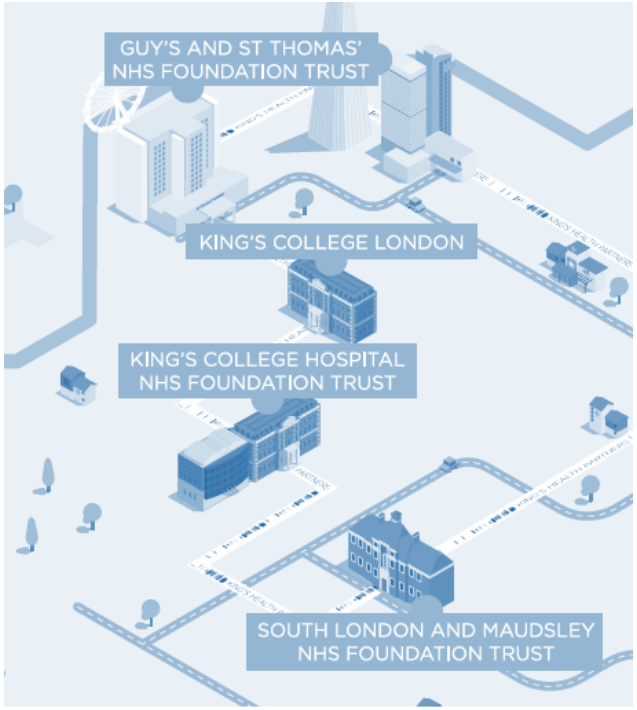
Better beginnings, healthy lives

- A distinctive clinical-academic focus on conditions and diseases that affect large numbers of women and children across their life course
- A combined approach to mind and body health - working closely with the Centre for Children's and Young People's Mental Health
- State-of-the-art imaging modalities, clinical expertise and basic science strengths
- A life course approach and a vision that includes both local and global health
- Interprofessional education and training as exemplified by the MSc in Women and Children's Health, MSc in Women's Health and MSc in Advanced Paediatrics
- Key publications in *the Lancet, NEJM, Nature, Nature Medicine* and others, with more than £84 million in funding for major projects
- Key initiatives will include the creation of a dedicated Clinical Trials Unit, development of Clinical Research Facilities.



Clinical Academic Groups – key highlights

- Many compelling initiatives from Clinical Academic Groups
- Partnership opportunities



Education impact

- NIHR Integrated Academic Training programme, unique in London
- 2019 Learning Hub relaunch with nearly 100 resources, including resources available to national and international learners
- New MBBS Curriculum 2020 focused on developing a workforce trained to deliver holistic care
- Education Academy coordinating CAG and institute educational progress
- New PGCert in Advanced Medical Training (Children's Health, Haematology, or Women's Health) aimed at international learners – enrolling September 2019.

The impact of Mind & Body

- IMPARTS now in 60 outpatient clinics, 17% increase on last year, with more than 65,000 patient screened
- COMPASS online Cognitive Behavioural Therapy tailored for long-term conditions - 12-month pilot May 2019
- Funding from the Maudsley Charity for a three-year Integrating our Mental and Physical Healthcare Systems (IMPHS) project
- Massive open online course (MOOC), 'Integrating Care: Depression, Anxiety and Physical Illness' - more than 12,000 staff, patients and members of the public signed-up
- Health and wellbeing toolkit available to all staff
- Mind & Body Champion's Network –now reached 600 staff
- Research on personalised medicine in psychiatry, seizures and stress, and the effects of nutrition on compulsive behaviours.

The impact of informatics

Building towards London becoming a health data capital of the world

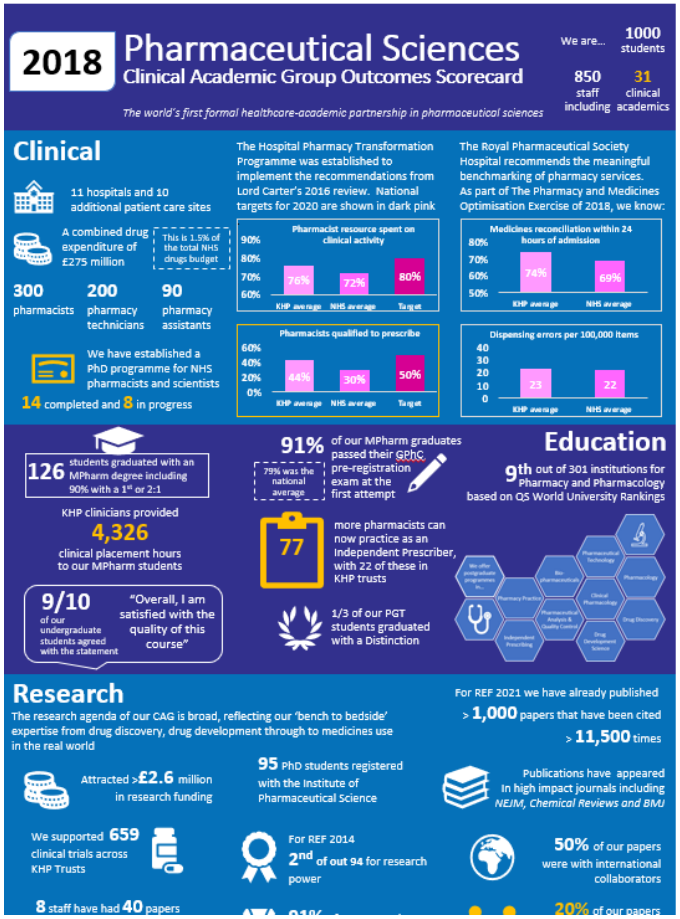
- **London Local Health and Care Record Exemplar – One London**
- **Health Data Research UK – London**
- **Bid for Digital Innovation Hub**

- Joined up electronic patient records across south east London, covering population of 1.7m
- One team across institutes and networks
- Potential to scale-up innovation from within King's Health Partners – CogStack, IMPARTS, HealthLocker, Lambeth DataNet, CRIS for clinical benefit

The impact of Value Based Healthcare

- Capability to measure and share outcomes and costs to make value-based decisions – pathway pilots in
  - cardiovascular, orthopaedics, depression in older adults
- Increasing influence and securing external funding
- Joined the European University Hospitals Alliance to further develop our work in value based healthcare
- The Vital 5 – an innovative new approach to population health to improve value and reduce health inequalities

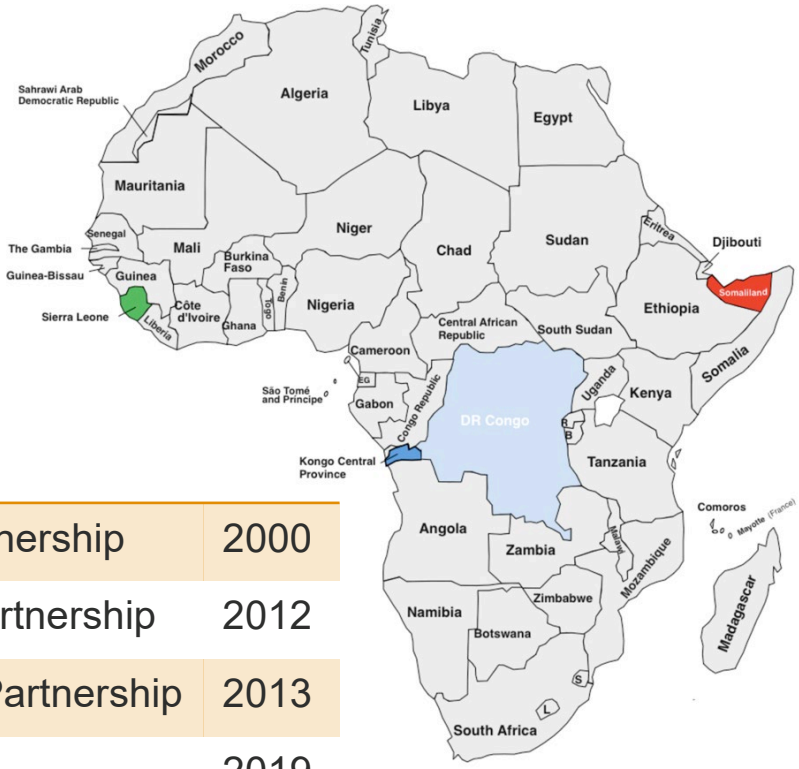
Vital 5	Aim
Blood pressure	to reduce stroke and heart attack, and improve well being
Obesity	to reduce diabetes, renal dialysis, liver transplants, amputations and other comorbidities, and improve well being
Mental health score	to reduce the burden of mental illness, improve physical health, recovery and well being
Alcohol intake	to reduce liver transplants and malignant disease, to improve well being
Smoking habits	to reduce respiratory and malignant disease, and improve well being



- 17 outcomes books – developing an outcomes scorecard approach

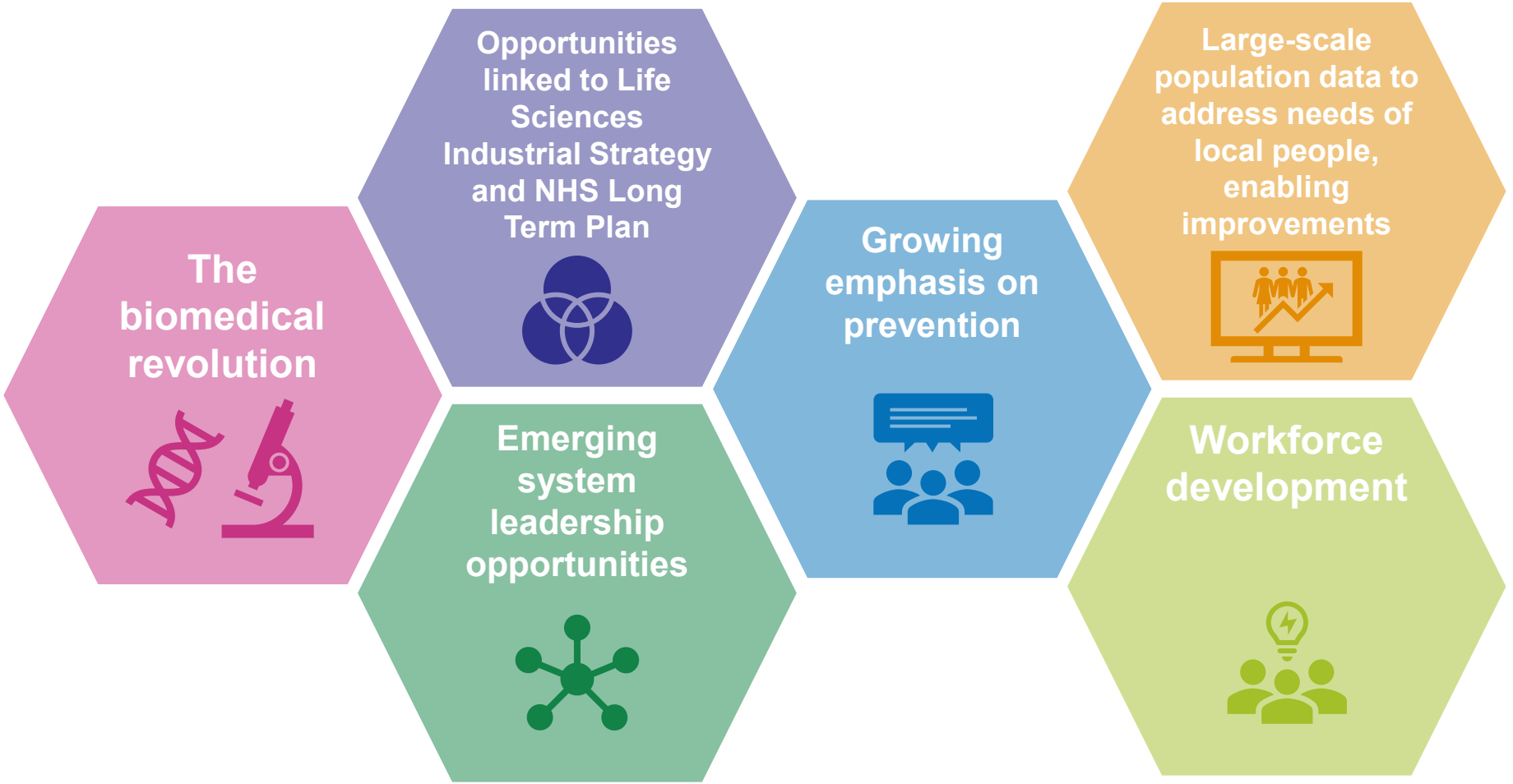
The impact of Global Health programmes

- King's Centre for Global Health & Health Partnerships 10-year strategy published
- Opportunities for King's Health Partners staff (clinical and non-clinical) to volunteer time and skills

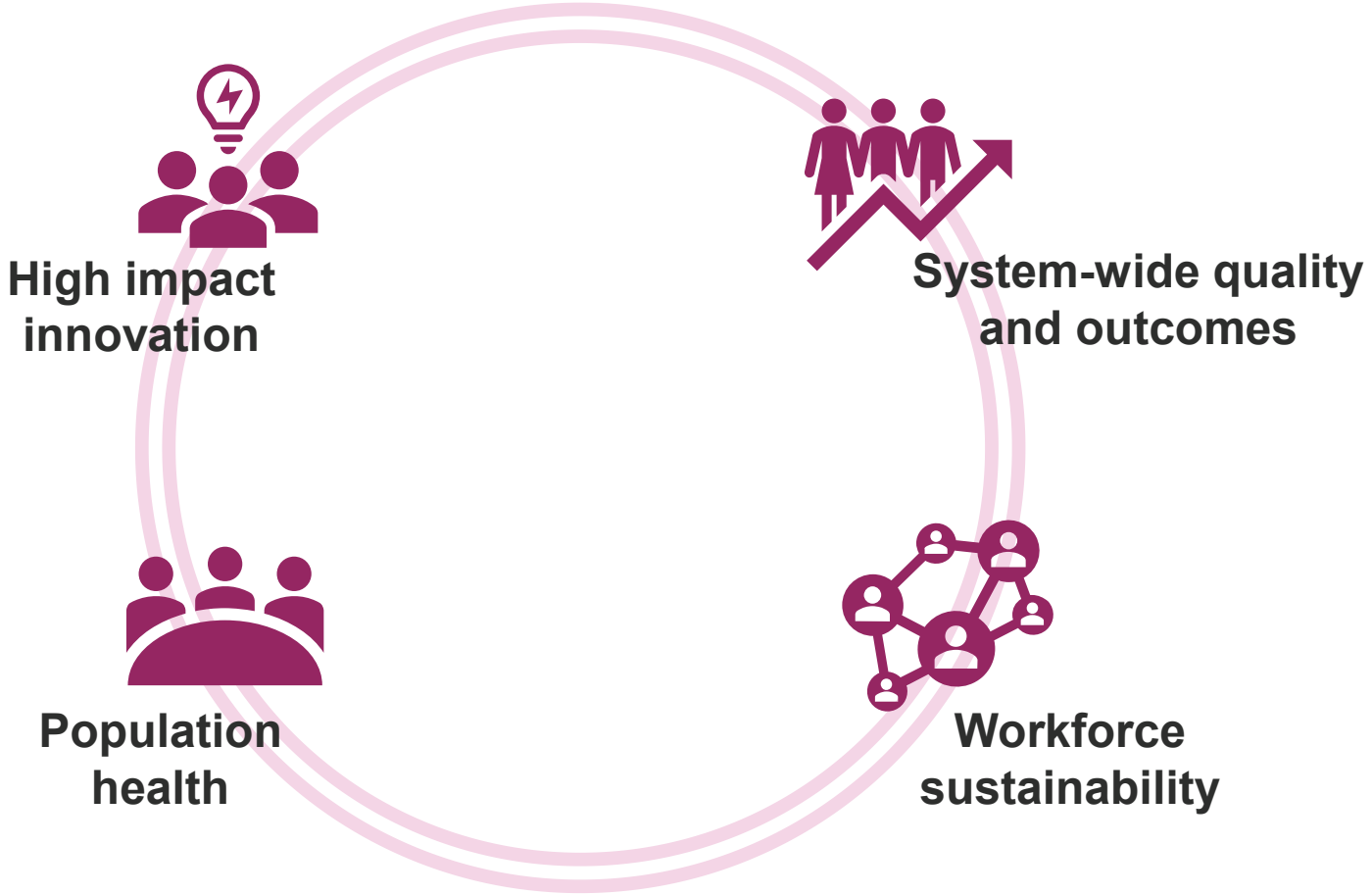


Somaliland Partnership	2000
Sierra Leone Partnership	2012
Kongo Central Partnership	2013
Zambia	2019

Looking to the future – building on our clinical academic opportunities



Setting the scene for the next five-years



Impact 7x7

King's Health Partners Annual Conference 2019

#KHP10Years

Using PET-CT to treat Hodgkin Lymphoma

Sally Barrington

NIHR Research Professor of PET Imaging

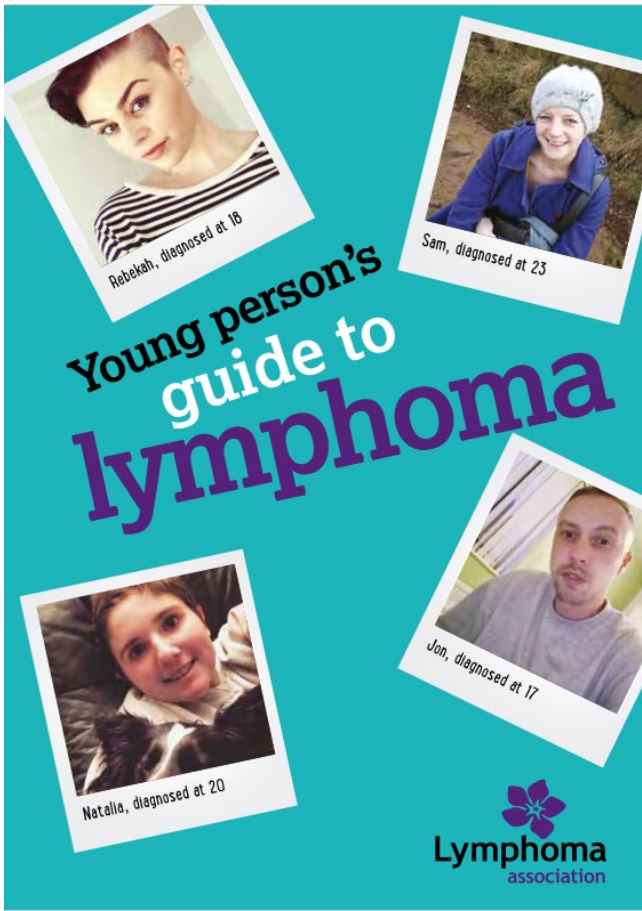
NHS National Institute for Health Research

Hodgkin Lymphoma

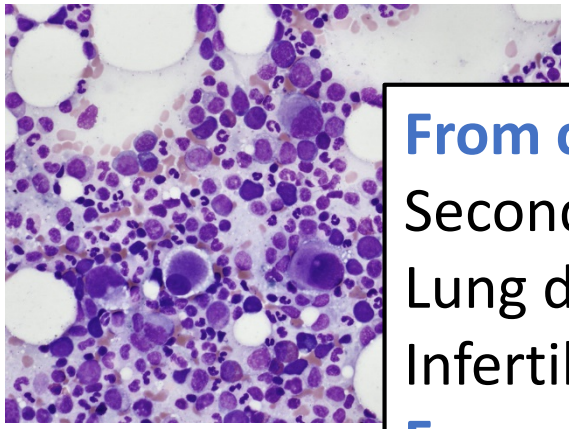
First described 1832 Thomas Hodgkin
Physician at Guy's and St Thomas'

Commonest cancer in young adults
2nd peak in people aged over 60

Treatment improved over 30 years
80% of patients are cured
95% early stage, 75% advanced stage



15 years after treatment more patients die from side-effects than disease



From chemotherapy:

Second blood cancers

Lung damage

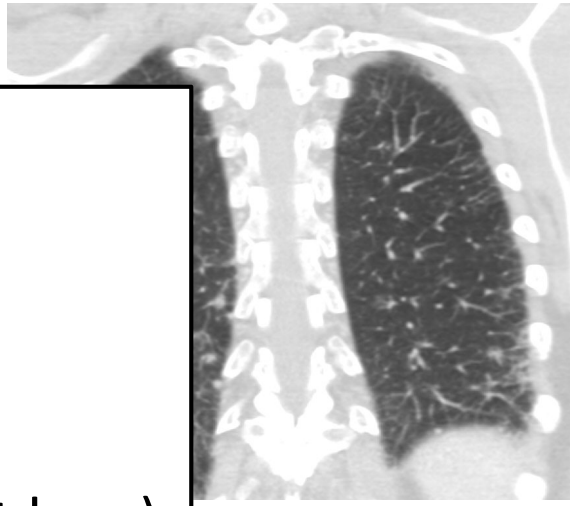
Infertility

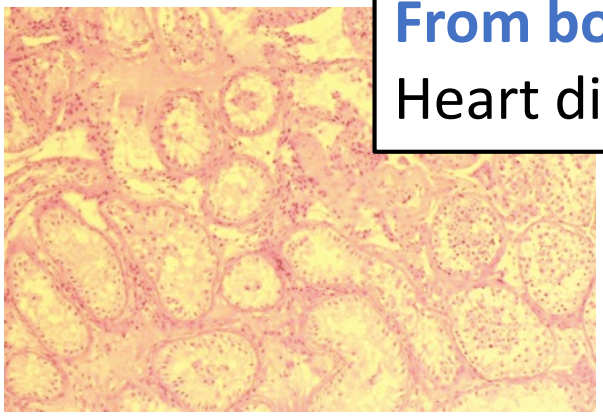
From radiotherapy:

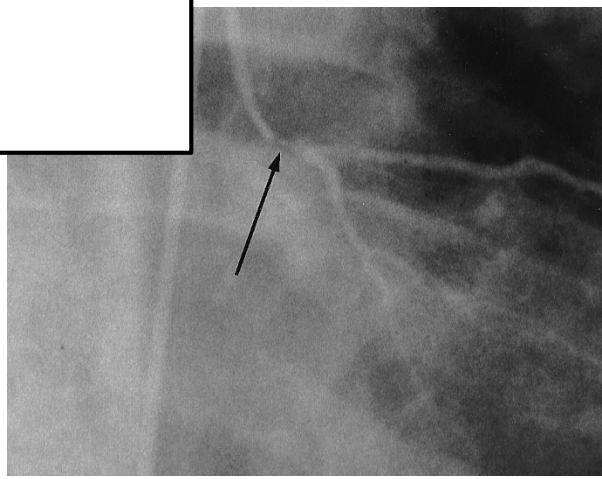
Second solid cancers (e.g. breast lung)

From both

Heart disease





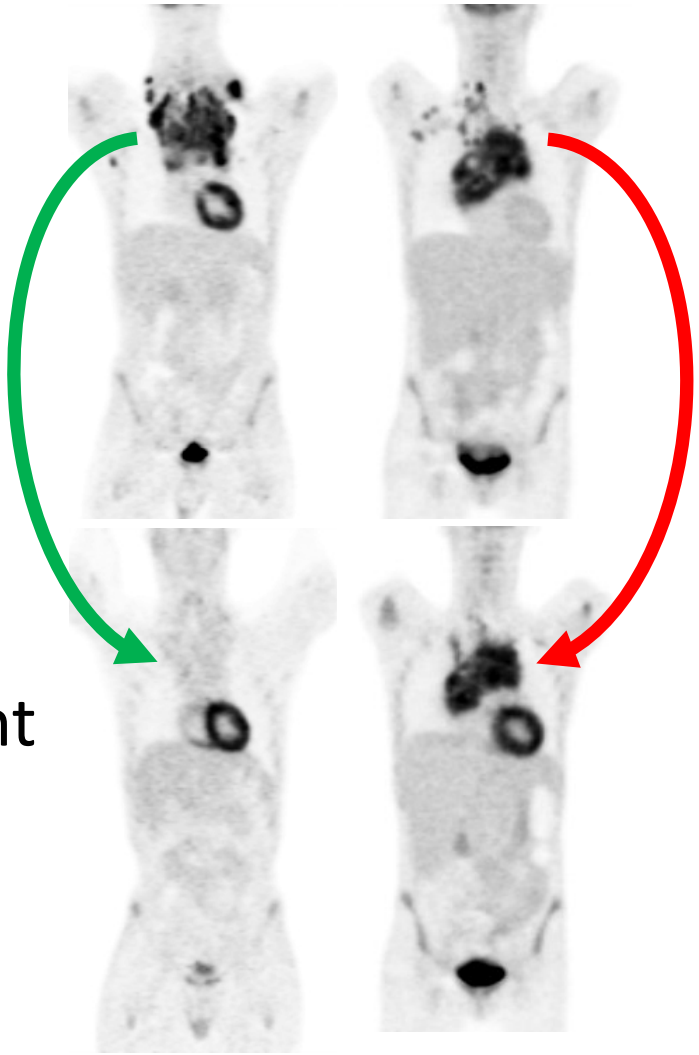


PET scans using radioactive tracers

Show metabolic changes in cancer

Allow earlier and more accurate monitoring of treatment

Have potential to modify treatment for individual patients



Good response

Poor response

King's College London & Guy's and St Thomas' PET Centre

PET Guided Therapy changes practice

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Results of a Trial of PET-Directed Therapy for Early-Stage Hodgkin's Lymphoma

John Radford, M.D., Tim Illidge, M.D., Ph.D., Nicholas Counsell, M.Sc., Barry Hancock, M.D., Ruth Pettengell, M.D., Peter Johnson, M.D., Jennie Wimperis, D.M., Dominic Culligan, M.D., Bilyana Popova, M.Sc., Paul Smith, M.Sc., Andrew McMillan, M.B., Alison Brownell, M.B., Anton Kruger, M.B., Andrew Lister, M.D., Peter Hoskin, M.D., Michael O'Doherty, M.D., and Sally Barrington, M.D.

Can we reduce the need for radiotherapy ?

The NEW ENGLAND JOURNAL of MEDICINE

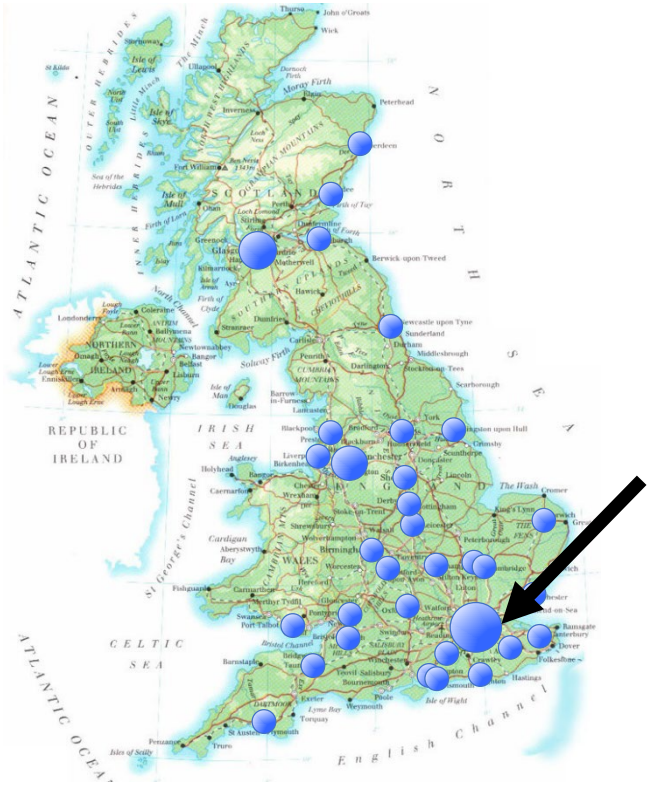
ESTABLISHED IN 1812 JUNE 23, 2016 VOL. 374 NO. 25

Adapted Treatment Guided by Interim PET-CT Scan in Advanced Hodgkin's Lymphoma

Peter Johnson, M.D., Massimo Federico, M.D., Amy Kirkwood, M.Sc., Alexander Fossâ, M.D., Leanne Berkahn, M.D., Angelo Carella, M.D., Francesco d'Amore, M.D., Gunilla Enblad, M.D., Antonella Franceschetto, M.D., Michael Fulham, M.D., Stefano Luminari, M.D., Michael O'Doherty, M.D., Pip Patrick, Ph.D., Thomas Roberts, B.Sc., Gamal Sidra, M.D., Lindsey Stevens, Paul Smith, M.Sc., Judith Trotman, M.D., Zaid Viney, M.D., John Radford, M.D., and Sally Barrington, M.D.

UK PET Core Lab

Quality Control for PET Clinical Trials



Can we safely reduce chemotherapy with fewer side-effects ?

Can we switch chemotherapy for patients with poor response on PET?

Standardised reading of PET scans

Crucial if treatment changed based on PET

Simple, reliable and reproducible

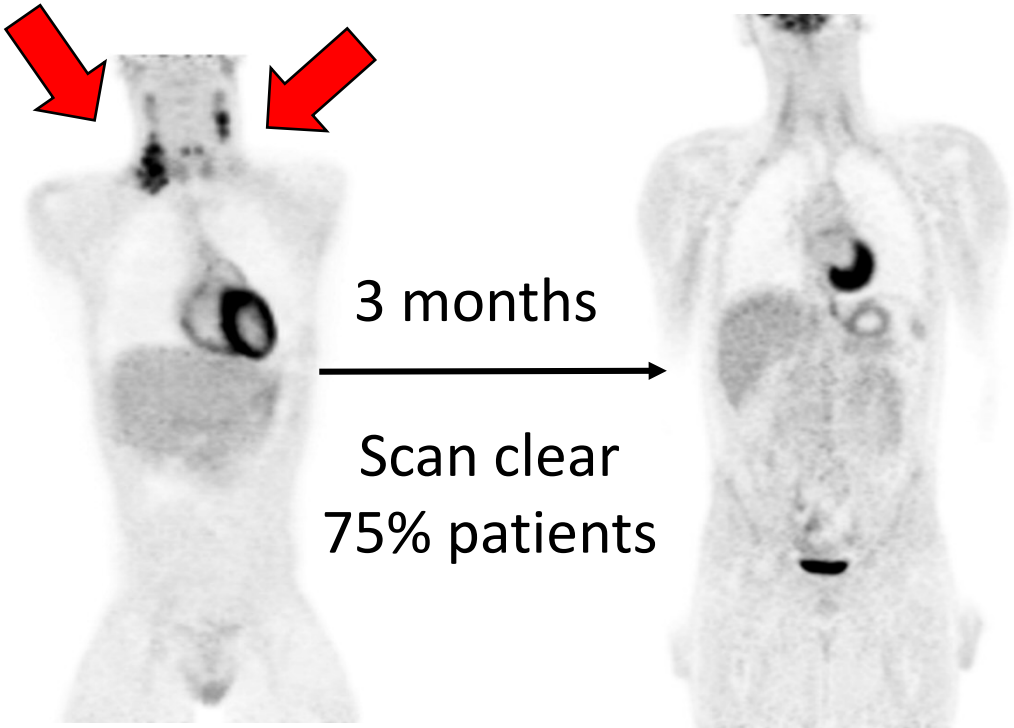
so everyone can use !

JOURNAL OF CLINICAL ONCOLOGY SPECIAL

Role of Imaging in the Staging and Response Assessment of Lymphoma: Consensus of the International Conference on Malignant Lymphomas Imaging Working Group

Sally F. Barrington, N. George Mikhaeel, Lale Kostakoglu, Michel Meignan, Martin Hutchings, Stefan P. Müeller, Lawrence H. Schwartz, Emanuele Zucca, Richard I. Fisher, Judith Trotman, Otto S. Hoekstra, Rodney J. Hicks, Michael J. O'Doherty, Roland Hustinx, Alberto Biggi, and Bruce D. Cheson

RAPID trial (early stage)



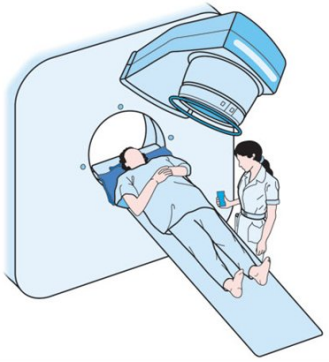
3 months

Scan clear
75% patients

90% disease free 3 y after treatment

Radiotherapy

97% disease free at 3 y

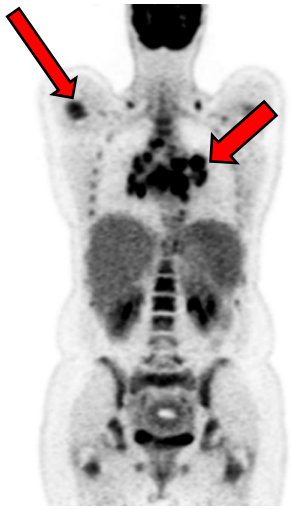


No treatment

91% disease free at 3 y

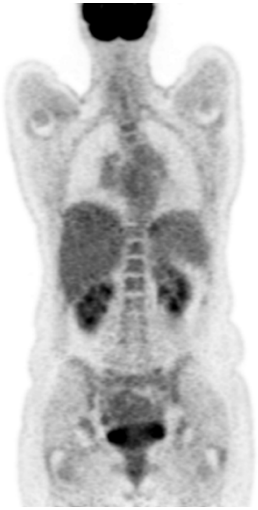
Many patients can be cured without radiotherapy treatment
Patients at high-risk of side-effects can choose not to receive RT
We hope this will mean fewer late side effects :
in Hodgkin lymphoma survivors

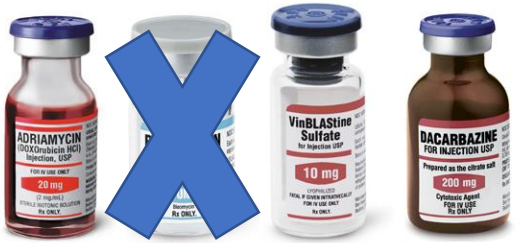
IL trial (advanced stage)



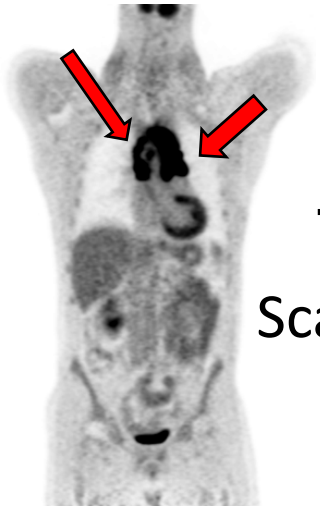
2 months

Scan clear
86% patients



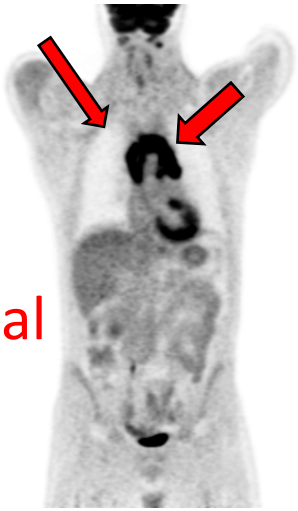


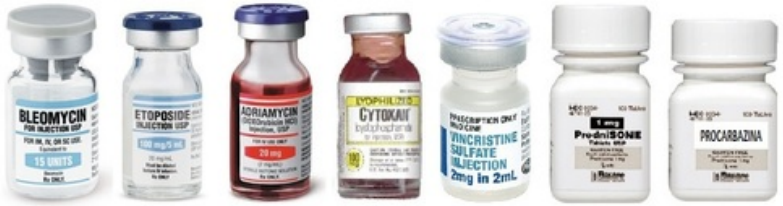
Same survival with fewer side-effects



2 months

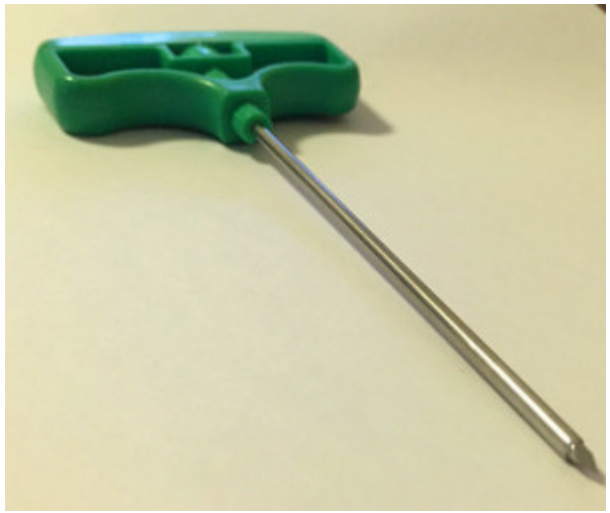
Scan still abnormal
14% patients

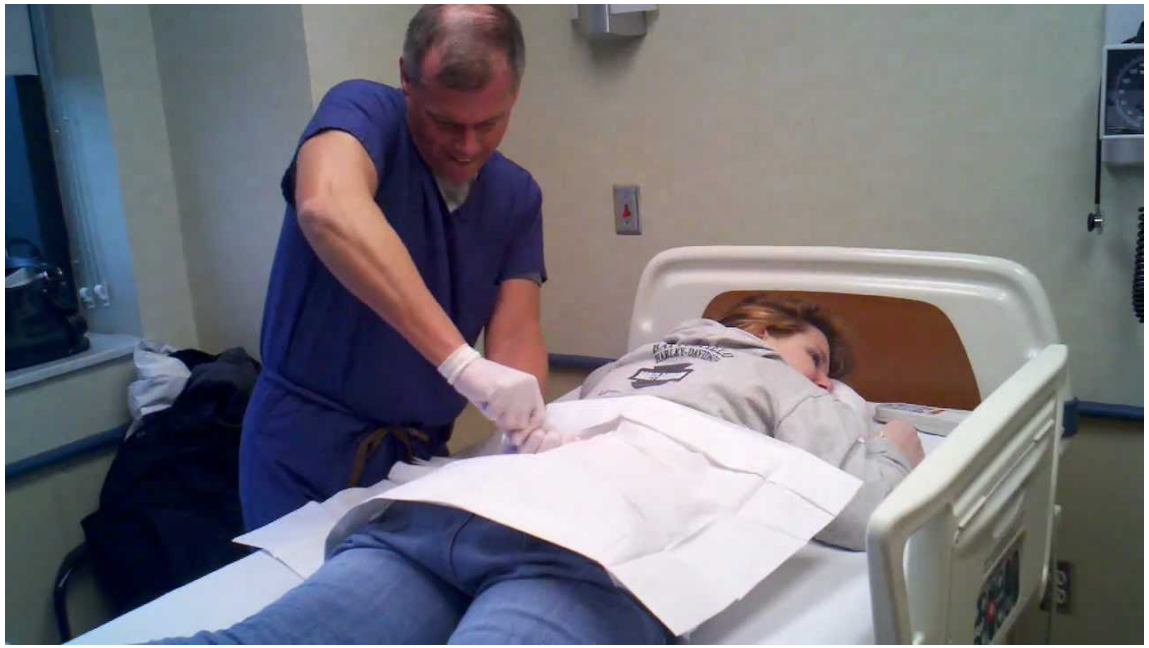




More intense chemotherapy to improve chance of cure

RATHL :
Can PET replace Bone Marrow Biopsy?





'As a cancer survivor I can tell you this procedure hurts like no other and generally all doctors downplay the pain'.

(You Tube posted 2011)

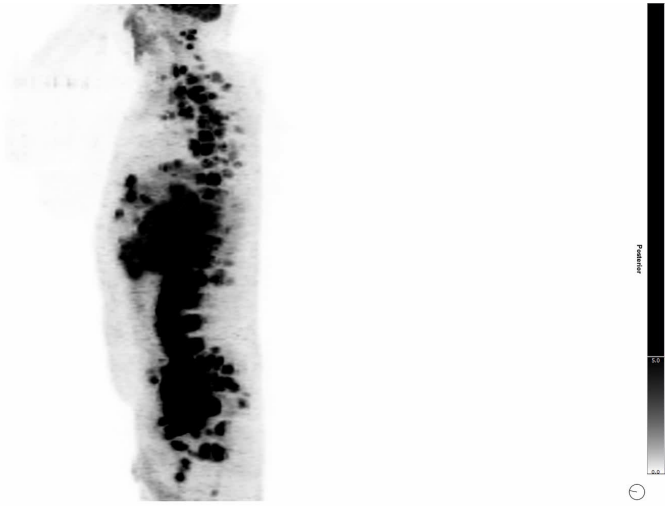
Yes: PET can reliably detect bone marrow spread
Doing a biopsy does not affect treatment

Plenary Paper

LYMPHOID NEOPLASIA

PET-CT for staging and early response: results from the Response-Adapted Therapy in Advanced Hodgkin Lymphoma study

Sally F. Barrington,[1] Amy A. Kirkwood,[2] Antonella Franceschetto,[3] Michael J. Fulham,[4,5] Thomas H. Roberts,[2] Helén Almquist,[6] Eva Brun,[7] Karin Hjorthaug,[8] Zaid N. Viney,[9] Lucy C. Pike,[1] Massimo Federico,[10] Stefano Luminari,[10] John Radford,[11] Judith Trotman,[5,12] Alexander Fossâ,[13] Leanne Berkahn,[14] Daniel Molin,[15] Francesco D'Amore,[16] Donald A. Sinclair,[1] Paul Smith,[2] Michael J. O'Doherty,[1] Lindsey Stevens,[2] and Peter W. Johnson[17]



insideblood commentary

24 MARCH 2016 | VOLUME 127, NUMBER 12

LYMPHOID NEOPLASIA

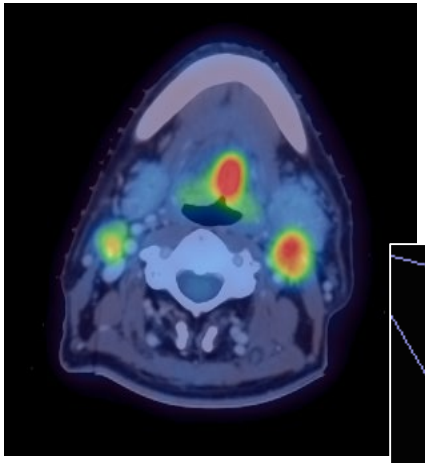
Comment on Barrington et al, page 1531

PET-CT: reliable cornerstone for Hodgkin lymphoma treatment?

Josée M. Zijlstra VU UNIVERSITY MEDICAL CENTER

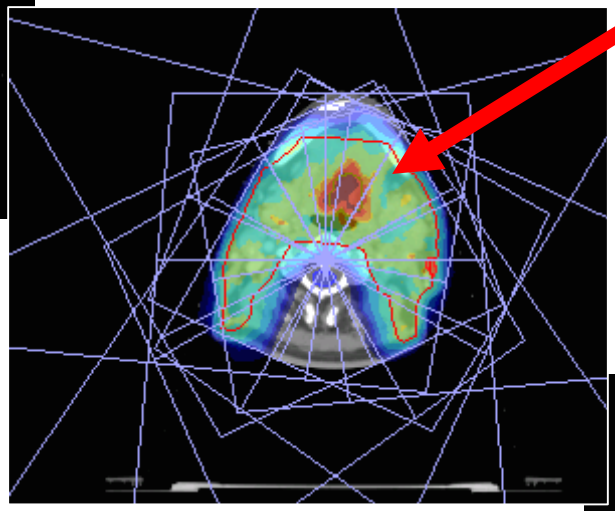
while maintaining the relatively good outcome. Accurate staging is of utmost importance to selecting the appropriate treatment regimen, which nowadays consists of 2 to 4 cycles of ABVD and radiotherapy for early-stage HL, and, for advanced-stage HL, mainly chemotherapy (6-8 cycles of ABVD or 6 cycles of bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone [BEACOPPP] escalated). With

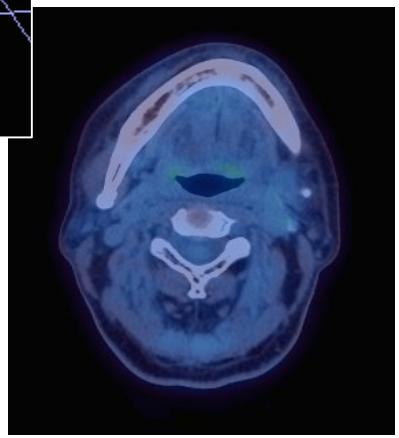
New targets : more cancers



Pre treatment
PET-CT

Boosting RT dose to improve cure in head & neck cancer



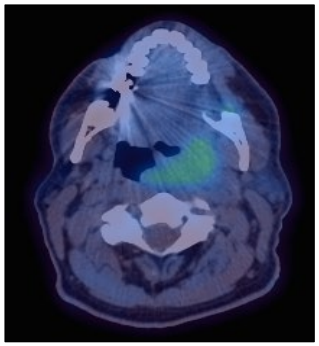


Post treatment
PET-CT

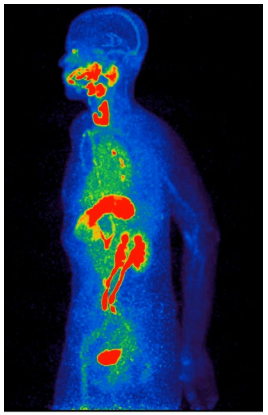
FiGaRO

F-FDG-PET in Guiding Dose-Painting with Intensity Modulated Radiotherapy in Oropharyngeal Tumours

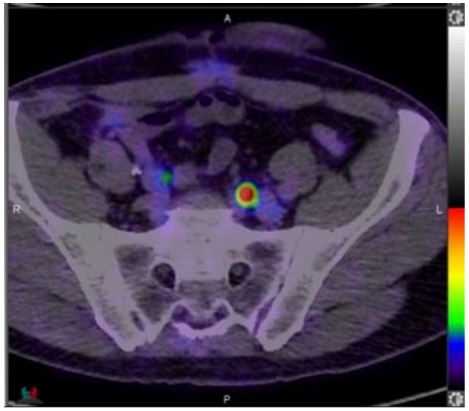
New targets : more tracers



^{64}Cu ATSM
Hypoxia in head and neck cancer

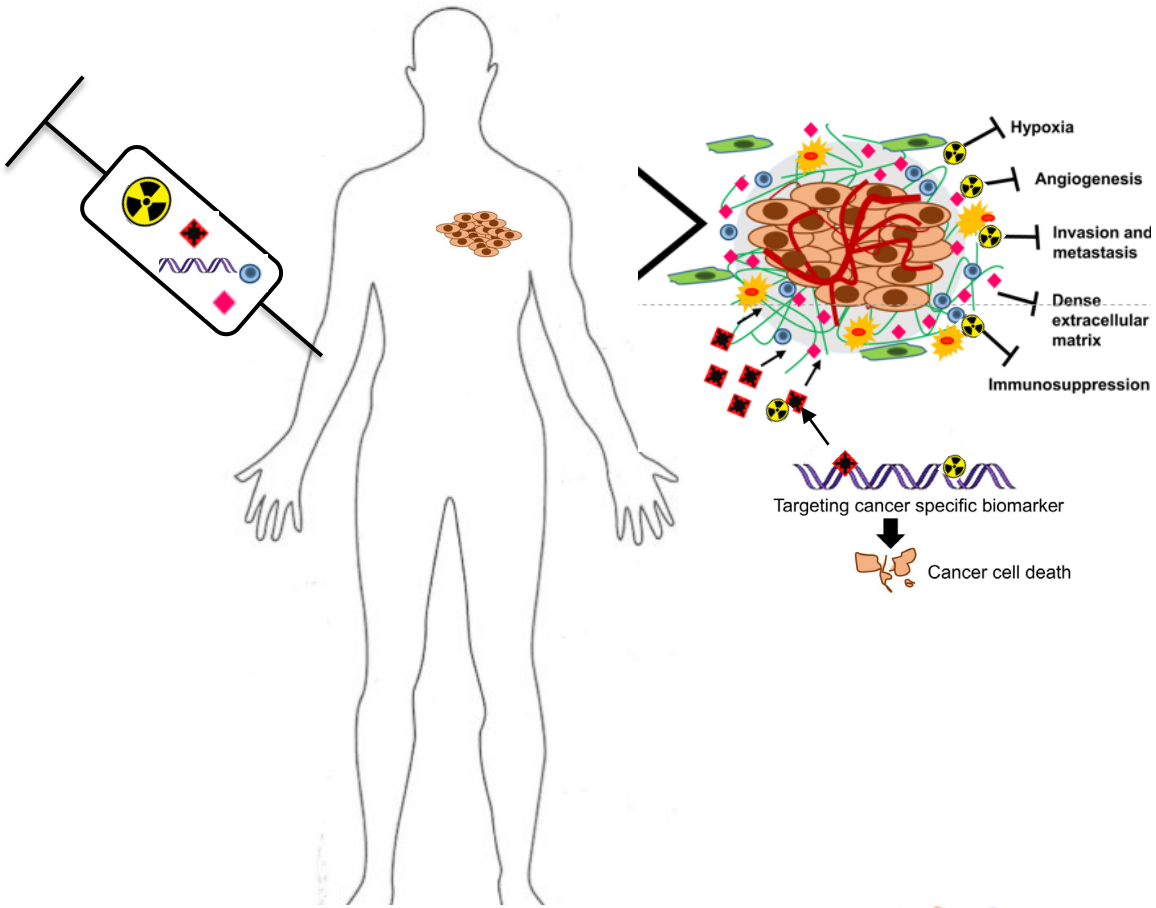


F18 tetrafluroborate
Thyroid cancer
Reporter gene imaging



Ga68 THP-PSMA
Prostate cancer

New targets : more cancers more tracers



EPSRC
Engineering and Physical Sciences Research Council

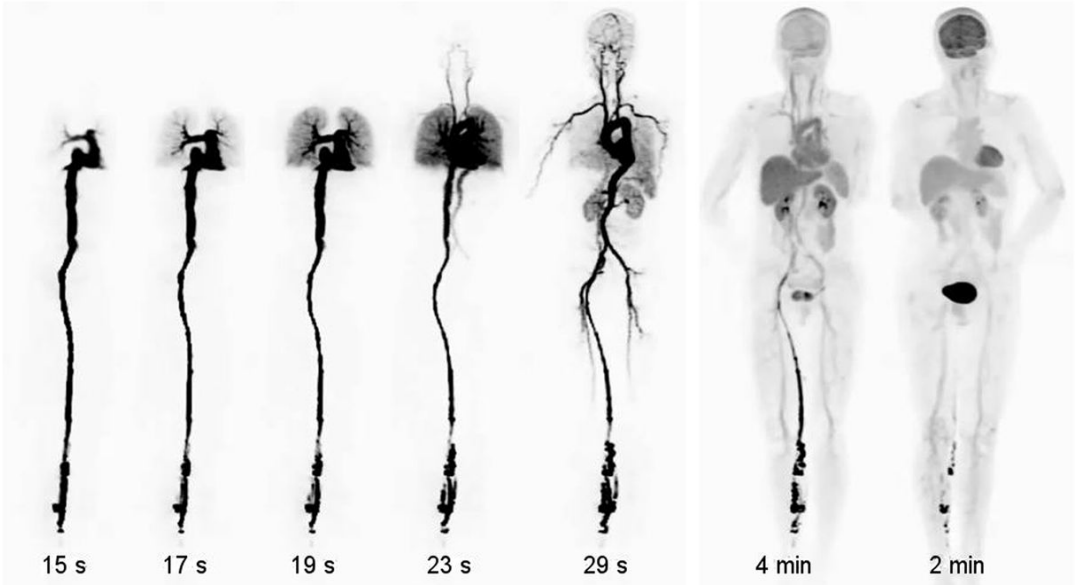
Programme grant Blower et al

KING'S HEALTH PARTNERS

modified from Lee YT et al Eur J Pharm 2018; 834: 189

Pioneering better health for all

New scanners: TOTAL BODY PET



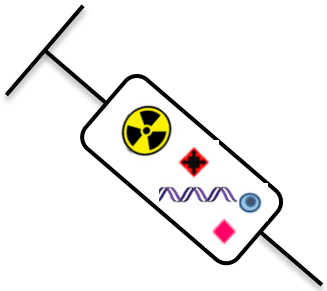
First in world 2019
Fudan University Shanghai
invented EXPLORER consortium USA

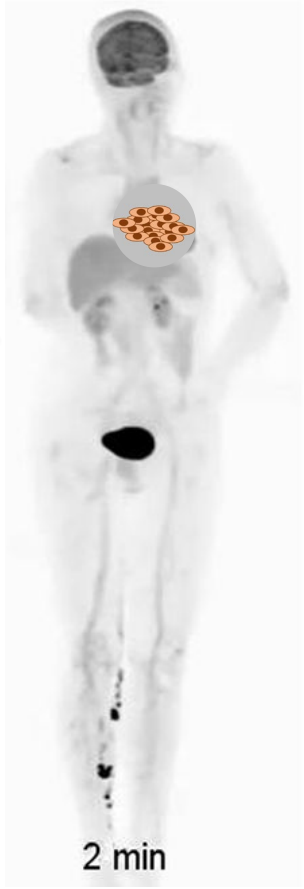
- Fast < 1min
- Very low dose (0.15mSv)
- Ultra sensitive

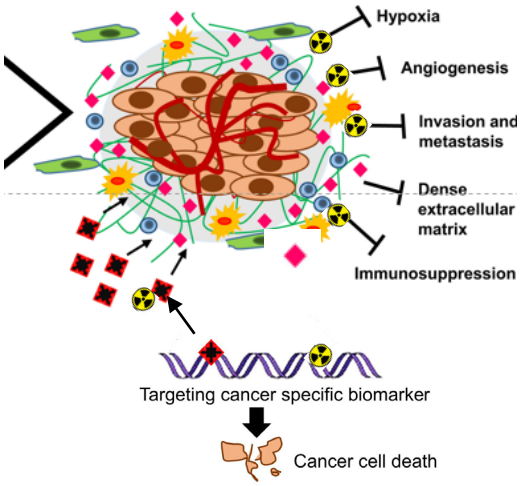
→ **Multiple tracers imaged at same (and over) time**

Badawi R et al J Nucl Med 2019; 60: 299-303

Future vision for next 10 years at KHP ?







Total body PET

Acknowledgements

Patients and their families

Kings College London

UK PET Core Lab

Paul Marsden

Lucy Pike

Cancer Imaging

Gary Cook

Clinical Oncology

Teresa Guerrero Urbano

Imaging Chemistry

Phil Blower

Michelle Ma

Sam Terry

Rafa Torres Martin de Rosales

My funder

NHS National Institute for Health Research

Kings College London & Guy's & St Thomas' PET Team

John Radford, **University of Manchester** and RAPID co-investigators

Peter Johnson, **University of Southampton** and RATHL co-investigators

National Addiction Centre

Institute of Psychiatry at The Maudsley

King's College London

Naloxone without the needle: Developing naloxone for public use

Professor Sir John Strang

National Addiction Centre, King's College London, UK

Declarations (personal & institutional)

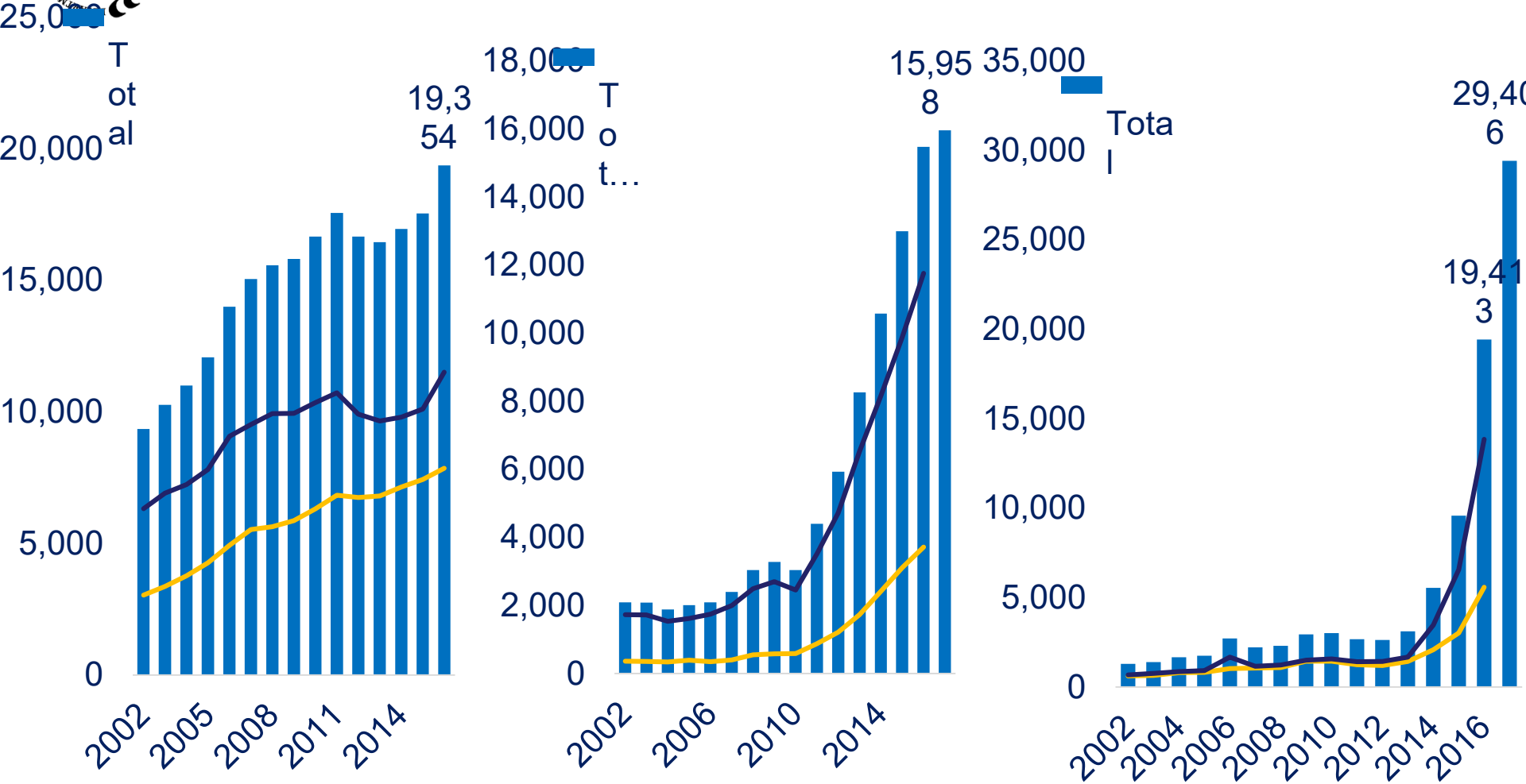
- NHS provider (community & in-patient); also Phoenix House, Lifeline, Clouds House, KCA (Kent Council on Addictions).
- Dept of Health, NTA, Home Office, NACD, EMCDDA, WHO, UNODC, NIDA.
- Dialogue and work with pharmaceutical companies re actual or potential development of new medicines for use in the addiction treatment field (incl re naloxone products), including (past 3 years) Martindale, Indivior, MundiPharma, Camurus and trial product supply from iGen and Camurus.
- SSA (Society for the Study of Addiction); UKDPC (UK Drug Policy Commission), and two Masters degrees (taught MSc and IPAS) and an Addictions MOOC.
- Work also with several charities (and received support) including Action on Addiction, and also with J Paul Getty Charitable Trust (JPGT) and Pilgrim Trust.
- The university (King's College London) has registered intellectual property on a buccal naloxone formulation, and JS has been named in a patent registration by a Pharma company as inventor of a novel concentrated naloxone nasal spray.

My thanks and acknowledgments

- PhD students/post-docs Dr Basak Tas & Dr Rebecca McDonald
- Colleagues - academic, clinical, policy
- Clinical teams - innovators and early adopters
- Drug users advocacy groups and individuals
- Diverse funders - government, research, charities
- Families and groups addressing overdose deaths

National Institute on Drug Abuse

U.S. National Opioid Overdose Deaths

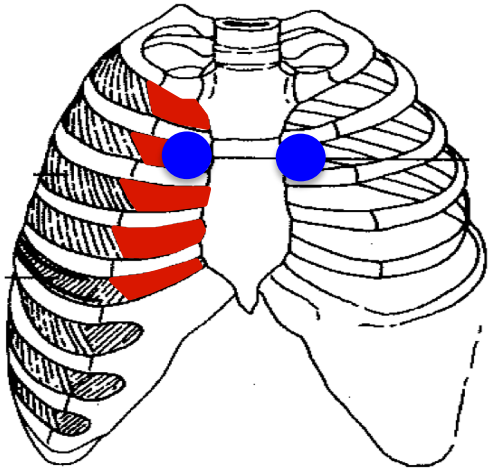


e: National Center for Health Statistics, CD

: National Center for Health Statistics, CDC V

Confidential - some new data from study of heroin intravenous administration at different doses - showing ‘normal dose’

work by Dr Basak Tas
with Professor Sir John Strang and Dr Caroline Jolley
- within the Clinical Research Facility



Keynote structure

Opioid overdose deaths: a global problem

Impact #1 - Concept of take-home naloxone

Impact #2 - Influence on policy & practice

Impact #3 - Non-injectable naloxone

Take-Home Naloxone - the concept

- Simple concept
  - most OD events in the presence of others,
  - willingness to resusc,
  - time is critical

(1996)

First serious consideration:

Strang J, Darke S, Hall W, Farrell M & Ali R (1996) **Heroin overdose: the case for take-home naloxone.** *British Medical Journal*, 312: 1435.

*** key points ***

Keynote structure

Opioid overdose deaths: a global problem

Impact #1 - Conception of take-home naloxone

Impact #2 - Influence on policy & practice

Impact #3 - Non-injectable naloxone

Current News

Archive Speeches and statements

Archive Media Briefings

News Archive

This week's news

Last week's news

Archive

Or search the news archive for:

Search

News archive by Topic

Agriculture

Arts and Culture

News

Listen

Naloxone kits issued across Scotland

31/07/2012

The Scottish Government today welcomed figures that show naloxone is being distributed the length and breadth of Scotland and is being made available to those at risk of opiate overdose.

Scotland was the first country in the world to announce a national naloxone programme, in November 2010. The programme is centrally coordinated and funded by the Scottish Government, empowering individuals, families, friends and communities to reverse an opiate overdose. Naloxone provides more time for an ambulance to arrive and further treatment to be given to those in opiate overdose situations.

Figures published today show that 3,445 naloxone kits were issued in Scotland in 2011/12 through this national programme. Scottish Government investment in the programme funds a national coordinator based at the Scottish Drugs Forum and support to Alcohol and Drugs Partnerships and Health Boards to enable them to deliver naloxone training and supply naloxone kits to people at risk.

(2015; updated 2019)

GOV.UK

Guidance

Widening the availability of naloxone

Updated 18 February 2019

Contents

Naloxone is the emergency antidote for overdoses caused by heroin and other opiates or opioids (such as methadone, morphine and fentanyl).

The main life-threatening effect of heroin and other opiates is to slow down and stop breathing. Naloxone blocks this effect and reverses the breathing difficulties.

Naloxone is a prescription-only medicine, so pharmacies cannot sell it over the counter. But drug services can supply it without a prescription. And anyone can use it to save a life in an emergency.

1. Drug services can supply naloxone without a prescription

Under regulations that came into force in October 2015, people working in or for drug treatment services can, as part of their role, supply naloxone to others that their drug

(2014)

Community management of opioid overdose

Recommendation

People likely to witness an opioid overdose should have access to naloxone and be instructed in its administration to enable them to use it for the emergency management of suspected opioid overdose.

World Health Organization

UNODC
United Nations Office on Drugs and Crime

(2013; UNGASS 2016)

World Health Organization

DISCUSSION PAPER
UNODC/WHO 2013

Opioid overdose: preventing and reducing opioid overdose mortality

Keynote structure

Opioid overdose deaths: a global problem

Impact #1 - Concept of take-home naloxone

Impact #2 - Influence on policy & practice

Impact #3 - Non-injectable naloxone

Contents lists available at ScienceDirect

Drug and Alcohol Dependence (2016)

journal homepage: www.elsevier.com/locate/drugalcdep

Review

Naloxone without the needle – systematic review of candidate routes for non-injectable naloxone for opioid overdose reversal

John Strang[a,*,1], Rebecca McDonald[a,1], Abdulmalik Alqurshi[b], Paul Royall[b], David Taylor[b,c], Ben Forbes[b]

[a] National Addiction Centre, Addictions Department, Institute of Psychiatry, Psychology and Neuroscience (IoPPN), King's College London, 4 Windsor Walk, Denmark Hill, London SE5 8BB, UK
[b] Institute of Pharmaceutical Science, King's College London, 150 Stamford Street, London SE1 9NH, UK
[c] Pharmacy Department, South London and Maudsley NHS Foundation Trust (SLaM), Maudsley Hospital, Denmark Hill, London SE5 8AZ, UK

ARTICLE INFO

Article history:
Received 4 November 2015
Received in revised form 24 February 2016
Accepted 28 February 2016
Available online xxx

Keywords:
Naloxone
Drug development
Heroin
Opioid
Overdose
Deaths
Nasal
Buccal
Sublingual

ABSTRACT

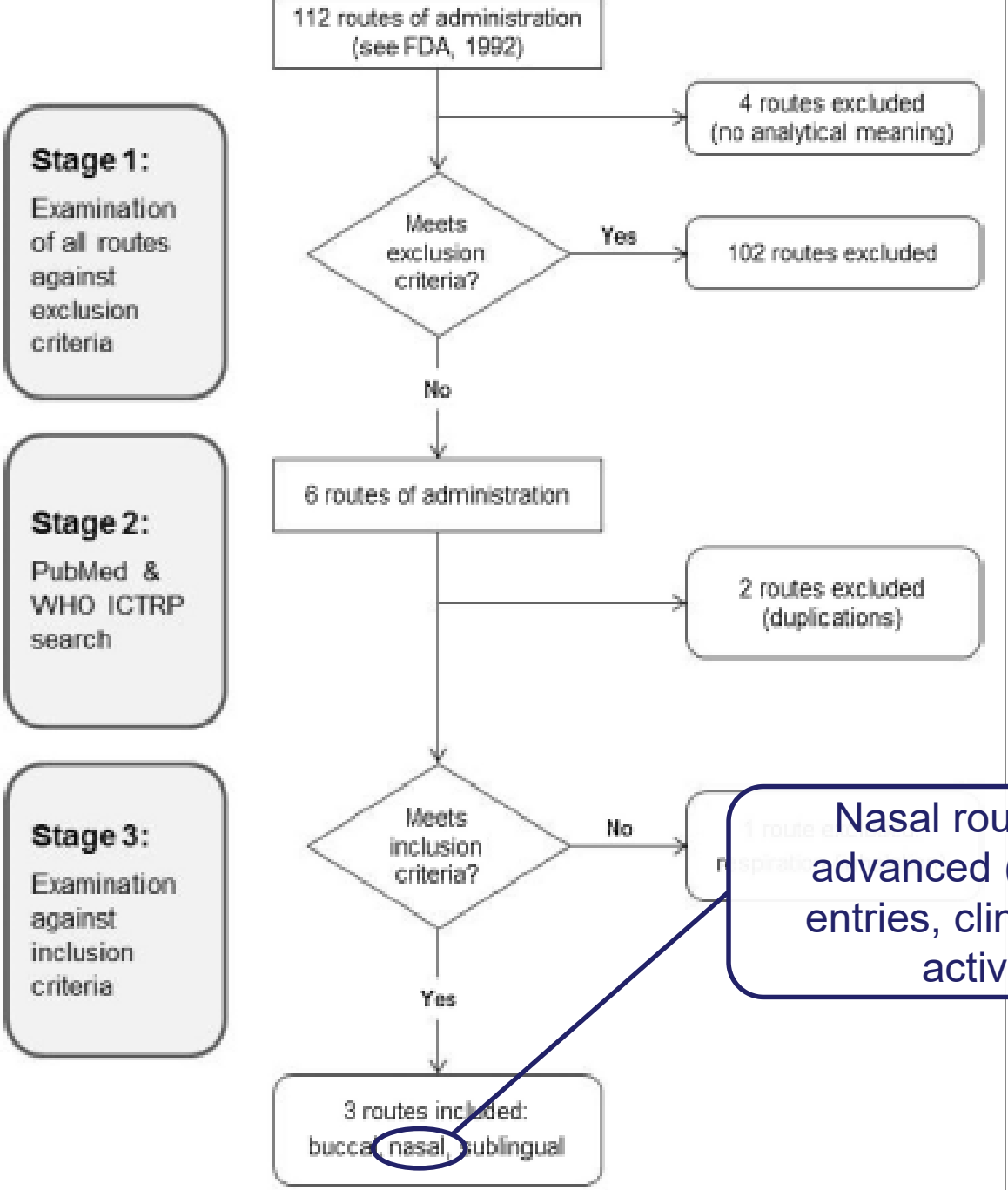
Introduction: Deaths from opioid overdose can be prevented through administration of the antagonist naloxone, which has been licensed for injection since the 1970s. To support wider availability of naloxone in community settings, novel non-injectable naloxone formulations are being developed, suitable for emergency use by non-medical personnel.

Objectives: 1) Identify candidate routes of injection-free naloxone administration potentially suitable for emergency overdose reversal; 2) consider pathways for developing and evaluating novel naloxone formulations.

Methods: A three-stage analysis of candidate routes of administration was conducted: 1) assessment of all 112 routes of administration identified by FDA against exclusion criteria. 2) Scrutiny of empirical data for identified candidate routes, searching PubMed and WHO International Clinical Trials Registry Platform using search terms "naloxone AND [route of administration]". 3) Examination of routes for feasibility and against the inclusion criteria.

Results: Only three routes of administration met inclusion criteria: nasal, sublingual and buccal. Products are currently in development and being studied. Pharmacokinetic data exist only for nasal naloxone, for which product development is more advanced, and one concentrated nasal spray was granted licence in the US in 2015. However, buccal naloxone may also be viable and may have different characteristics.

Conclusion: After 40 years of injection-based naloxone treatment, non-injectable routes are finally being developed. Nasal naloxone has recently been approved and will soon be field-tested, buccal naloxone holds promise, and it is unclear what sublingual naloxone will contribute. Development and approval of reliable non-injectable formulations will facilitate wider naloxone provision across the community internationally.



Nasal route most advanced (PubMed entries, clinical trials activity)

Fig. 1. Selection process of candidate routes of administration.

ADDICTION

RESEARCH REPORT

(2018)

doi:10.1111/add.14033

Pharmacokinetics of concentrated naloxone nasal spray for opioid overdose reversal: Phase I healthy volunteer study*

Rebecca McDonald[1], Ulrike Lorch[2], Jo Woodward[3], Björn Bosse[4], Helen Dooner[3], Gill Mundin[3], Kevin Smith[3] & John Strang[1]

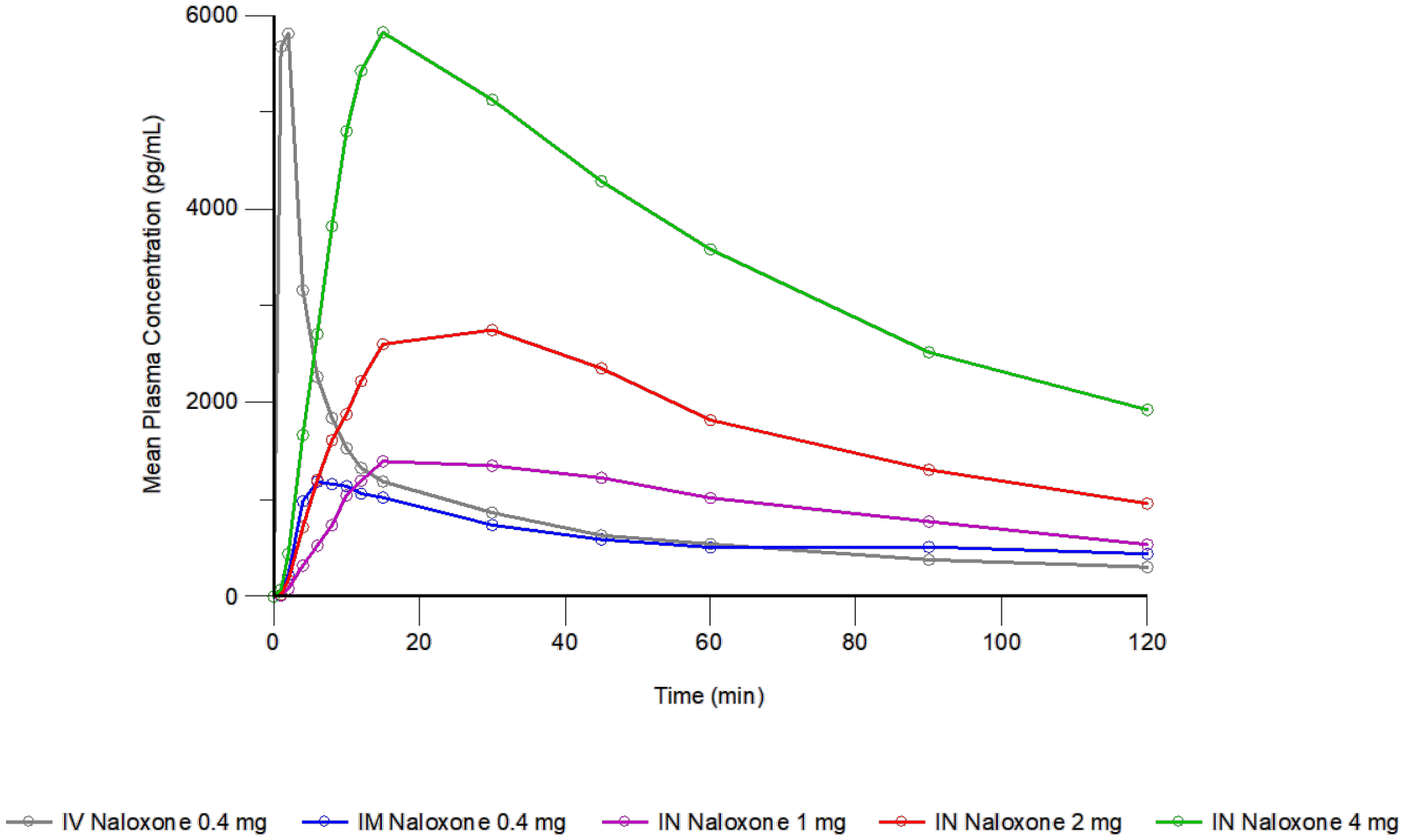
National Addiction Centre, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK,[1] Richmond Pharmacology Ltd, Croydon University Hospital (Woodcroft Wing), Croydon, UK,[2] Mundipharma Research Ltd, Cambridge Science Park, Cambridgeshire, UK[3] and Mundipharma Research GmbH and Co. KG, Limburg, Germany[4]

ABSTRACT

Background and Aims Take-home naloxone can prevent death from heroin/opioid overdose, but pre-provision is difficult because naloxone is usually given by injection. Non-injectable alternatives, including naloxone nasal sprays, are currently being developed. To be effective, the intranasal (i.n.) spray dose must be adequate but not excessive, and early absorption must be comparable to intramuscular (i.m.) injection. We report on the pharmacokinetics (PK) of a specially produced concentrated novel nasal spray. The specific aims were to: (1) estimate PK profiles of i.n. naloxone, (2) compare early systemic exposure with i.n. versus i.m. naloxone and (3) estimate i.n. bioavailability. **Design** Open-label, randomized, five-way cross-over PK study. **Setting** Clinical trials facility (Croydon, UK). **Participants** Thirty-eight healthy volunteers (age 20–54 years; 11 female). **Intervention and comparator** Three doses of i.n. (1 mg/0.1 ml, 2 mg/0.1 ml

Key findings: Naloxone mean PK profile

Adding PK data for IntraNasal (IN 2mg)




Nasale
Anwendung
NYXOID 1.8 mg
naloxone
nasal spray
NYXOID 1.8 mg
naloxone
nasal spray
NYXOID 1.8 mg
nasal spray, solution
in a single-dose container
Naloxone

molecular pharmaceutics

(2016)

Article

pubs.acs.org/molecularpharmaceutics

Amorphous Formulation and *in Vitro* Performance Testing of Instantly Disintegrating Buccal Tablets for the Emergency Delivery of Naloxone

Abdulmalik Alqurshi,[†] Zahrae Kumar,[†] Rebecca McDonald,[‡] John Strang,[‡] Asma Buanz,[§] Shagufta Ahmed,[∥] Elizabeth Allen,[∥] Peter Cameron,[⊥] James A. Rickard,[⊥] Verity Sandhu,[⊥] Chris Holt,[⊥] Rebecca Stansfield,[⊥] David Taylor,[†] Ben Forbes,[†] and Paul G. Royall*[,†]

[†]Institute of Pharmaceutical Science, King's College London, Franklin-Wilkins Building, 150 Stamford Street, London, U.K., SE1 9NH

[‡]Institute of Psychiatry, Psychology & Neuroscience (IoPPN), King's College London (National Addiction Centre), Addictions Sciences Building, 4 Windsor Walk, Denmark Hill, London, U.K., SE5 8BB

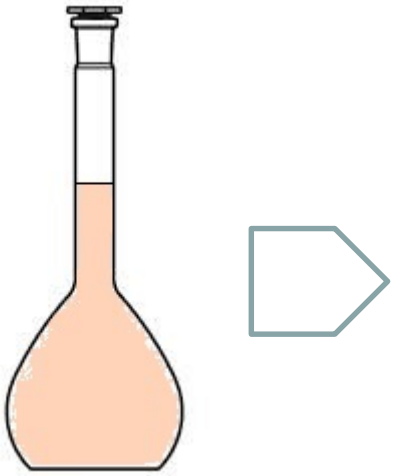
[§]UCL School of Pharmacy, University College London, 29-39 Brunswick Square, London, U.K., WC1N 1AX

[∥]Quintiles Ltd, Quintiles Drug Research Unit at Guy's Hospital, 6 Newcomen Street London, U.K., SE1 1YR

[⊥]Guy's and St Thomas' NHS Foundation Trust Pharmacy Manufacturing Unit, Guy's Hospital, Great Maze Pond, London, U.K., SE1 9RT

3 | Naloxone Instant Melt Tablet Development

SOLUTION → FREEZE → DRY → TABLET



Ice Water vapour

Temperature / Pressure

Stock solution
Naloxone and pharmaceutical grade excipients in water for injection

Solution pipetted into blister wells (top) and frozen (bottom) ready for lyophilisation

Frozen tablets lyophilised using tailored temperature and pressure cycle

Instant melt tablet

Conclusion

Impact #1 - Concept of take-home naloxone

Impact #2 - Influence on policy & practice

Impact #3 - Non-injectable naloxone

thebmj

BMJ 2014;349:g6580 doi: 10.1136/bmj.g6580

EDITORIALS

(2014)

Take-home emergency naloxone to prevent deaths from heroin overdose

Now enough experience to justify it

John Strang *professor*[1], Sheila M Bird *professor*[2], Paul Dietze *professor*[3], Gilberto Gerra *chief*[4], A Thomas McLellan *chief executive officer*[5]

[1]National Addiction Centre (Institute of Psychiatry and The Maudsley), King's College London, London SE5 8AF, UK; [2]Biostatistics Unit, Cambridge CB2 0SR, UK ; [3]Burnet Institute, Melbourne, Australia; [4]UNODC Drug Prevention and Health Branch Division, United Nations Office on Drugs and Crime, Vienna, Austria; [5]Treatment Research Institute, Philadelphia, PA 19106, USA

A paradigm shift is occurring in the treatment of heroin overdose. On 5 November the World Health Organization launched guidelines on the community management of heroin

In 2012, a United Nations resolution identified the need for more effective prevention of drug overdose, including the use of naloxone.[6] The same year, the first large scale randomised

Naloxone Monograph from EMCDDA (European Monitoring Centre on Drugs and Drug Addiction) (2016)

European Monitoring Centre for Drugs and Drug Addiction

INSIGHTS EN 20

264

Preventing opioid overdose deaths with take-home naloxone

(2016)

Editors
John Strang and Rebecca McDonald
National Addiction Centre, Addictions Department, Institute of Psychiatry, Psychology & Neuroscience, King's College London, United Kingdom

EMCDDA project group
Dagmar Hedrich and Roland Simon

http://www.emcdda.europa.eu/news/2016/1/preventing-opioid-overdose-naloxone

Thank you

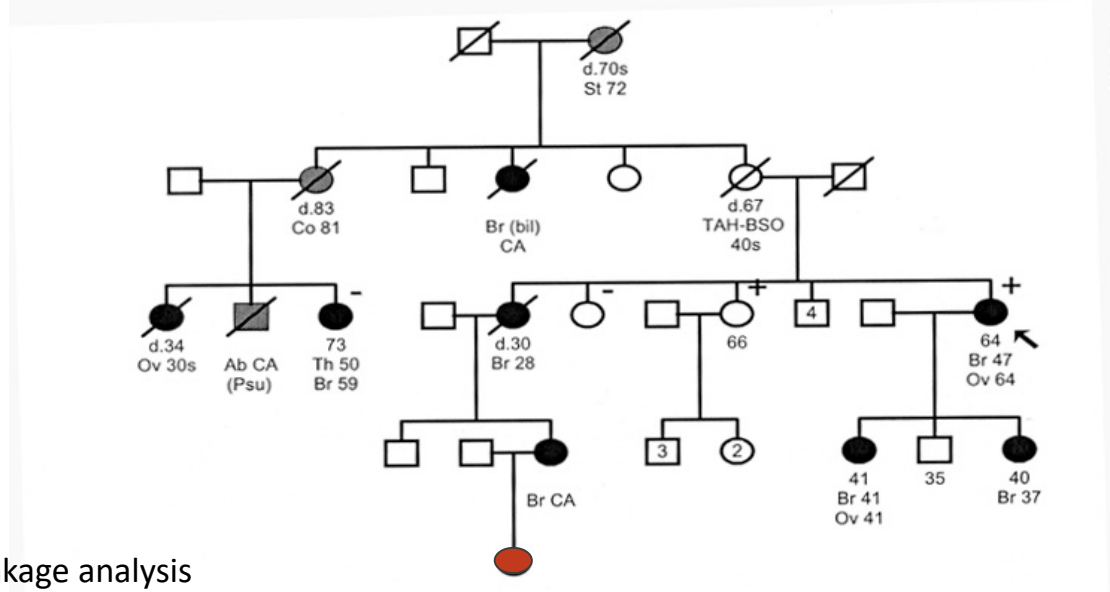
First Targeted Treatment for Hereditary Cancer

Professor Andrew Tutt // 16th May 2019

Director - Breast Cancer Now Research Centre, King's Health Partners and Institute of Cancer Research London

In mid 90s a global team tracked DNA in families to find 2 gene loci causing breast/ovarian cancer

Families with many members with
Breast and ovarian cancer



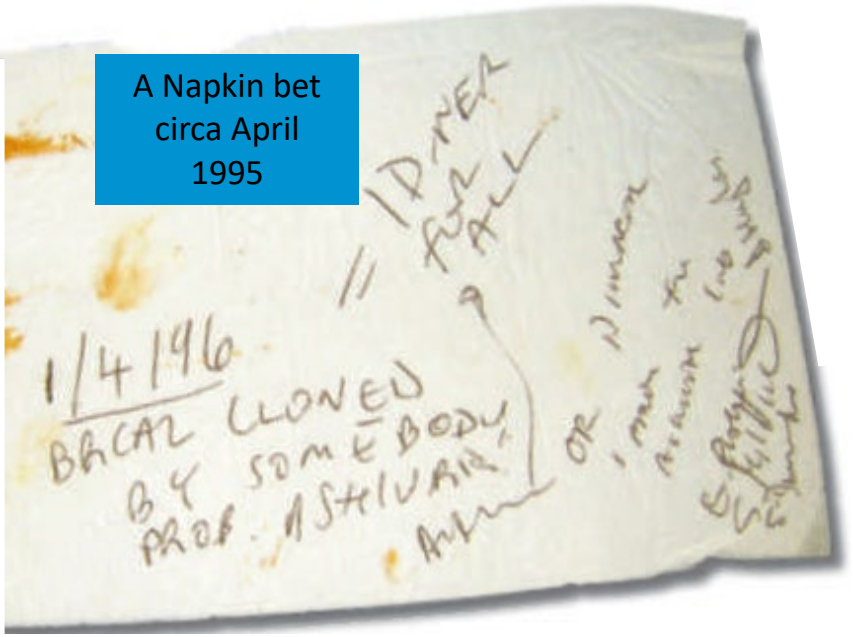
DNA linkage analysis
Linked cancer risk to changes DNA somewhere in small region of chromosome 13

Science teams race to clone responsible genes (BRCA1&2) to change practice in the clinic - UK Academics win on BRCA2

Dec 1995 **LETTERS TO NATURE**

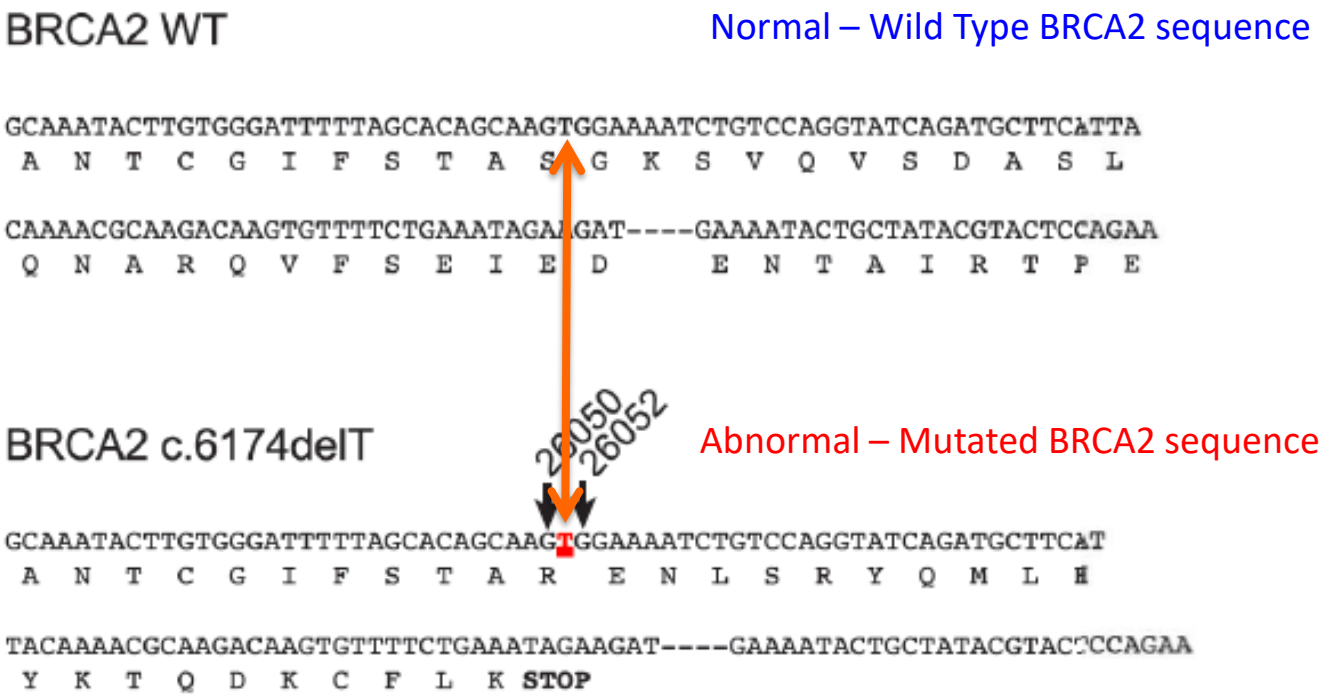
Identification of the breast cancer susceptibility gene *BRCA2*

Richard Wooster*, Graham Bignell*, Jonathan Lancaster‡, Sally Swift†, Sheila Seal*, Jonathan Mangion*, Nadine Collins*, Simon Gregory§, Curtis Gumbs‖, Gos Micklem§, Rita Barfoot*, Rifat Hamoudi*, Sandeep Patel*, Catherine Rice§, Patrick Biggs*, Yasmin Hashim*, Amanda Smith†, Frances Connor†, Adalgeir Arason¶, Julius Gudmundsson¶, David Ficenec¶*** David Kelsell#, Deborah Ford☆, Patricia Tonin**, D. Timothy Bishop††, Nigel K. Spurr#, Bruce A. J. Ponder‡‡, Rosalind Eeles*, Julian Peto☆, Peter Devilee§§, Cees Cornelisse§§, Henry Lynch‖ , Steven Narod**☆☆, Gilbert Lenoir¶¶, Valdgardur Egilsson¶, Rosa Bjork Barkadottir¶, Douglas F. Easton##, David R. Bentley§, P. Andrew Futreal , Alan Ashworth† & Michael R. Stratton*



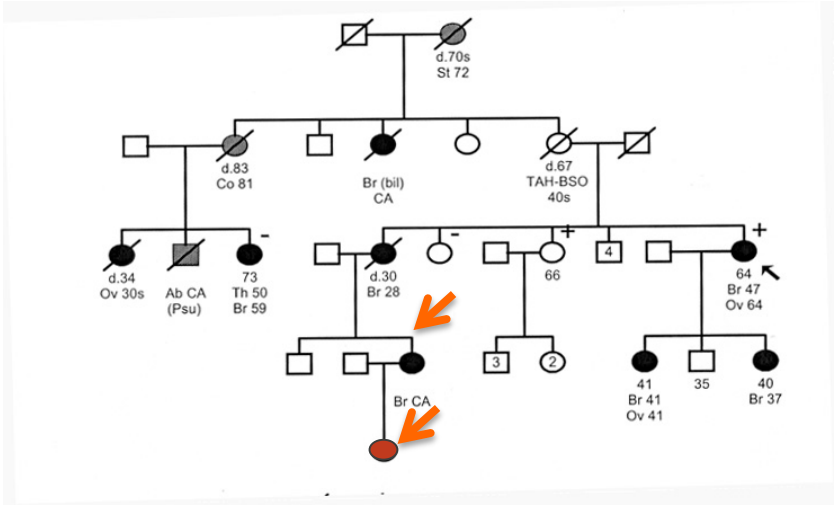
Approximately 10000 bases of coding sequence within a huge gene locus

One missing coding "base" in gene sequence is enough to truncate protein and cause cancer



BRCA2 c.6174delT A common founder mutation in Ashkenazi community

Reading the DNA sequence for the mutation could tell a daughter if she shares mothers risk



NEWS

Gene test spares mother surgery

By Celia Hall
Medical Editor

A WOMAN who decided to have her breasts removed rather than risk developing cancer has avoided surgery thanks to the discovery of a gene.

Healthy and happily married with a baby and a two-year-old, Annmarie Blomfield was within weeks of surgery when she was advised that the discovery of the BRCA1 gene would lead to a test to establish her risk of developing breast cancer.

Three weeks ago, she learned that although she comes from a family with a high incidence of the disease, her chances of getting it are the same as the next woman.

Mrs Blomfield, 30, had her breast cancer gene test as part of a research programme but, from early next year, it will be available for other women whose family history shows a high risk of breast cancer.

The discovery has transformed her life, saved her from surgery and has given her the knowledge that has not passed a dangerous gene mutation to her daughters.

"You hear a lot about gene discoveries and you wonder how they are helping people. It is wonderful to be able to know definitely if you have a problem or not," she said.

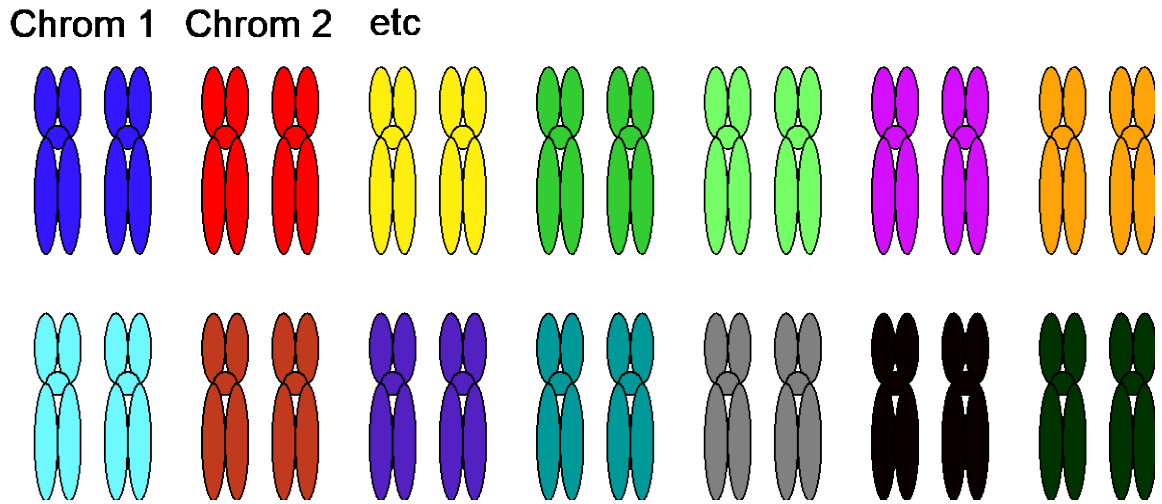
She was one of a growing number of women from "breast cancer families" who opt for mastectomies rather

Bright future: Annmarie Blomfield with her daughters Becky, left, and Joanne

dawned on me slowly," she Mrs Blomfield was setting up tation at the Royal Marsden Hospital, Chelsea. A second

This young mother had a 50% risk of carrying the mutation but could now have sequencing and be spared bilateral prophylactic surgery

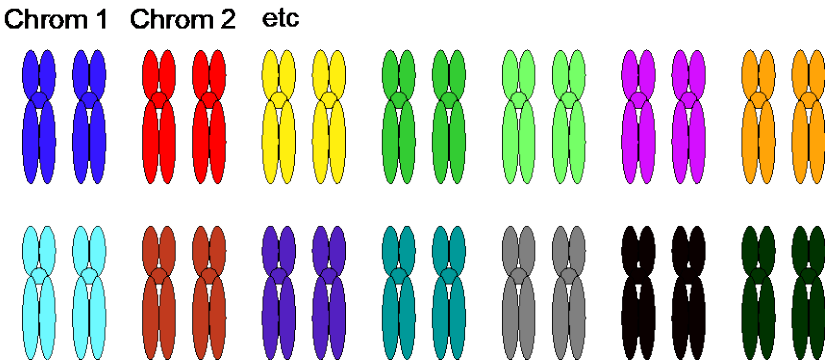
But to treat these genetic cancers in a more targeted way need to understand gene function

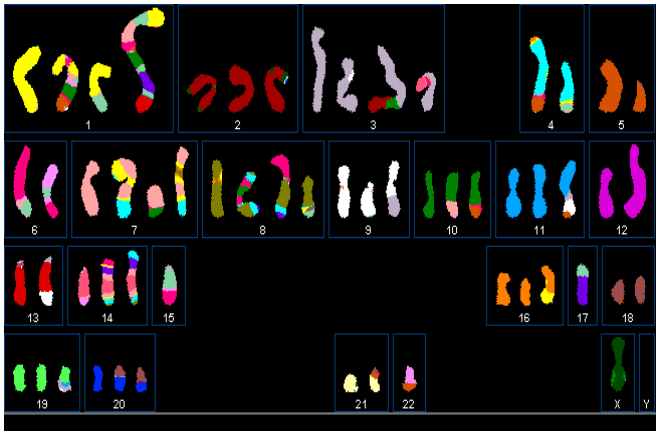


BRCA1 and 2 genes control specialized house keeping DNA repair

Having at least 1 normal copy maintains stability in our genome - preventing cancer

When carriers back up copy fails in ovarian or breast cell the genome scrambles and it gets what needs for malignancy





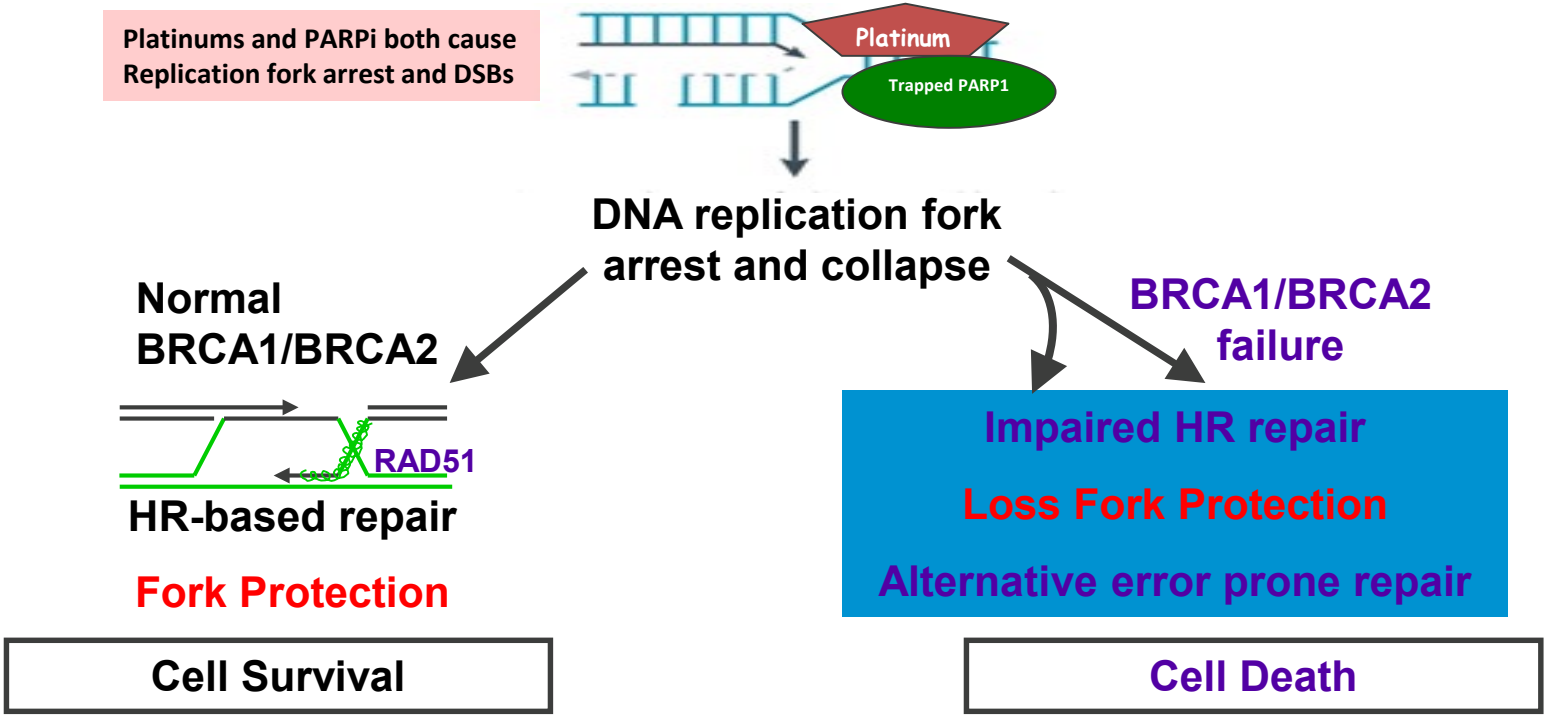
Homologous Recombination
DNA repair

Genome
House keeping

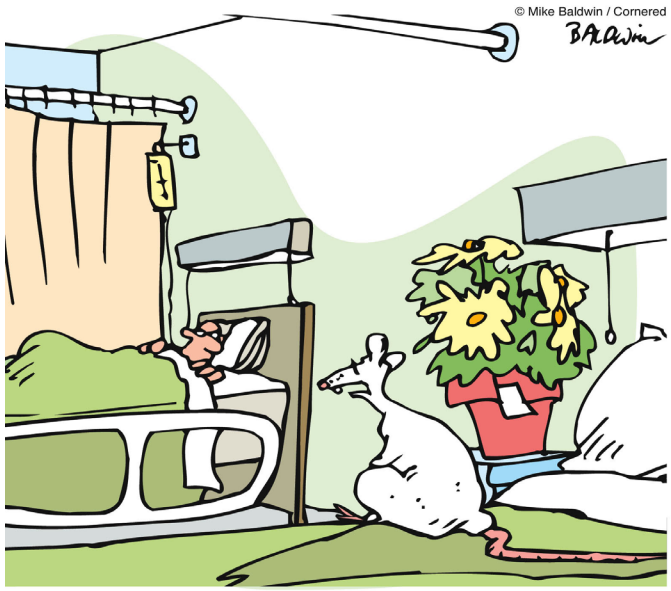
How could we use knowledge to help in those where gene fault had already caused cancer?

- Should my cancer be treated differently by an oncologist?
- Needed re-positioning of current treatments to that target DNA repair defect
- Develop new targeted treatments
- Clinical trials specifically for genetic HBOC

Trapped PARP1 or platinum adducts on DNA stall DNA replication forks and create DNA double strand breaks

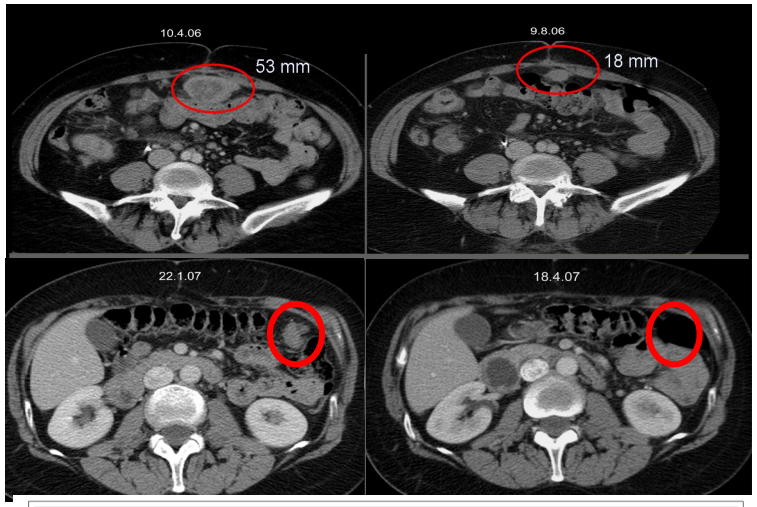


Rapidly partnered pharma and translated to clinic



"I go home today. They cured me using this new miracle drug. I'm afraid it'll be years before it's approved for humans."

Fong P *et al*. N Engl J Med 2009;361:123-34



The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JULY 9, 2009 VOL. 361 NO. 2

Inhibition of Poly(ADP-Ribose) Polymerase in Tumors from *BRCA* Mutation Carriers

Peter C. Fong, M.D., David S. Boss, M.Sc., Timothy A. Yap, M.D., Andrew Tutt, M.D., Ph.D., Peijun Wu, Ph.D., Marja Mergui-Roelvink, M.D., Peter Mortimer, Ph.D., Helen Swaisland, B.Sc., Alan Lau, Ph.D., Mark J. O'Connor, Ph.D., Alan Ashworth, Ph.D., James Carmichael, M.D., Stan B. Kaye, M.D., Jan H.M. Schellens, M.D., Ph.D., and Johann S. de Bono, M.D., Ph.D.

We drove genetic testing biomarker selection trials in *BRCA1/2* mutation carriers with breast and ovarian cancer proving concept

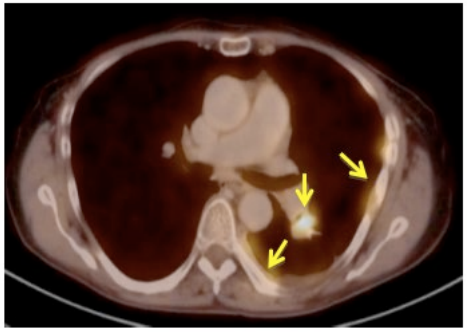
THE LANCET

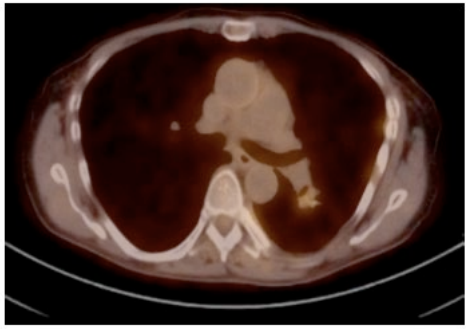
Oral poly(ADP-ribose) polymerase inhibitor olaparib in patients with *BRCA1* or *BRCA2* mutations and advanced breast cancer: a proof-of-concept trial

Andrew Tutt, Mark Robson, Judy E Garber, Susan M Domchek, M William Audeh, Jeffrey N Weitzel, Michael Friedlander, Banu Arun, Niklas Loman, Rita K Schmutzler, Andrew Wardley, Gillian Mitchell, Helena Earl, Mark Wickens, James Carmichael

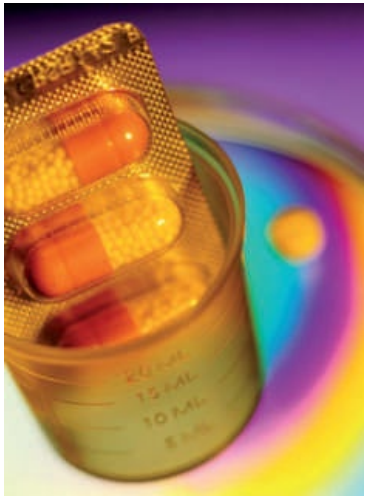
Oral poly(ADP-ribose) polymerase inhibitor olaparib in patients with *BRCA1* or *BRCA2* mutations and recurrent ovarian cancer: a proof-of-concept trial

M William Audeh, James Carmichael, Richard T Penson, Michael Friedlander, Bethan Powell, Katherine M Bell-McGuinn, Clare Scott, Jeffrey N Weitzel, Ana Oaknin, Niklas Loman, Karen Lu, Rita K Schmutzler, Ursula Matulonis, Mark Wickens, Andrew Tutt



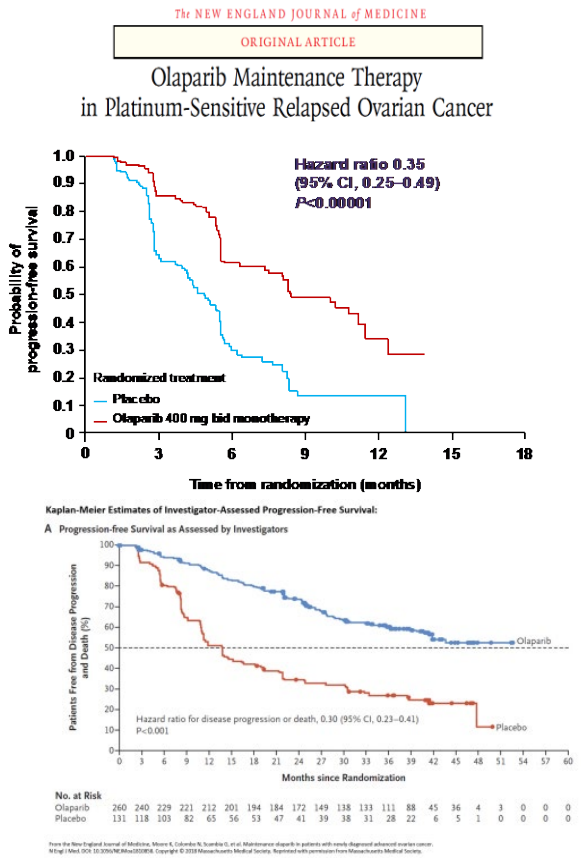


Tutt et al *The Lancet* 2010 376(9737)
Audeh et al *The Lancet* 2010 376(9737)



Patients demand to be tested more rapidly and frequently

Our work stimulated global trials of PARP inhibitors to delay recurrence in *BRCA1/2* mutated ovarian Cancer



FDA News Release

FDA approves Lynparza to treat advanced ovarian cancer

First LDT companion diagnostic test also approved to identify appropriate patients

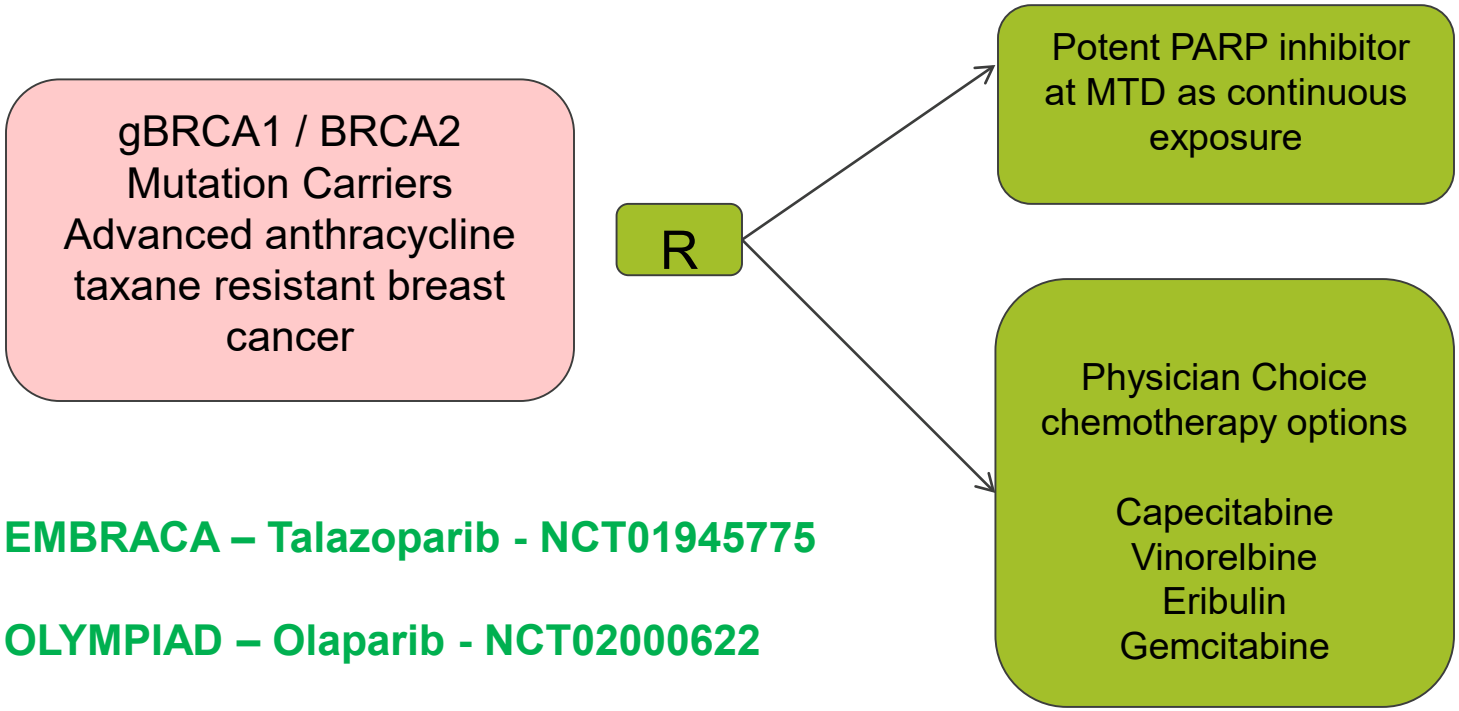
For Immediate Release December 19, 2014

"Today's approval constitutes the first of a new class of drugs for treating ovarian cancer," said Richard Pazdur, MD, director of the Office of Hematology and Oncology Products in the FDA's Center for Drug Evaluation and Research. "Lynparza is approved for patients with specific abnormalities in the BRCA gene and is an example of how a greater understanding of the underlying mechanisms of disease can lead to targeted, more personalized treatment.

Licenses for 3 other PARP inhibitors followed in ovarian cancer

Ledermann J *et al*. *N Engl J Med* 2012;366:1382–1392
Moore et al N Engl J Med. 2018 Dec 27;379(26):2495-2505

We led academic genetic oncologists to work with Pharma to test PARP inhibitors Vs Chemo



EMBRACA – Talazoparib - NCT01945775

OLYMPIAD – Olaparib - NCT02000622

PARPi improve disease control and quality of life preservation compared to chemotherapy

FDA U.S. FOOD & DRUG ADMINISTRATION

Home | Food | Drugs | Medical Devices

News & Events

Home > News & Events > Newsroom > Press Annou

FDA News Release

FDA approves first tre with a certain inherite

SHARE TWEET LINKEDIN PIN IT EM

For Immediate Release January 12, 2018

FDA U.S. FOOD & DRUG ADMINISTRATION

A to Z Index | Follow FDA | En Español

Search FDA

Home | Food | Drugs | Medical Devices | Radiation-Emitting Products | Vaccines, Blood & Biologics | Animal & Veterinary | Cosmetics | Tobacco Products

Drugs

Home > Drugs > Drug Approvals and Databases > Approved Drugs

- Approved Drugs
- Hematology/Oncology (Cancer) Approvals & Safety Notifications
- Drug Information Soundcast in Clinical Oncology (D.I.S.C.O.)
- Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book)

FDA approves talazoparib for gBRCAm HER2-negative locally advanced or metastatic breast cancer

SHARE TWEET LINKEDIN PIN IT EMAIL PRINT

On October 16, 2018, the Food and Drug Administration approved talazoparib (TALZENNA, Pfizer Inc.), a poly (ADP-ribose) polymerase (PARP) inhibitor, for patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm), HER2-negative locally advanced or metastatic breast cancer. Patients must be selected for therapy based on an FDA-approved companion diagnostic for talazoparib.

Approval was based on EMBRACA (NCT01945775), an open-label trial randomizing 431 patients (2:1) with gBRCAm HER2-negative locally advanced or metastatic breast cancer to receive talazoparib (1 mg) or physician's choice of chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine). All patients were required to have a known deleterious or suspected deleterious gBRCA mutation and must have received no more than 3 prior cytotoxic chemotherapy regimens for locally advanced or metastatic disease. Patients were required to have received treatment with an anthracycline and/or a taxane (unless contraindicated) in the neoadjuvant, adjuvant, and/or metastatic treatment setting.

Time from randomisation (months)

Number of patients at risk															
Olaparib	201	164	134	93	77	56	40	20	15	7	4	2	1	1	0
TPC	93	54	30	19	13	8	7	4	1	0	0	0	0	0	0

Duration of PFS (months)

No. at risk (event/cumulative events)															
Talazoparib	262 (0/0)	212 (26/26)	139 (18/44)	78 (17/61)	44 (7/68)	28 (3/71)	26 (1/72)	20 (0/72)	14 (1/73)	7 (3/76)	4 (0/76)	2 (0/76)	0 (0/76)	0 (0/76)	0 (0/76)
Overall TPC	114 (0/0)	64 (22/22)	30 (17/39)	17 (3/42)	6 (2/44)	1 (3/47)	0 (1/48)	0 (0/48)	0 (0/48)	0 (0/48)	0 (0/48)	0 (0/48)	0 (0/48)	0 (0/48)	0 (0/48)

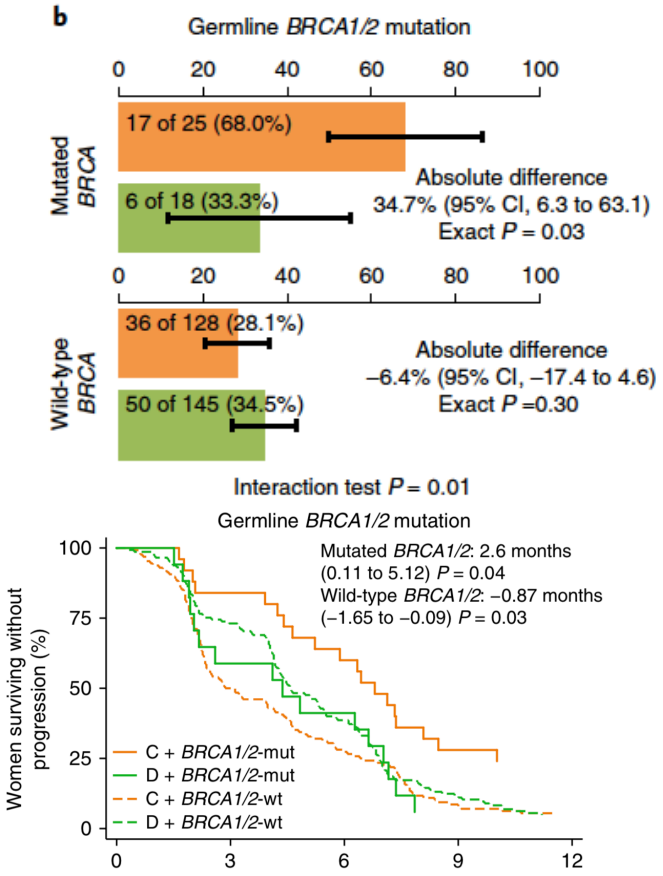
Affordable platinum chemo has double activity in genetic breast and can be applied globally

KHP–ICR TNT Trial is first biomarker stratified Ph III trial published by Nature Medicine

ARTICLES
https://doi.org/10.1038/s41591-018-0009-7
nature medicine

Carboplatin in *BRCA1/2*-mutated and triple-negative breast cancer BRCAness subgroups: the TNT Trial

Andrew Tutt[1,2*], Holly Tovey[3], Maggie Chon U. Cheang[3], Sarah Kernaghan[3], Lucy Kilburn[3], Patrycja Gazinska[2], Julie Owen[4], Jacinta Abraham[5], Sophie Barrett[6], Peter Barrett-Lee[5], Robert Brown[7,8], Stephen Chan[9], Mitchell Dowsett[1,10], James M Flanagan[7], Lisa Fox[3], Anita Grigoriadis[2], Alexander Gutin[11], Catherine Harper-Wynne[12], Matthew Q. Hatton[13], Katherine A. Hoadley[14], Jyoti Parikh[15], Peter Parker[16,17], Charles M. Perou[14], Rebecca Roylance[18], Vandna Shah[2], Adam Shaw[19], Ian E. Smith[20], Kirsten M. Timms[11], Andrew M. Wardley[21], Gregory Wilson[22], Cheryl Gillett[4,23], Jerry S. Lanchbury[11], Alan Ashworth[24], Nazneen Rahman[25,26], Mark Harries[27], Paul Ellis[27], Sarah E. Pinder[4,23] and Judith M. Bliss[3]



KHP leads design and delivery by global team of trial of PARPi as curative therapy for genetic breast cancer

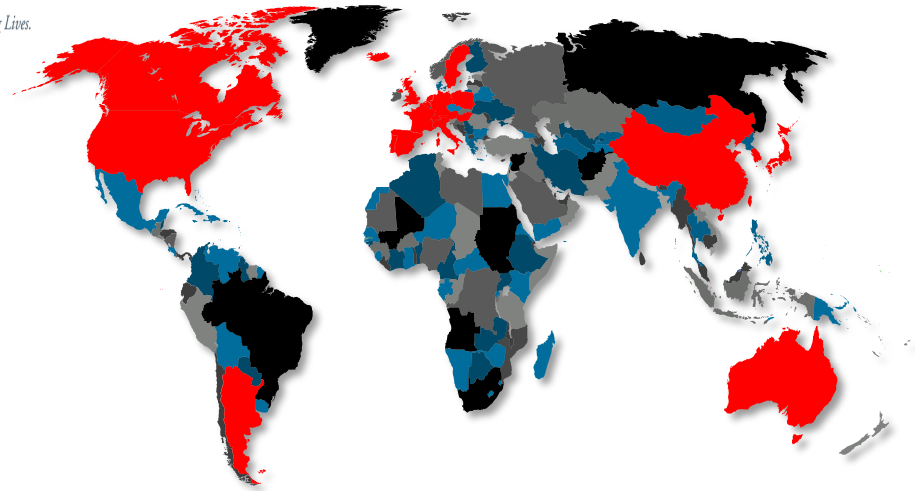
1st April 2019

Completes accrual of 1800 mutation carriers with breast cancer across >650 Hospitals

BIG
Breast International Group

OlympiA
OLaparib in Adjuvant
BRCAm breast cancer

NRG ONCOLOGY
Advancing Research. Improving Lives.



Adjuvant Breast Cancer Trial for 1800 women
***With BRCA1/2* mutation carriers**

AstraZeneca

frontier science

Impacts in clinic

- The first new licensed drug in the clinic for ovarian cancer for many years
- Global PARP inhibitor trials in over 5000 BRCA1/2 carriers across several cancer types with 4 major Pharma companies
- First FDA licensed biomarker selection targeted treatments for Genetic and Triple Negative Forms of Metastatic Breast Cancer
- BRCA1/2 genetics is now integrated in oncology teams globally
- Beyond expensive PARPi the KHP TNT Trial brings highly active affordable carboplatin chemotherapy to BRCA1/2 carriers globally

Acknowledgements

- Specialist BRCA Carrier Clinic Team at KHP
- KHP Breast Team
- TNT Trial Management Group
- OlympiA Trial Team
- Tutt Laboratory KCL and ICR
- Chris Lord laboratory ICR
- Alan Ashworth UCSF
- Jonathan Lederman UCL
- Mark Robson MSKCC
- Jennifer Litton MDACC

KCL BCN Unit at Guy's Cancer Centre

breast cancer now

CANCER RESEARCH UK

Changing antenatal care with pre-eclampsia research

KHP at 10: 2019

Lucy C Chappell
NIHR Research Professor in Obstetrics

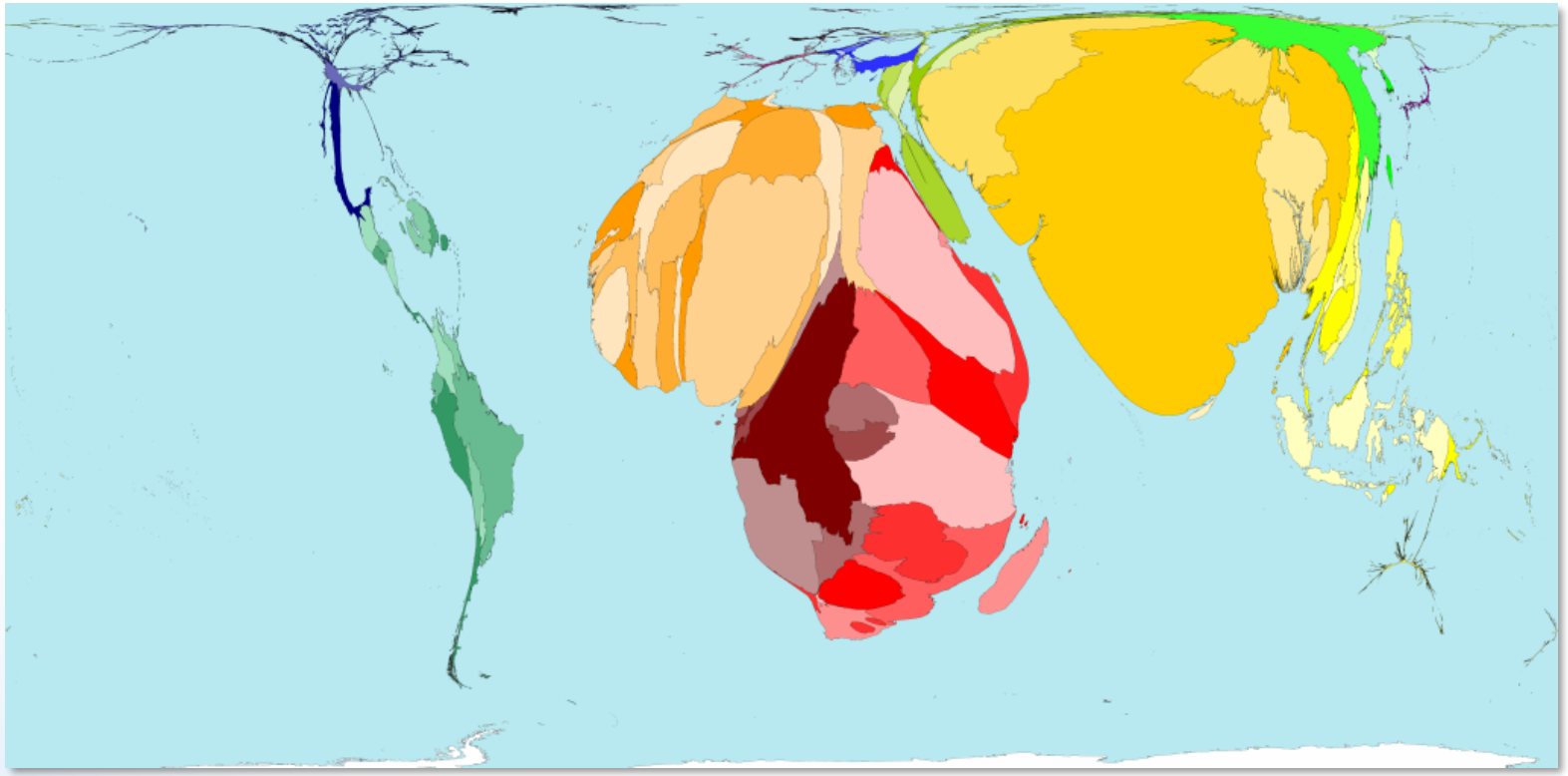
KING'S HEALTH PARTNERS

KING'S College LONDON

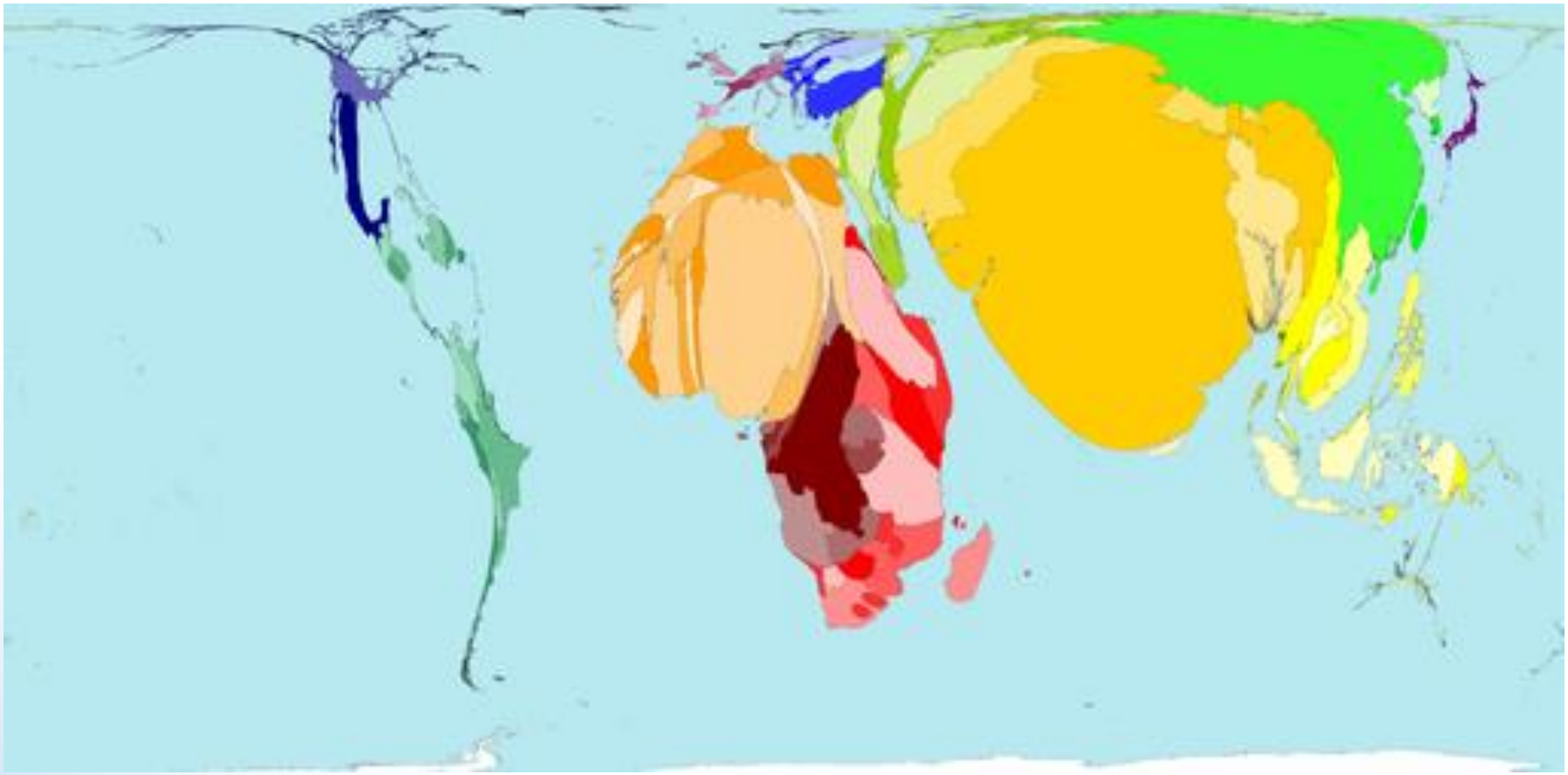
What’s the point of antenatal care?

Bumps in the road

Global map of maternal mortality



Parallel disease burden of stillbirths



Blood pressure checks at antenatal visits

The conundrum of pre-eclampsia: from origin…

Shanmugalingam J Human Hypertens 2019

To clinical manifestation

Antenatal care in 1914

A Case of "Pre-eclampsia" at the Twenty-fourth Week; Acute Toxæmia; Cæsarean Section.

By Victor Bonney, M.S.

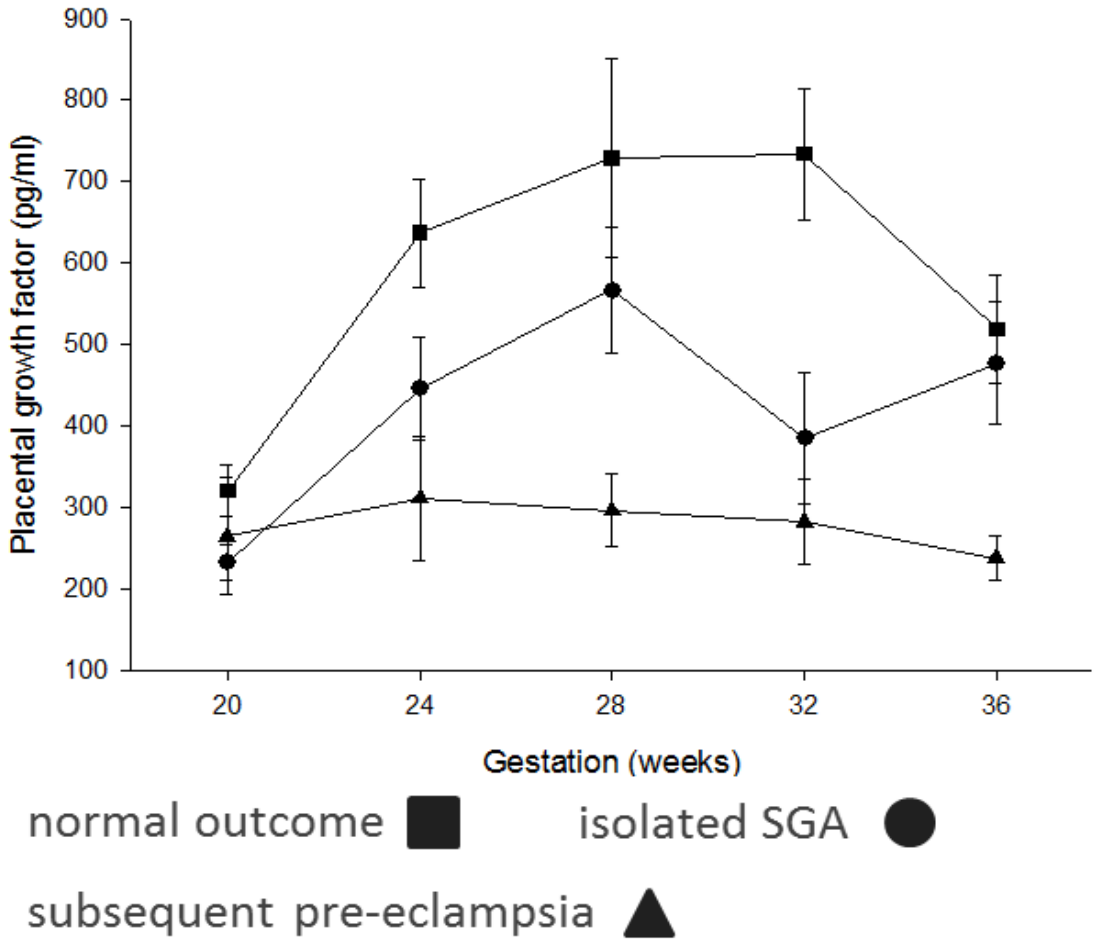
The pulse tension was very high and her sight was now so much impaired that she could only dimly distinguish the figures of those around her.

worse. The urine contained a good deal of blood and enough albumin to solidify on boiling, and the quantity passed *per diem* was much reduced. Moreover, the vomiting was incessant and she could not see

Bonney Proc Roy Soc Med 1914

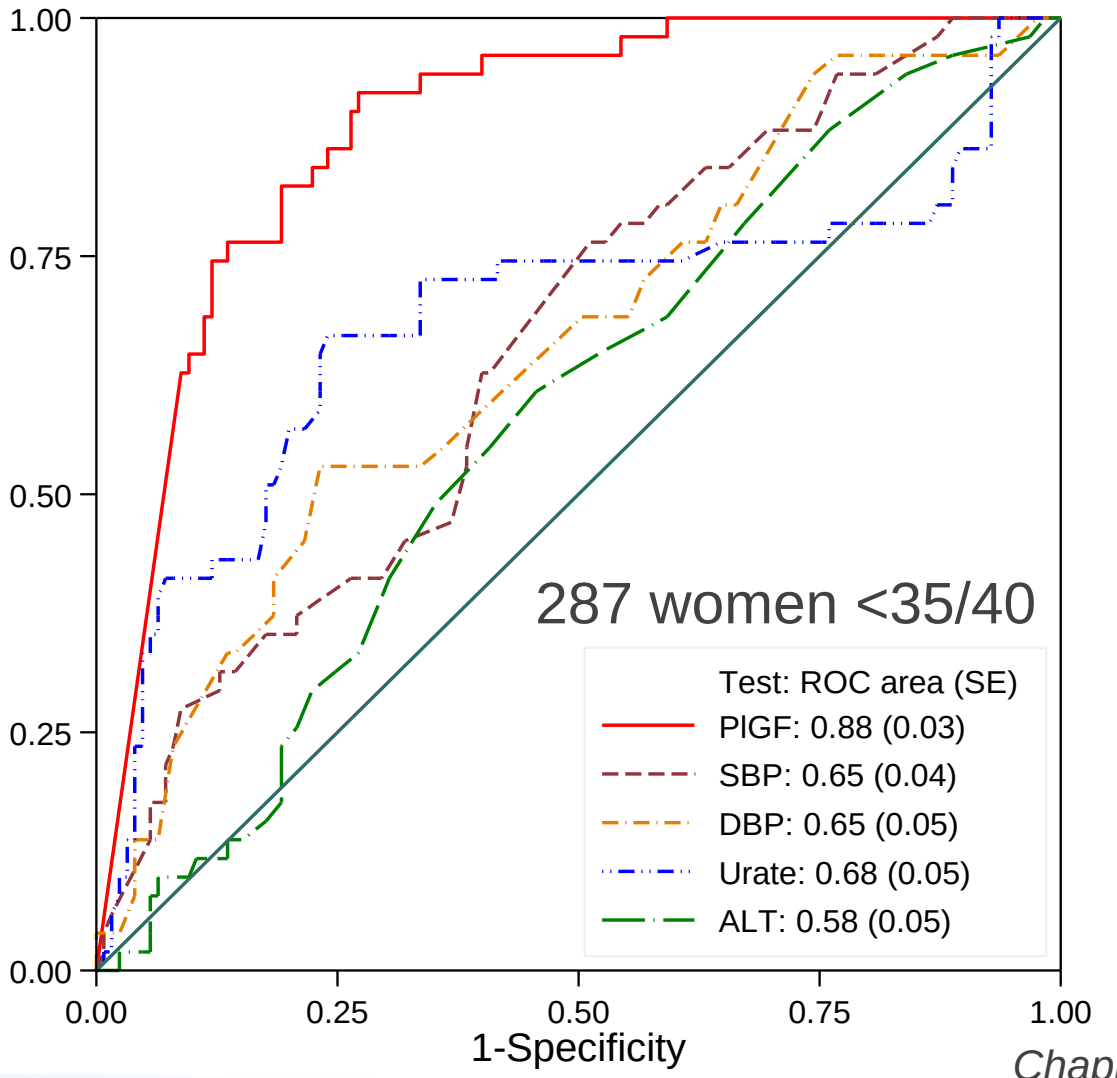
How has our understanding developed?

Prospective longitudinal cohort study (n=63)



Chappell et al 2002

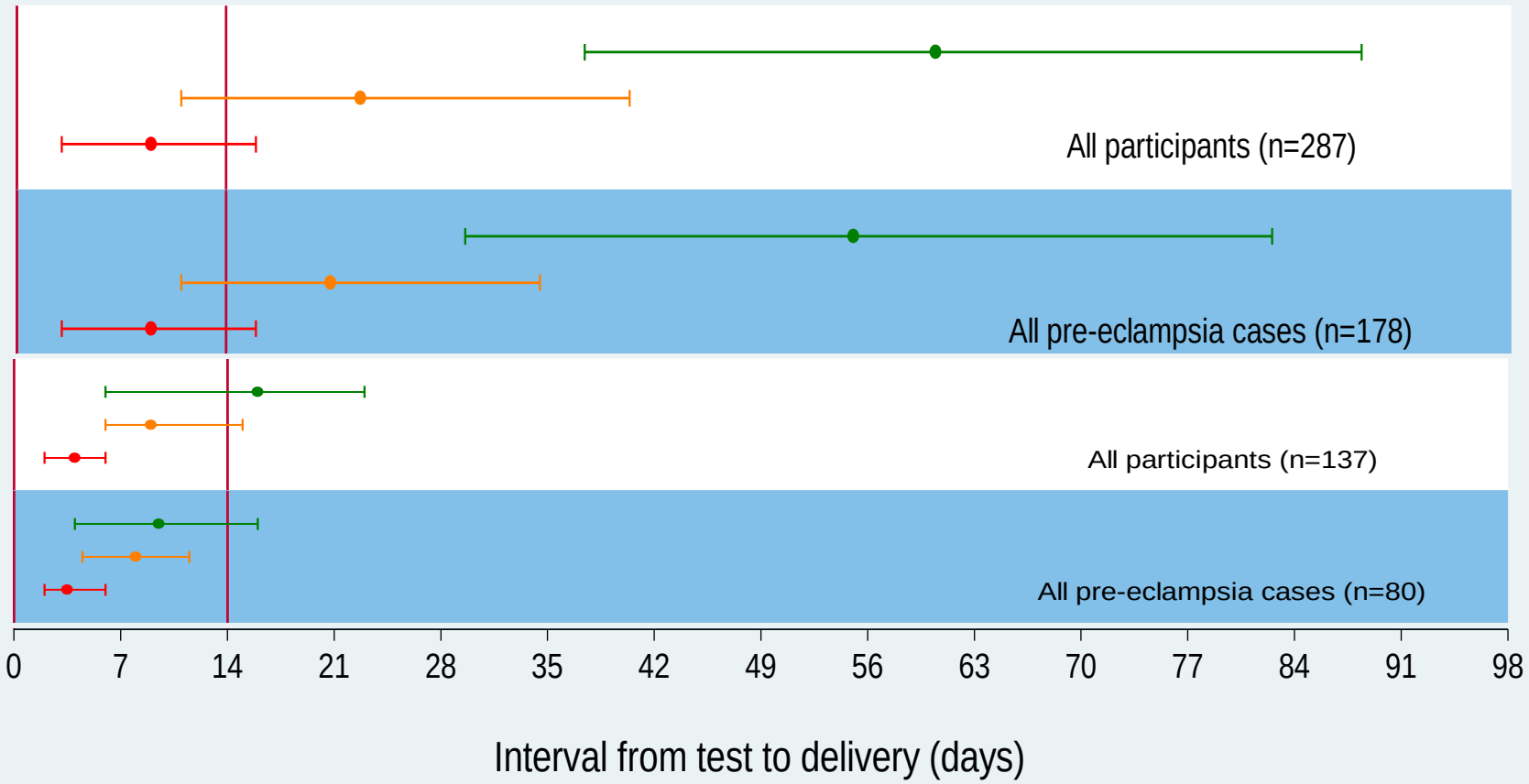
Prospective multi-centre cohort diagnostic accuracy study of PlGF (n=625)



Chappell et al 2013

Time to delivery with very low (red), low (amber), and norma (green) PlGF (results masked to clinicians)

Red line: very low PlGF (<12 pg/mL)
orange line, low PlGF (<5th centile)
green line, normal PlGF (≥5th centile)



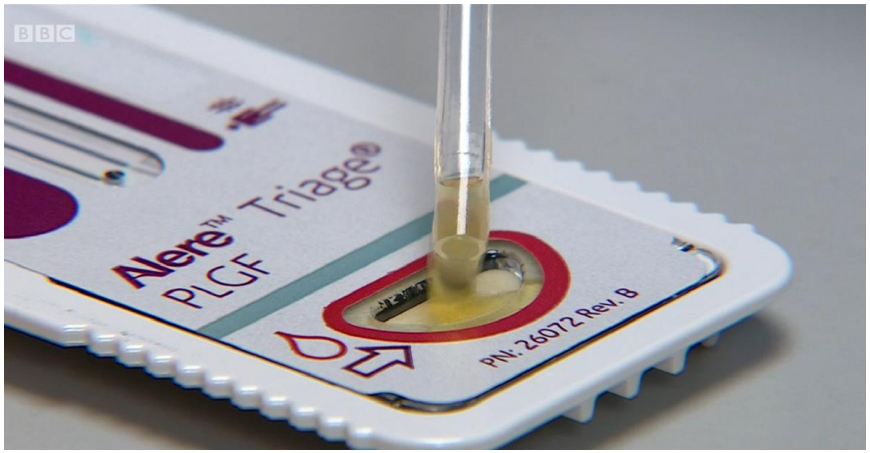
Chappell et al 2013

Trialling a diagnostic test

Placental growth factor testing to assess women with suspected pre-eclampsia: a multicentre, pragmatic, stepped-wedge cluster-randomised controlled trial

Kate E Duhig, Jenny Myers, Paul T Seed, Jenie Sparkes, Jessica Lowe, Rachael M Hunter, Andrew H Shennan, Lucy C Chappell*, on behalf of the PARROT trial group†*

Result in 15 mins



Hypertension in Pregnancy NICE Guidelines

with additional diagnostic test for the PARROT trial

Mild hypertension
BP up to 149/99 mmHg

- **Do not admit to hospital.**
- BP up to 149/99 mmHg
- **Do not treat** hypertension.
- **Measure BP no more than** x1/wk
- **Test for proteinuria** at each visit
- **Carry out routine** antenatal blood tests.
- **If presenting before** 32/40, or at high risk of pre-eclampsia, test for proteinuria and measure BP x2/ wk.

Moderate hypertension
BP 150/100–159/109 mmHg

Do not admit to hospital.

- **Treat hypertension** to keep BP <150/ 80–100 mmHg.
- **Measure BP at least** x2/ wk.
- **Test for proteinuria** at each visit
- **Test kidney function,** electrolytes, FBC, transaminases, bilirubin.
- **No further blood tests** if no subsequent proteinuria.
- Arrange fetal USS

Severe hypertension
BP ≥ 160/110 mmHg

- **Admit to hospital until** BP *≤159/109 mmHg* and **treat hypertension** to keep BP < 150/ 80–100 mmHg.
- **Measure BP at least** x4/ day
- **Test for proteinuria** daily
- **Test kidney function,** electrolytes, FBC, transaminases, bilirubin at presentation & then weekly.
- Arrange fetal USS

Continue care as in guidelines pathway; integrate additional information from PlGF test as shown below

PlGF >100 NORMAL	PlGF 12-100 LOW	PlGF <12 VERY LOW
CONTINUE WITH USUAL MANAGEMENT	CONSIDER INCREASED SURVEILLANCE	ASSESS AS PRE-ECLAMPSIA

Algorithm version 3.0 Jan 2016

Results: effect of PlGF on time to diagnosis

Primary Outcome	Revealed PlGF testing	Concealed PlGF testing	Effect size (adjusted means ratio)
Number of women diagnosed with pre-eclampsia	205 (36.8%)	155 (34.8%)	
Time to diagnosis of pre-eclampsia (days)	1.9 (0.5-9.2)	4.1 (0.8-14.7)	0.39 (0.17-0.91

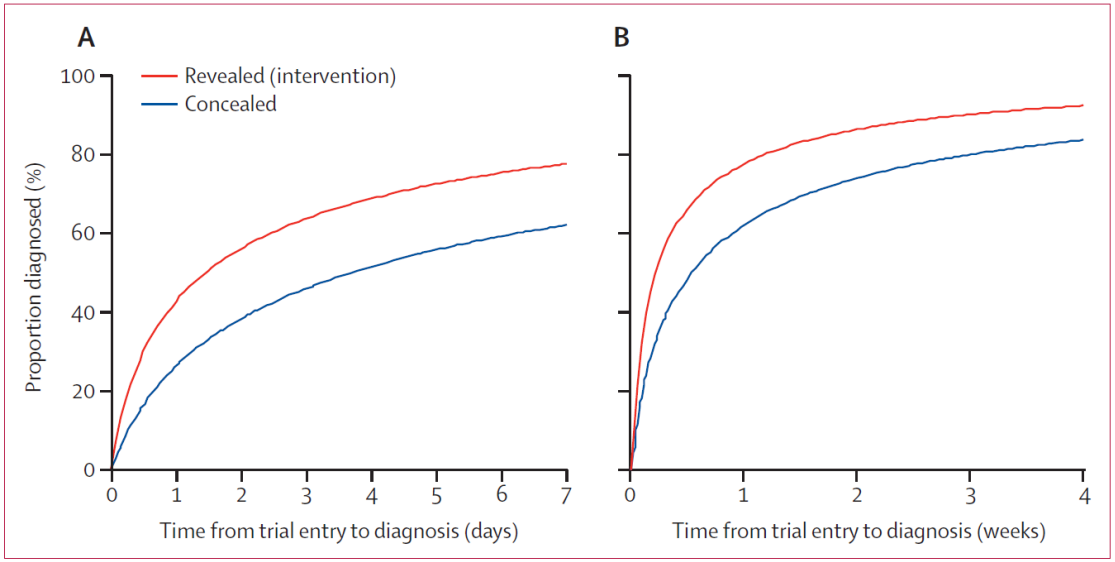


Figure 2: **Proportion of women diagnosed with pre-eclampsia when revealing versus concealing circulating placental growth factor concentrations from clinicians, over days (A) and weeks (B)**
Data are mixed-effects log-normal regression curves.

Duhig et al 2019

Results: effect of PlGF testing on maternal/ perinatal outcomes

Secondary outcomes	Revealed PlGF testing	Concealed PlGF testing	Effect size (adjusted odds ratio)
Maternal severe morbidity	22 (3.8%)	24 (5.4%)	0.32 (0.11-0.96)
Neonatal admission	195 (34.5%)	146 (33.0%)	1.09 (0.66-1.80)
Perinatal adverse outcome	86 (15%)	63 (14.1%)	1.45 (0.73-2.90)

Duhig et al 2019

Impact: new UK national guidance (NICE 2016 and 2019)

PlGF-based testing to help diagnose suspected pre-eclampsia (Triage PlGF test, Elecsys immunoassay sFlt-1/PlGF ratio, DELFIA Xpress PlGF 1-2-3 test, and BRAHMS sFlt-1 Kryptor/BRAHMS PlGF plus Kryptor PE ratio) (DG23)

1 Recommendations

1.1 The Triage PlGF test and the Elecsys immunoassay sFlt-1/PlGF ratio, used with standard clinical assessment and subsequent clinical follow-up, are recommended to help rule-out pre-eclampsia in women presenting with suspected pre-eclampsia between 20 weeks and 34 weeks plus 6 days of gestation.

Table 1 Management of pregnancy with gestational hypertension [2019]

	Degree of hypertension	
	Hypertension: blood pressure of 140/90–159/109 mmHg	**Severe hypertension: blood pressure of 160/110 mmHg or more[a]**
Admission to hospital	Do not routinely admit to hospital.	Admit, but if BP falls below 160/110 mmHg then manage as for hypertension
Antihypertensive pharmacological treatment	Offer pharmacological treatment if BP remains above 140/90 mmHg	Offer pharmacological treatment to all women
Target blood pressure once on antihypertensive treatment	Aim for BP of 135/85 mmHg or less	Aim for BP of 135/85 mmHg or less
Blood pressure measurement	Once or twice a week (depending on BP) until BP is 135/85 mmHg or less	Every 15–30 minutes until BP is less than 160/110 mmHg
Dipstick proteinuria testing[a]	Once or twice a week (with BP measurement)	Daily while admitted
Blood tests	Measure full blood count, liver function and renal function at presentation and then weekly	Measure full blood count, liver function and renal function at presentation and then weekly
PlGF-based testing	Carry out PlGF-based testing on one occasion (in accordance with NICE guidance, see recommendation 1.4.4) if there is suspicion of pre-eclampsia	Carry out PlGF-based testing on one occasion (in accordance with NICE guidance, see recommendation 1.4.4) if there is suspicion of pre-eclampsia

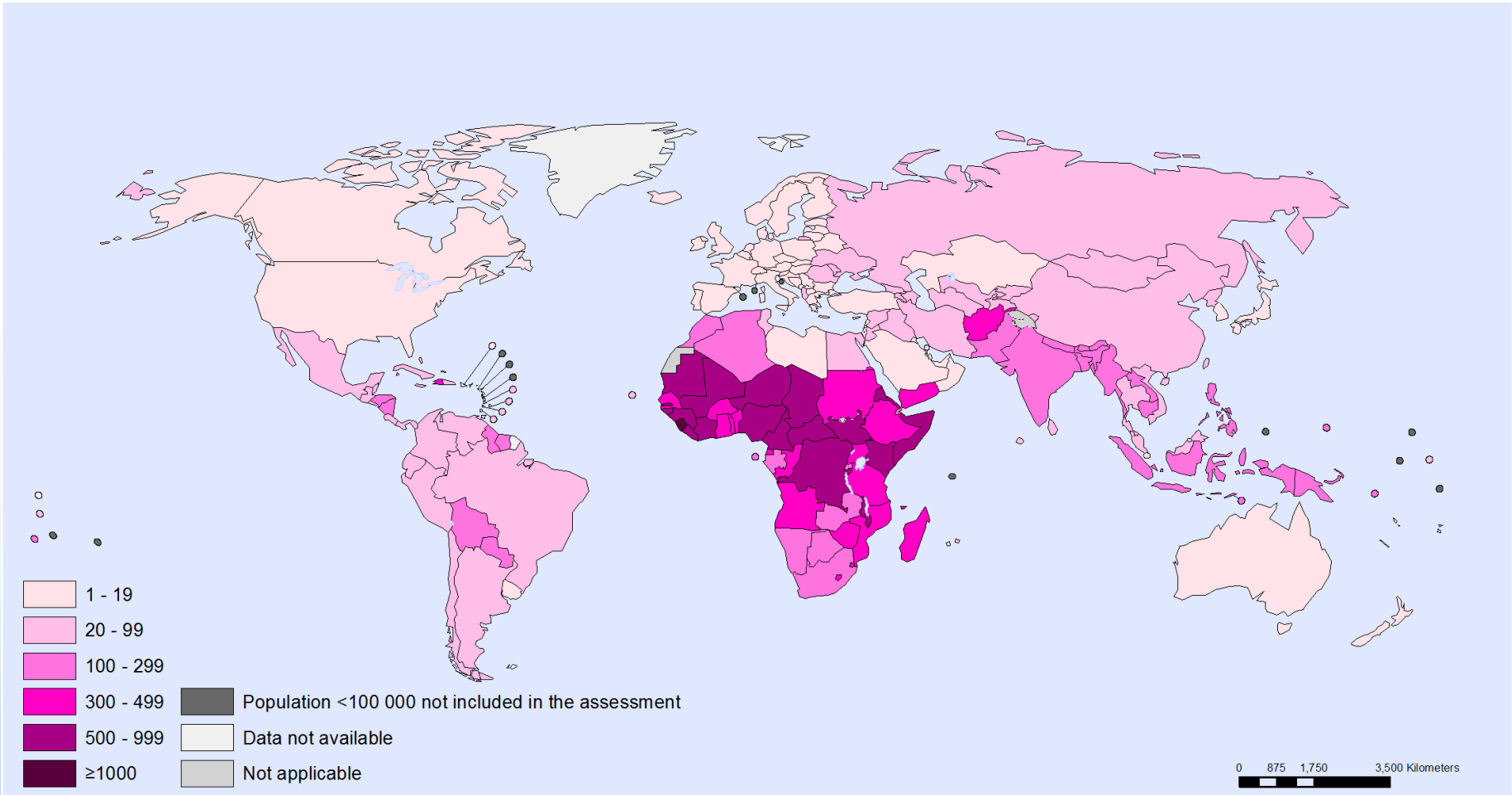
From ivory tower into clinical practice

The power of media coverage

What will the next 100 years of antenatal care hold?

Changing maternal mortality on a global scale

Maternal mortality ratio (per 100 000 live births), 2015

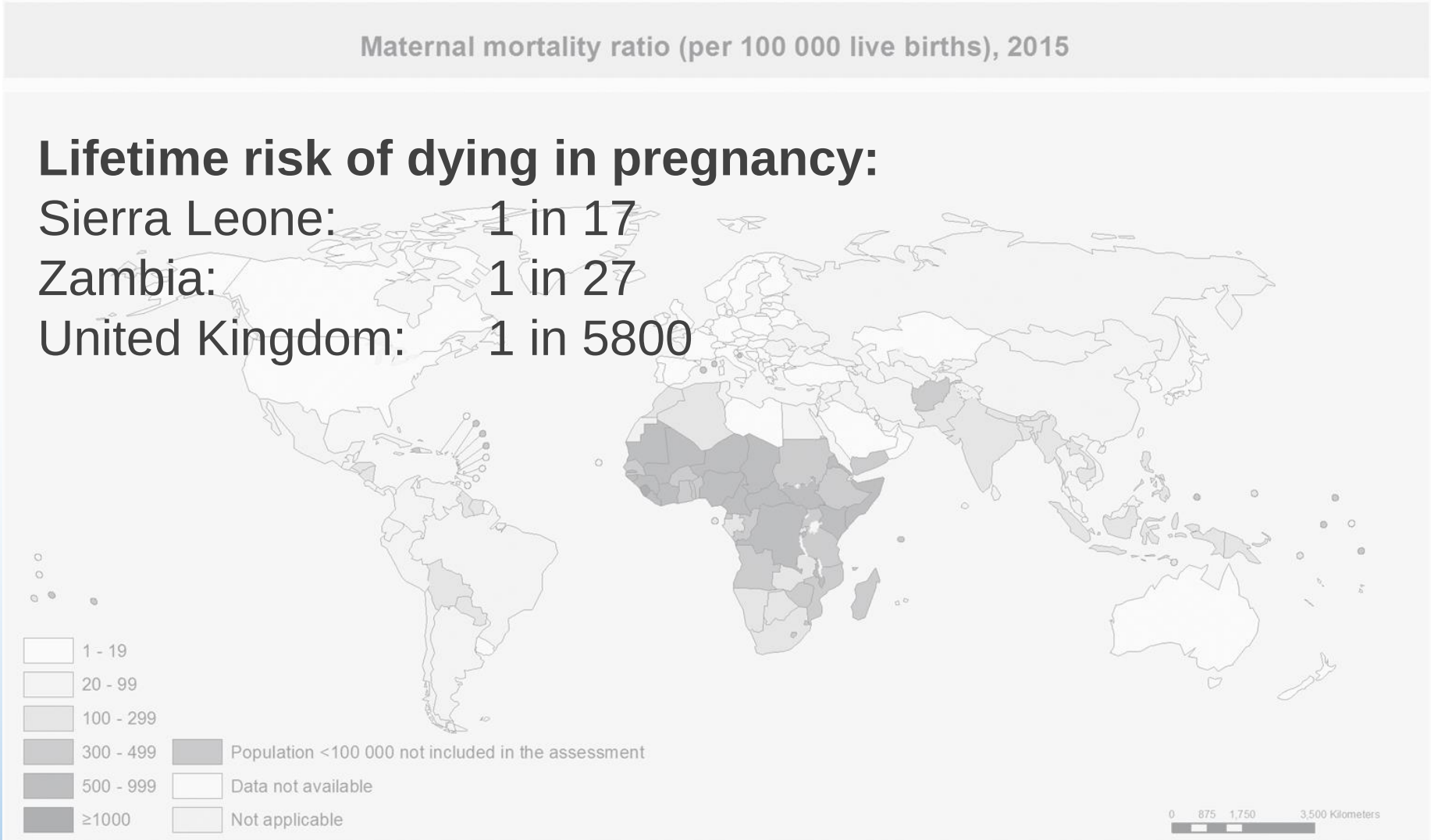


The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Health Statistics and Information Systems (HSI)
World Health Organization

World Health Organization

What does this mean for a woman today?



Whether in Ndola, Zambia…

Or at Guy's and St Thomas'

Advances in MRI-Guided Electrophysiology

Reza Razavi
Professor of Paediatric Cardiovascular Science
Director Wellcome Trust EPSRC Centre for Medical Engineering

Why improve treatment of cardiac arrhythmias such as Ventricular Tachycardia?

KING'S College LONDON

Sudden Cardiac Death is the single most important cause of adult death in developed world[1]

13-18% of all natural deaths

Ventricular tachyarrhythmias (VT) account for up to 80% of episodes[1]

At present, ICD implantation is the mainstay of treatment for patients with the highest risk

Non-curative: long-term morbidity and mortality burden

Expensive: complications, repeat implantations, monitoring, imperfect patient selection

VT ablation- the current 'curative' treatment- is not widely used and has recurrence rates of up to 50%[2]

[1] Priori et al, "Task Force on Sudden Cardiac Death" (2002)
[2] Ghanbari et al, VT Ablation and Outcomes, (2014)

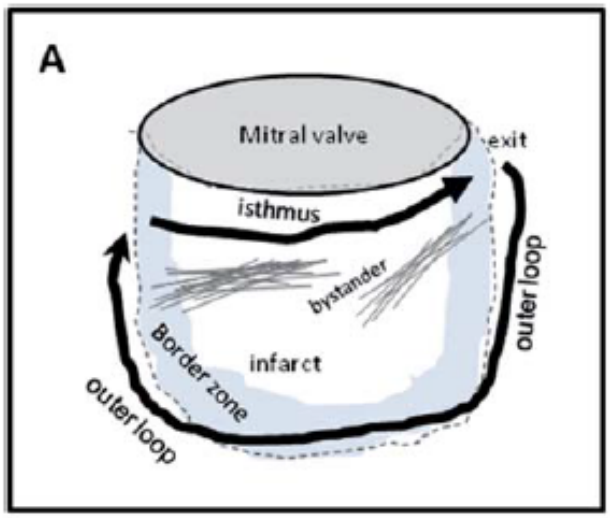
Why does VT ablation have a low success rate?

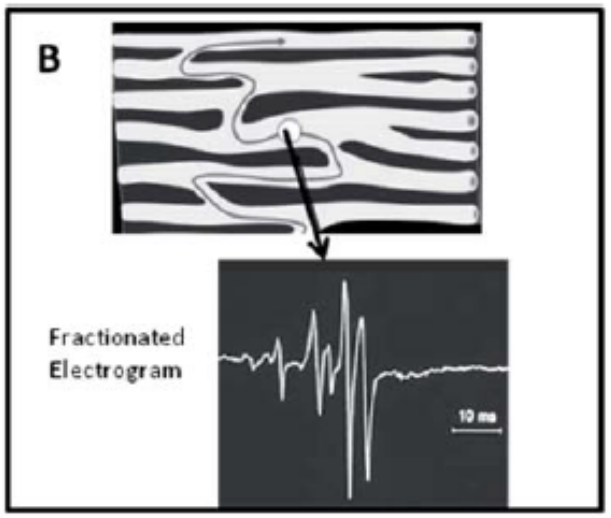
KING'S College LONDON

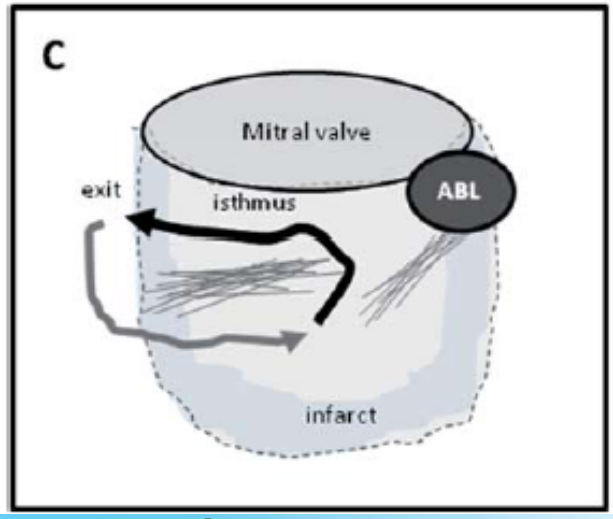
1. Identification of correct substrate for ablation

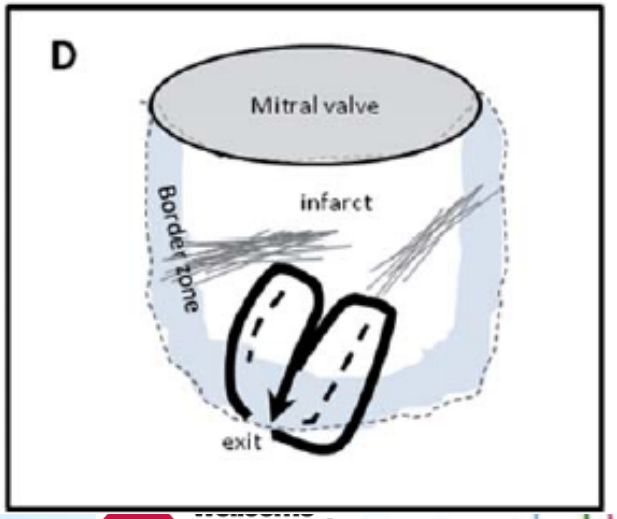
2. Achievement of sufficient injury to ablation target

Ablation substrate identification





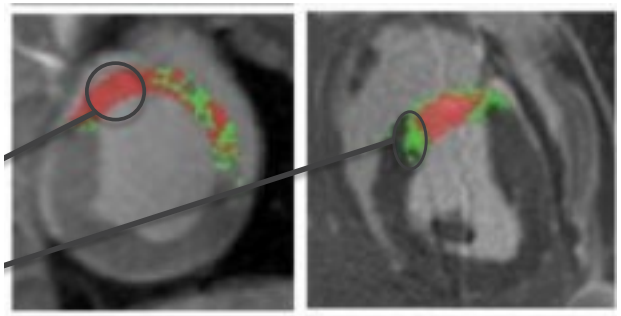




thmus sites of ischemic ventricular tachycardia are
ssue heterogeneity, visualized by magnetic
aging

M. Muz Zviman, PhD,* Dan Herzka, PhD,† Frank Miller,* Valeria Castro,*
PhD,* Hiroshi Ashikaga, MD, PhD,* Yoav Dori, MD, PhD,§
PhD,*† Hugh Calkins, MD, PhD,* Albert C. Lardo, MD, PhD,*†
, MA*†‡

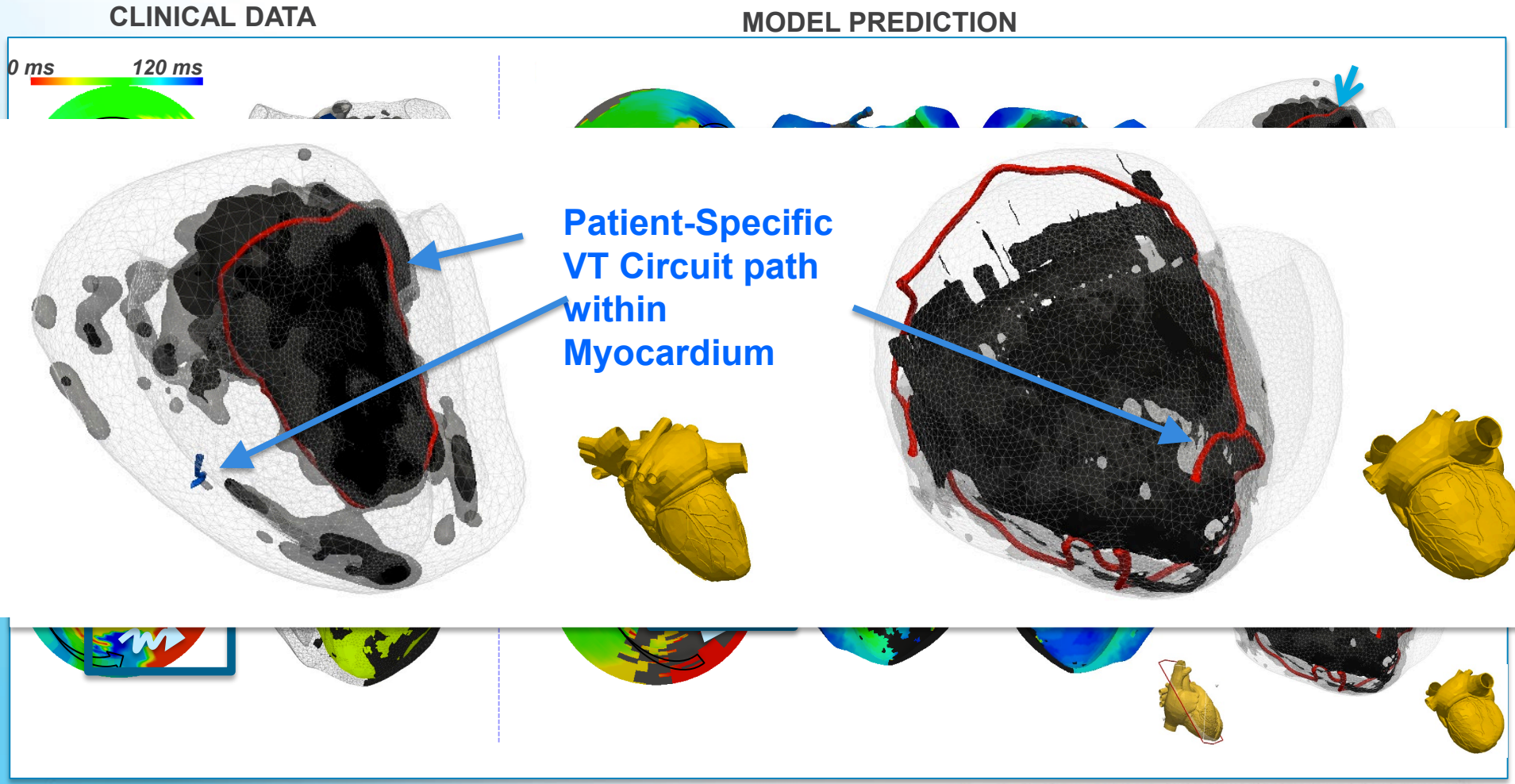
Heart Rhythm, Vol 8, No 12, December 2011



Zone of
slow conduction:
'Borderzone'

Model Prediction of Induced VT Isochrones & Circuits

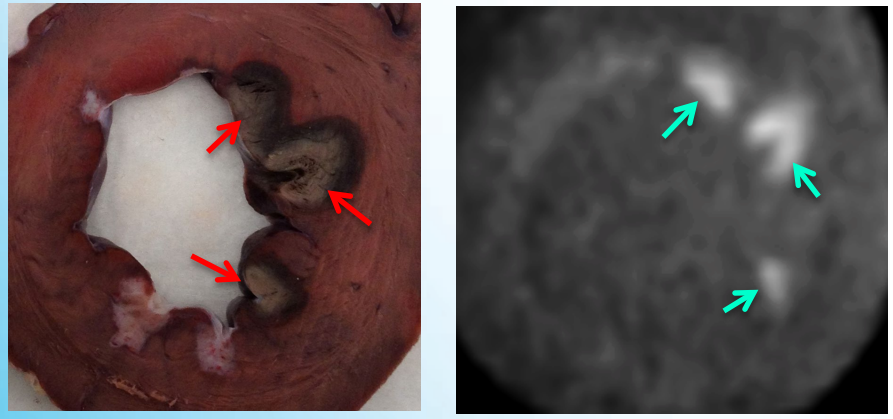
Comparison of activation isochrones for model predicted induced VT *in silico* with clinically observed induced VT



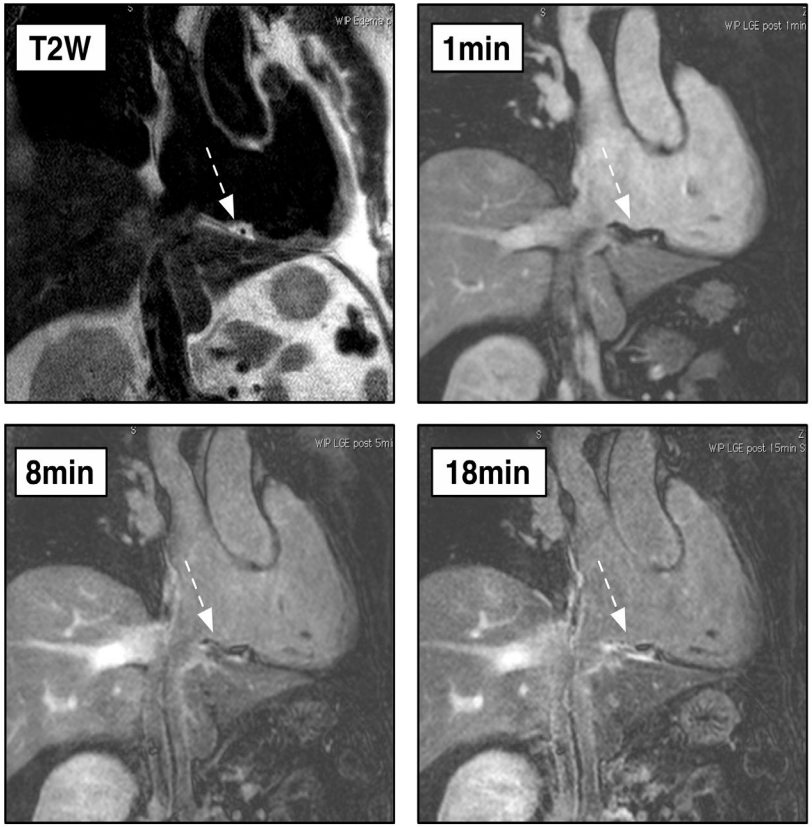
Chen Z, …..Razavi R.J Cardiovasc Electrophysiol. 2016 Apr 20

Achievement of sufficient injury to target

- **Inability to create a sufficiently deep lesion to ablate VT is an important cause of ablation failure[1]**
- **MRI is capable of identifying transmural lesions acutely**



Non-contrast T1w MRI accurately estimates dimensions of lesion core (shortens T1 relaxation time)



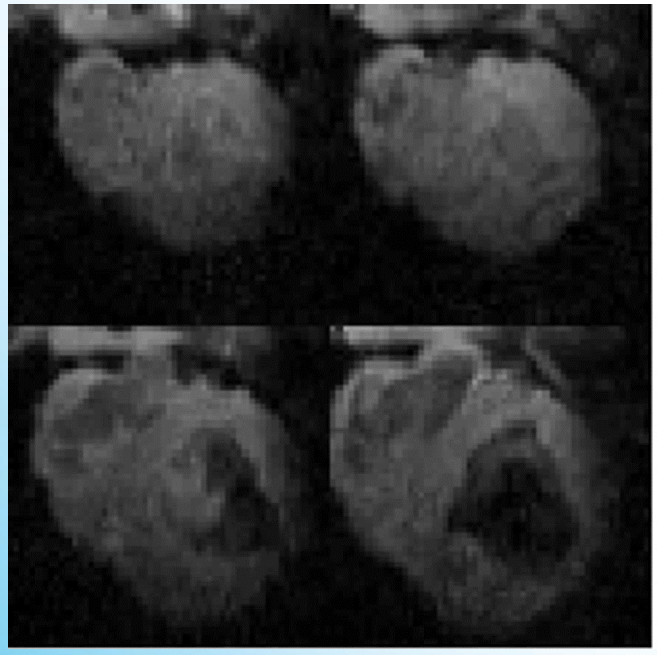
Early no-reflow with subsequent late gadolinium enhancement at the site of permanent ablation

[1] EHRA/HRS Expert Consensus on Catheter Ablation of Ventricular Arrhythmias (2009)

Real-time MR-thermometry

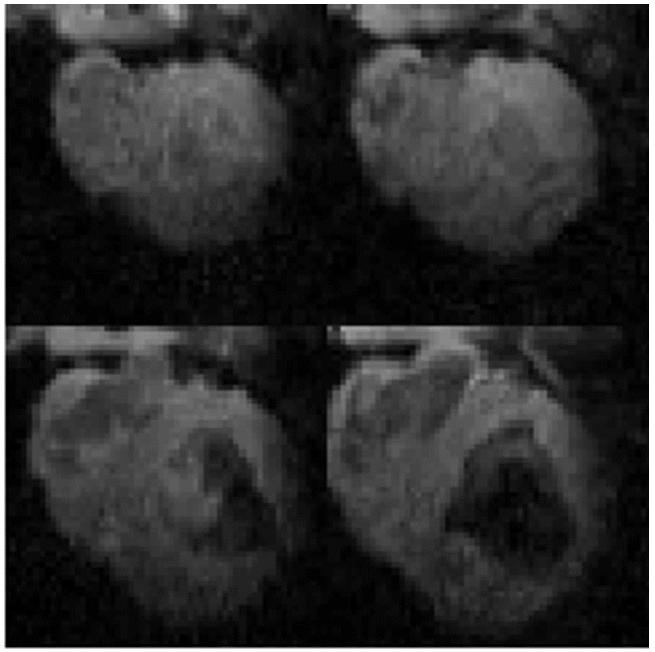
KING'S College LONDON

Temperature mapping



0°C 30°C

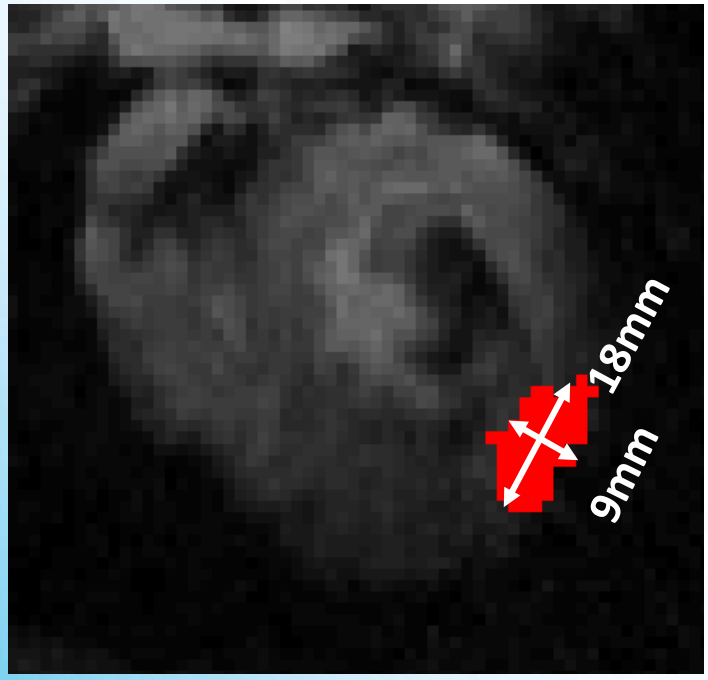
Thermal dose mapping



Thermal dose > Lethal dose

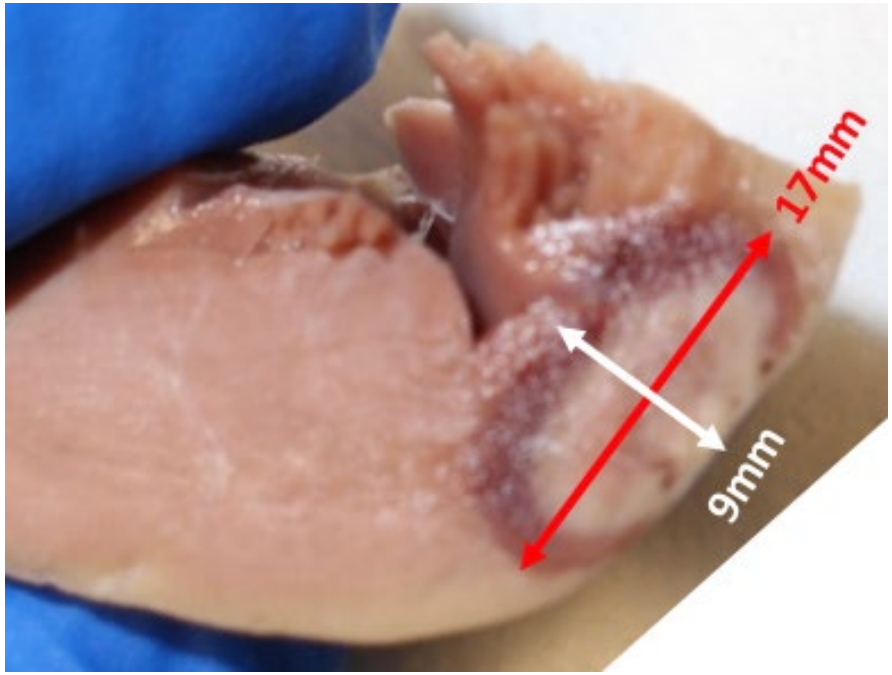
Real-time MR-thermometry

Thermal dose mapping

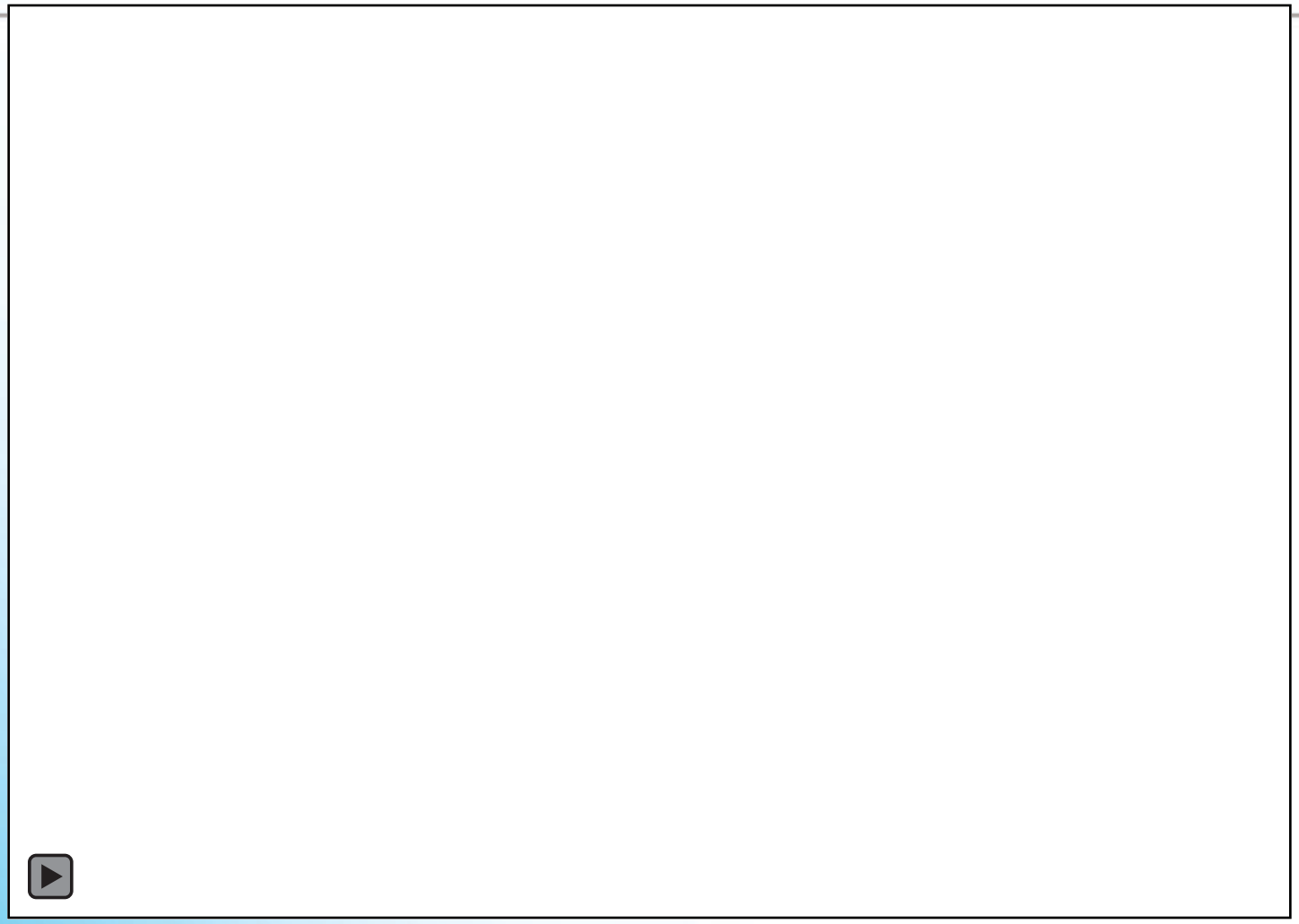


Thermal dose > Lethal dose

Gross macroscopy

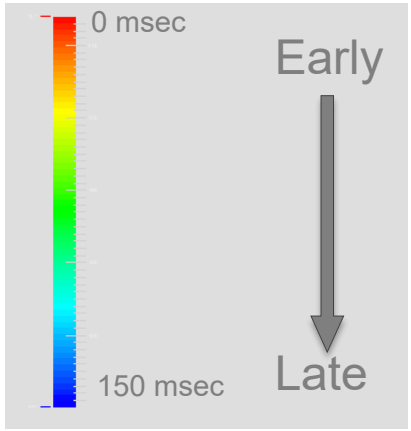


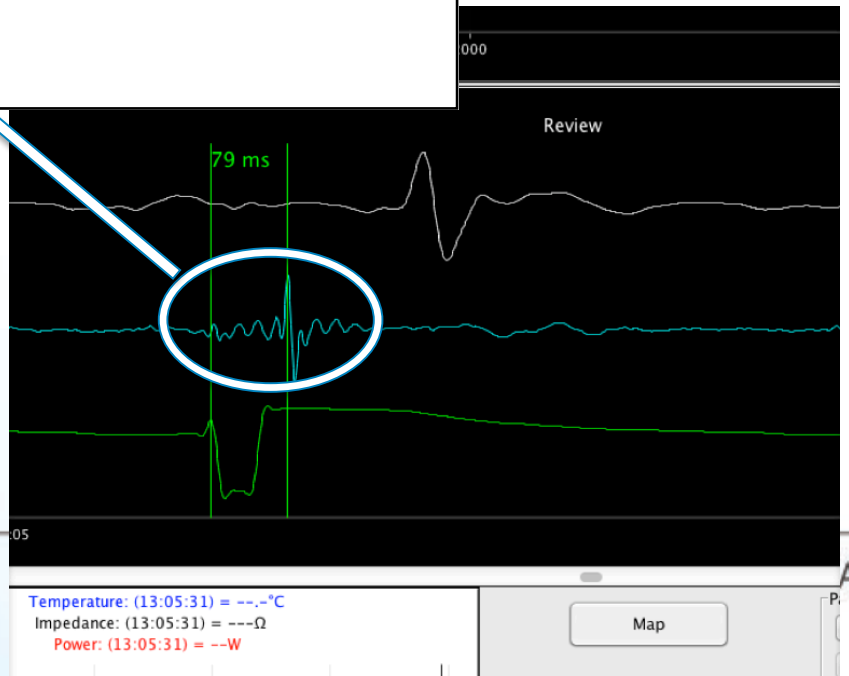
Feasibility of MR-guided ablation



Chubb H ….Razavi R JACC Clin EP 2017 3:89–103

Feasibility of MR-guided ablation



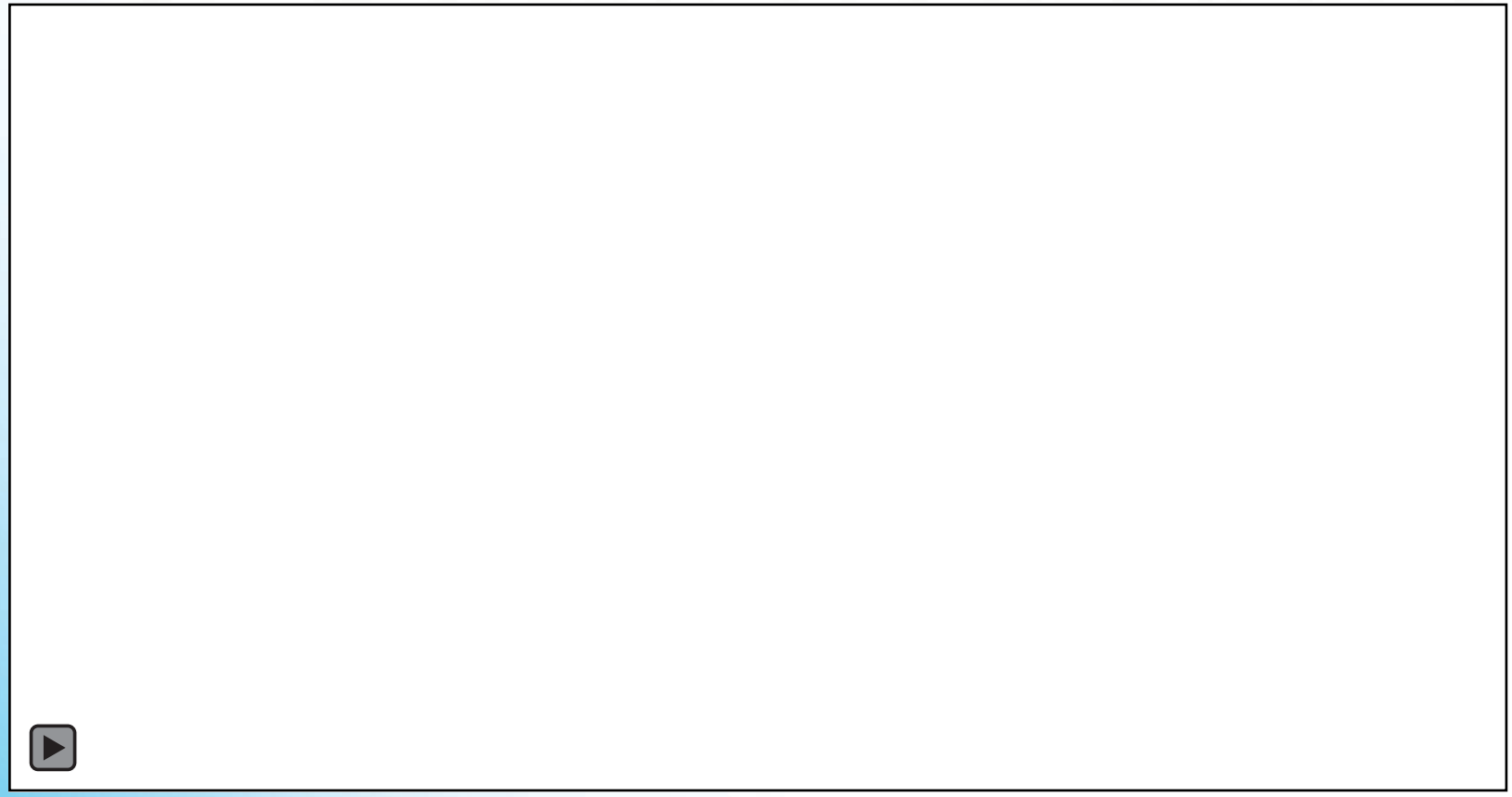


Local Activation Time

Isochrone map

Chubb H ….Razavi R JACC Clin EP 2017 3:89–103

Feasibility of MR-guided ablation

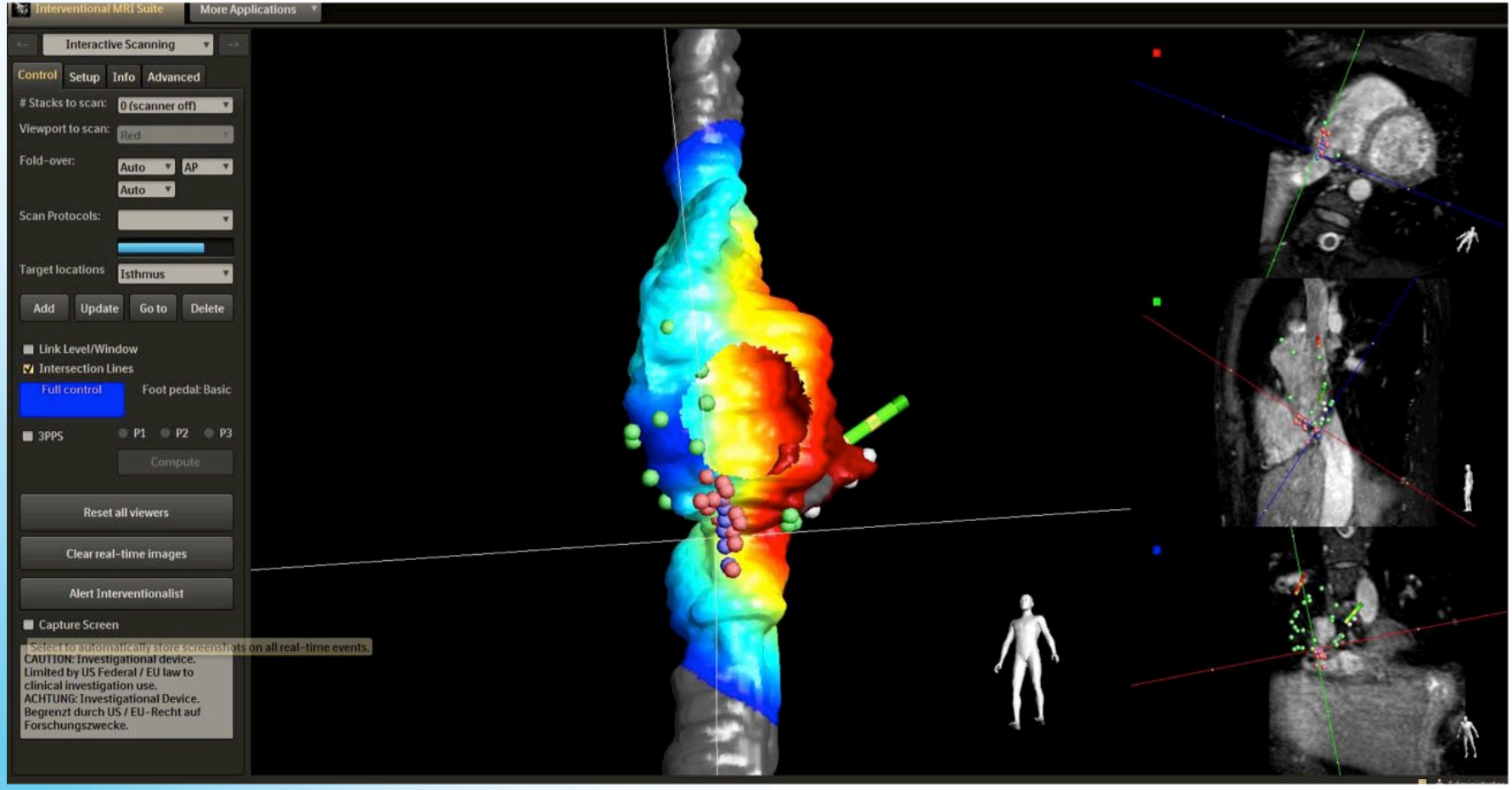


Point-by-point ablation

35-45W, 60s per lesion, 17ml/sec irrigation

Chubb H ….Razavi R JACC Clin EP 2017 3:89–103

Feasibility of MR-guided ablation



Bi-directional Block post-ablation

CENTRE for MEDICAL ENGINEERING

Chubb H ….Razavi R JACC Clin EP 2017 3:89–103

Conclusion

- Innovations in real-time MR technology are opening up new frontiers in electrophysiology
- For VT ablation the added value of MR over alternative methods of guiding interventions is:
  - Accurate visualization and targeting of the VT substrate
  - Evaluation of the ablation effect in real-time to titrate treatment
- We require:
  - Safe defibrillation inside the MR scanner
  - improvement in MR-safe EP catheters that can easily work in the left ventricle
- Ventricular tachycardia MR ablation will likely become the clinical method of choice

Acknowledgments

- KCL - Tobias Schaeffter, Derek Hill, Vivek Muthurangu, Sanjid Hedge, Mark Miquel, Rene Botnar, Sebastien Rojoul, Andy King, Kawal Rhode……..
- KCL - Mark O'Neill, Jas Gill, Shak Qureshi, Eric Rosenthal, Tarique Hussein, Gerlad Greil, Dennis Cauldfield, Aphrodite Tzifa, James Harrison, Henry Chub, Kuberan Pushparajah, James Wong, Mari Nieves Velasco Forte, John Whitaker, Rahul Mukerjee, Louisa O'Neill ……..
- Philips - Steffen Weiss, Holger Eggers, Sascha Kruger, Jouke Smink
- Imricor - Jennifer Weisz, Gregg Stenzel, Tom Iloyd, Steven Wedan
- Siemens – Radhouene Neji, Rainer Schneider, Thomas Pohl, Martin Oestermeier

Organ transplantation is the treatment of choice for endstage failure of:

Kidney

Liver

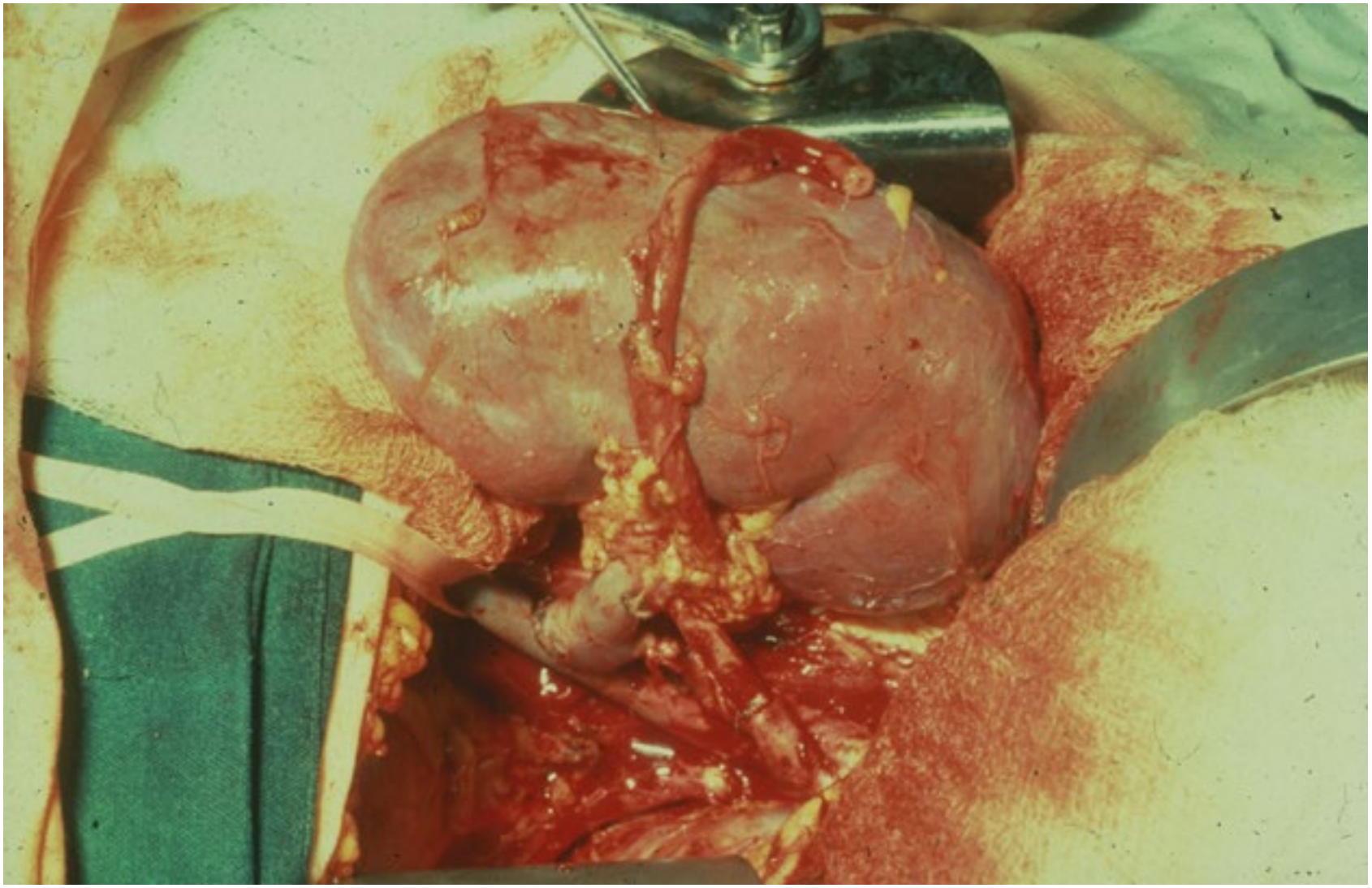
Heart

Lung

Cornea

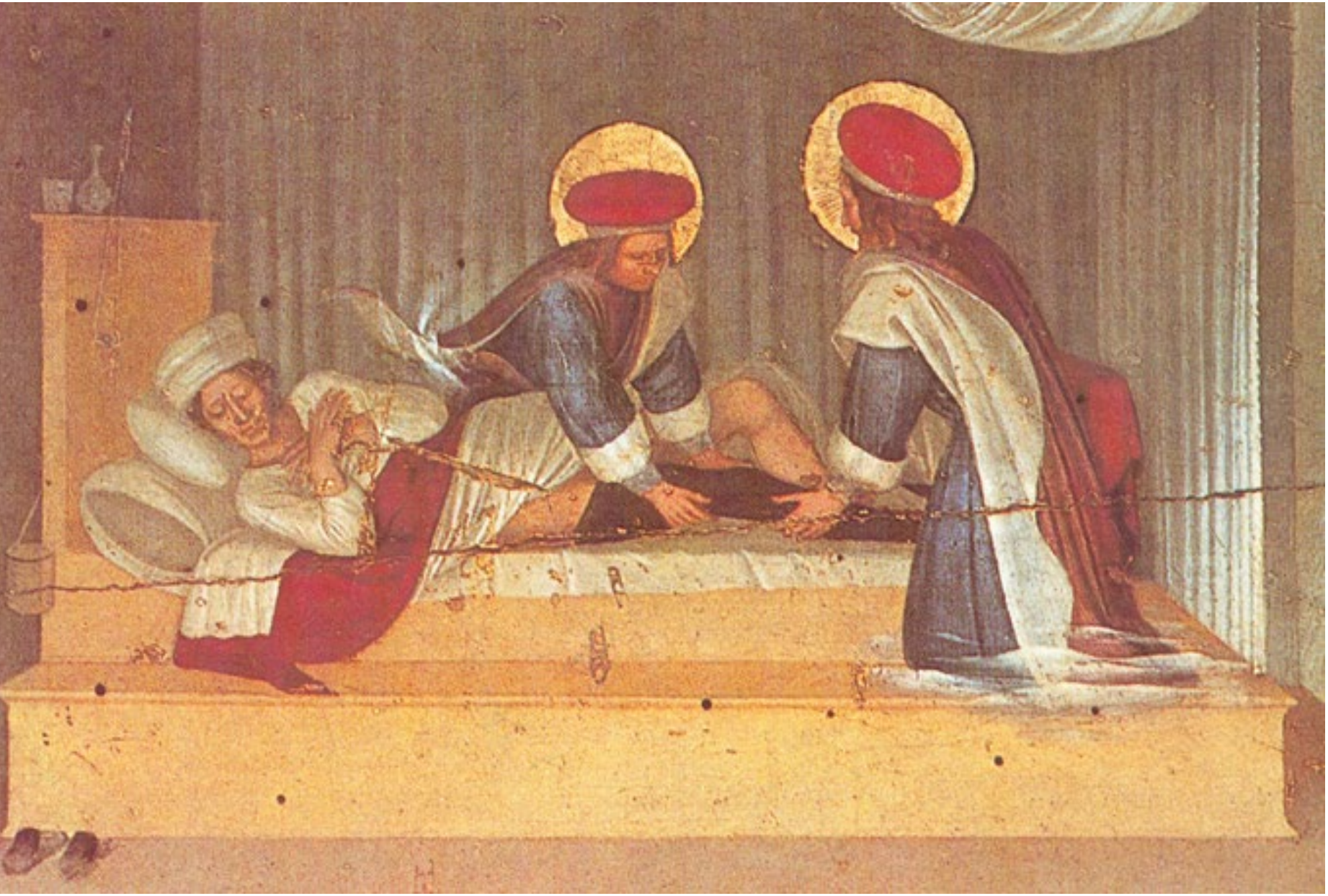
Pancreas

Brain…….

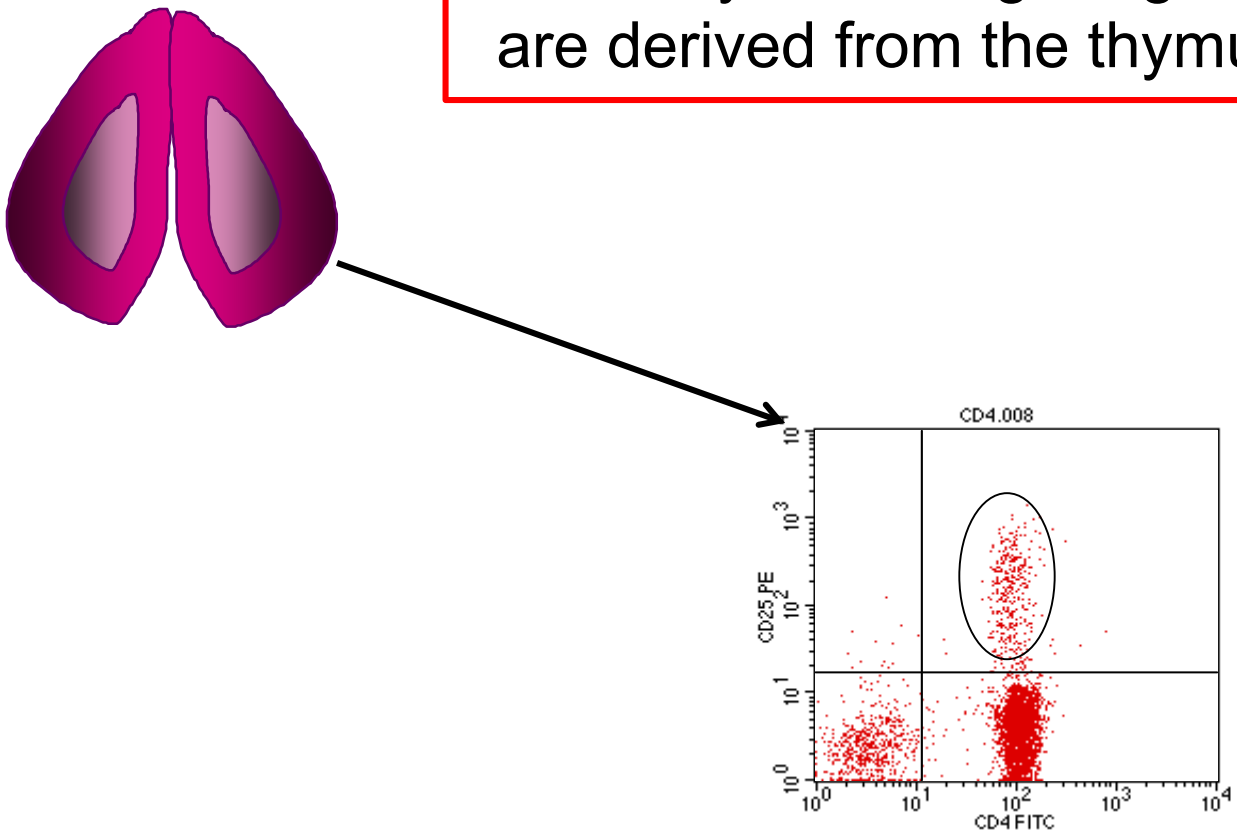


Three major problems that limit the clinical applications of transplantation are:

- morbidity/mortality associated with longterm immunosuppression
- “chronic rejection”
- shortage of organs…….

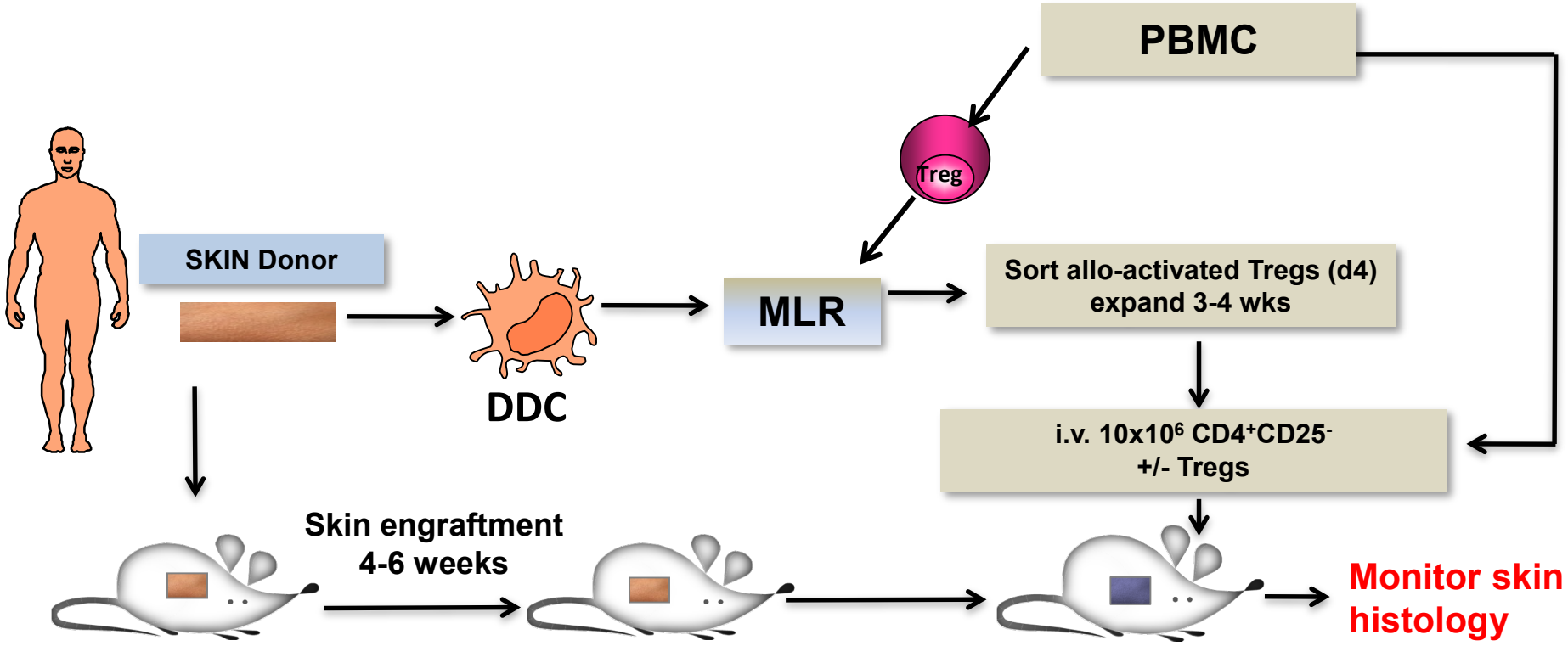


Naturally occurring Tregs are derived from the thymus



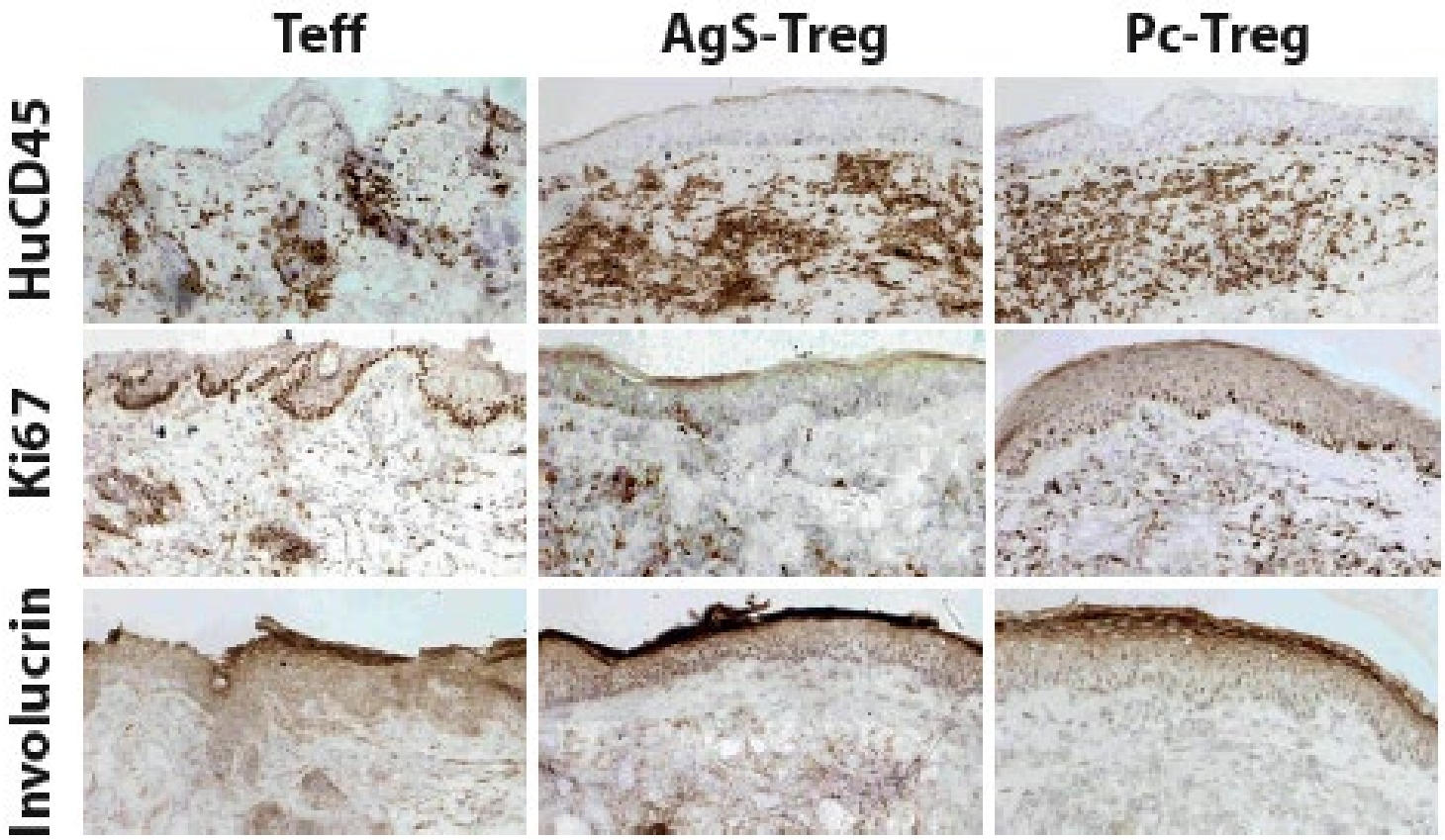
Mice and humans that fail to generate thymus-derived Tregs develop multiple autoimmune disorders

Protocol for testing the efficacy of Tregs in protecting human skin allografts from immune-mediated damage



Sagoo et al. Science Transl Med

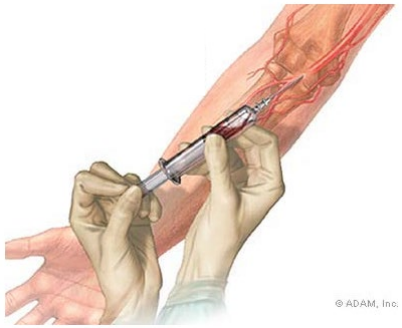
Histological analysis shows that both Tregs can mediate protection of skin allografts from alloimmune injury



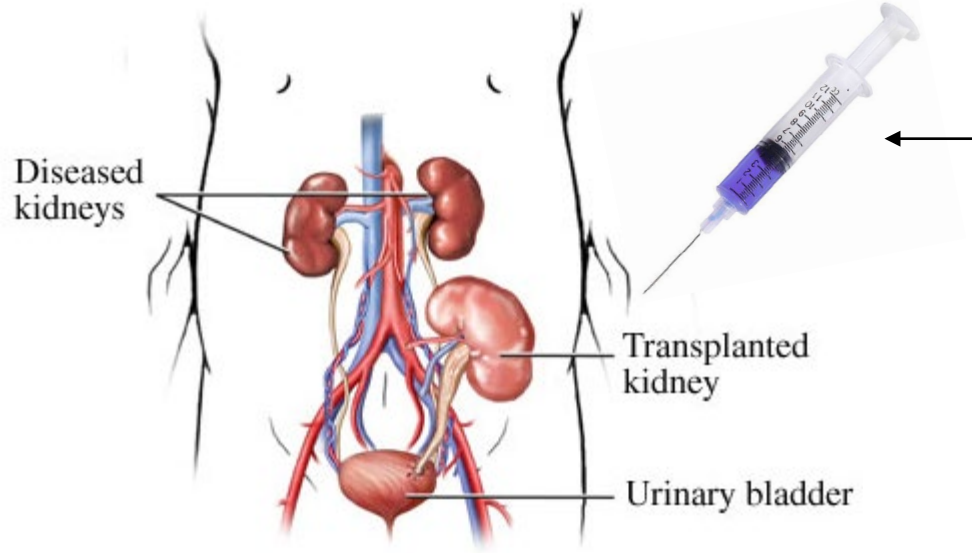
Clinical trials of tolerance....

Outlook-Concept

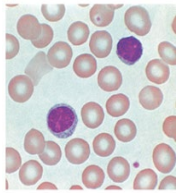
End stage organ failure and need for transplantation



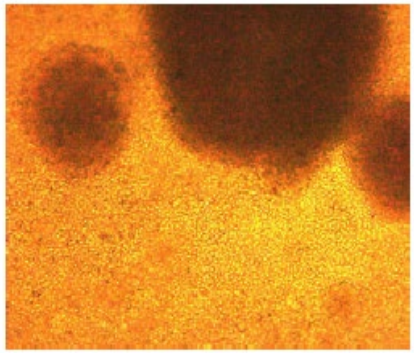
Regulatory T cell selection, expansion and modification



Tregs in transplantation-two clinical trials



Treg expansion



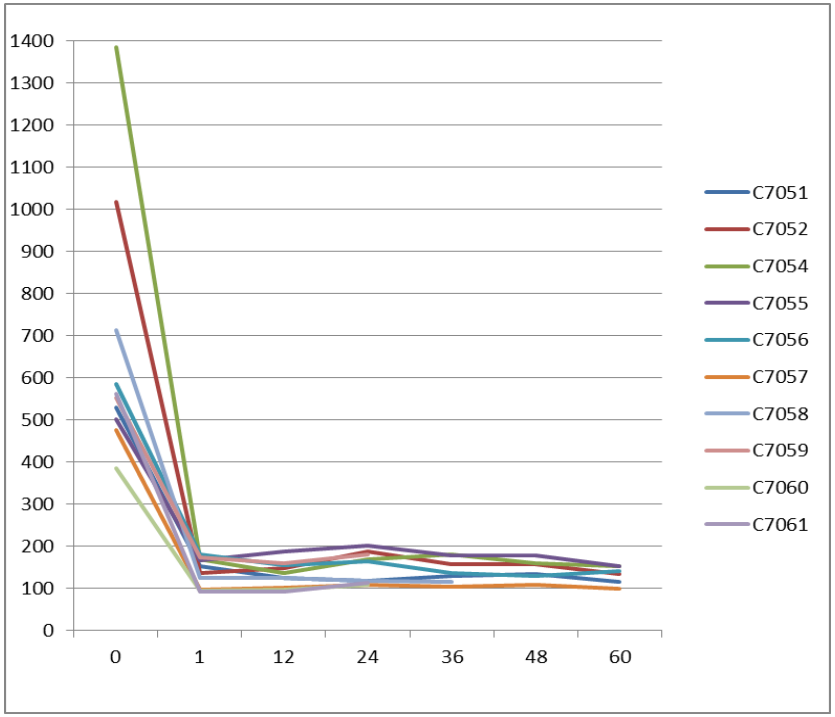
- The ONE Study – kidney – 12 patients
  - Infusion of Tregs (**1 - 10x10^6/kg)**
  - **Living donors**
- ThRIL – liver – 9 patients
  - Deletion of allospecific cells (ATG)
  - Infusion of Tregs - **0.5/1 - 4.5 x 10^6/kg Tregs** (Rapamycin)
  - **Deceased donors**

SEVENTH FRAMEWORK PROGRAMME

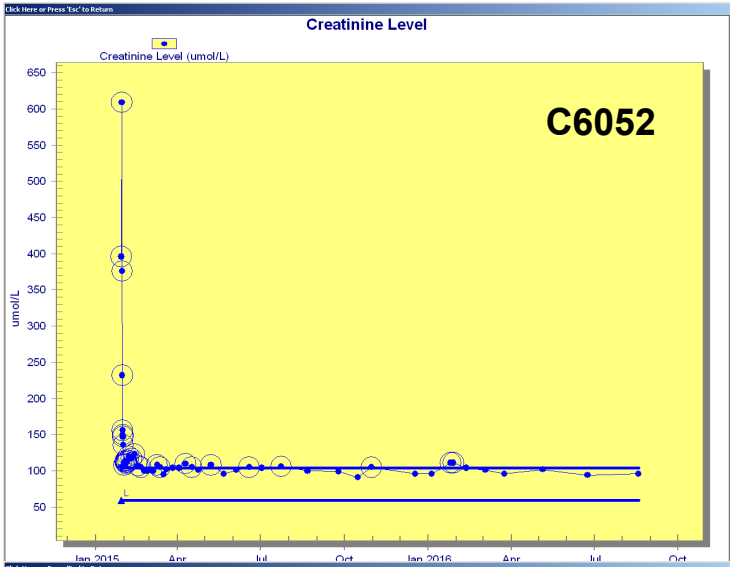
MRC Medical Research Council

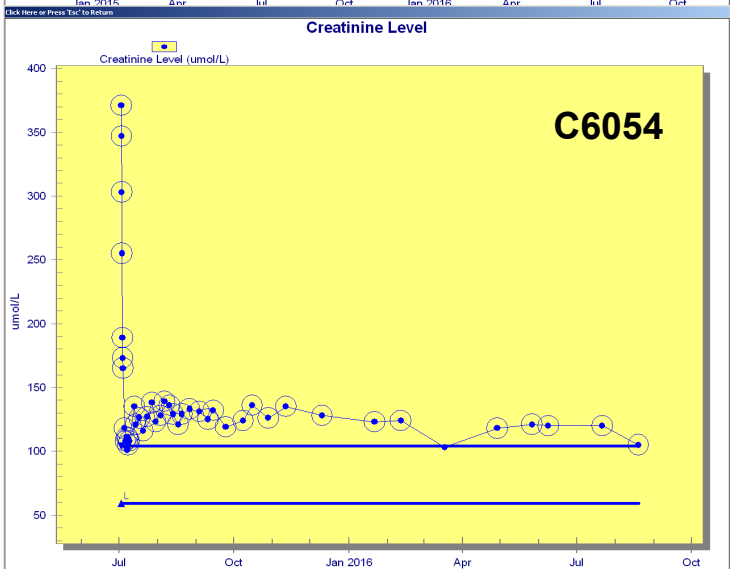
Renal Function: serum creatinine

Serum Creatinine Umol/L

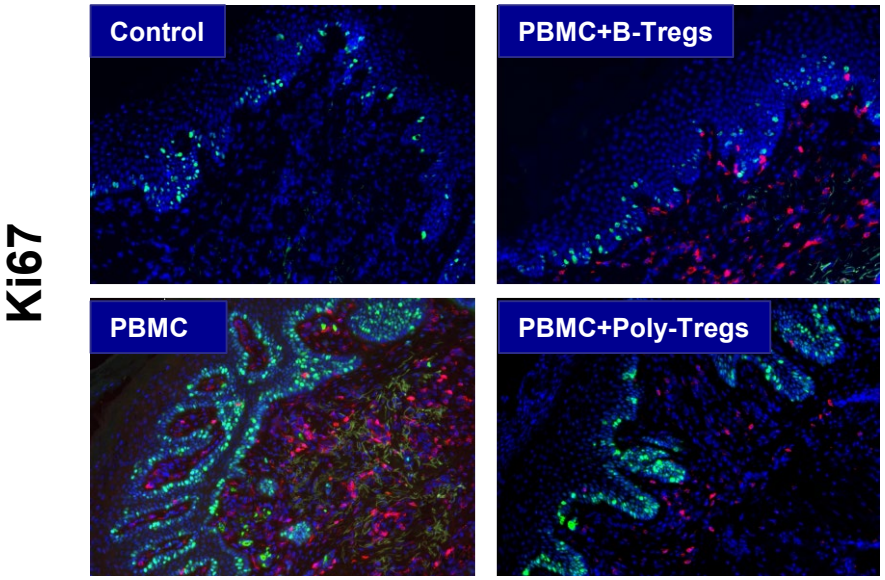


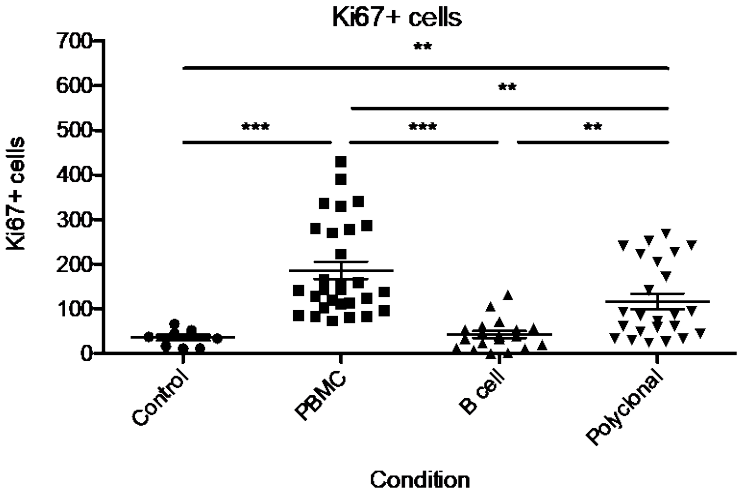
Time Post-Transplant (weeks)



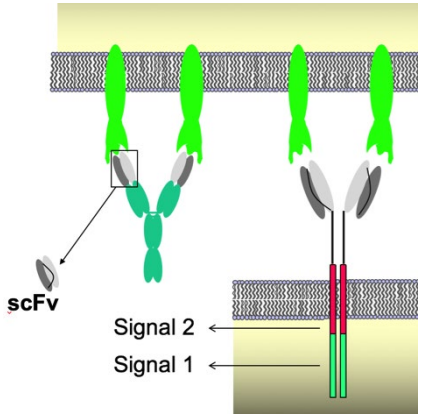


Graft-specific Tregs are superior in preventing skin graft damage compared to polyclonal Tregs





Putnam, Safinia et al. A.J.T. 2013

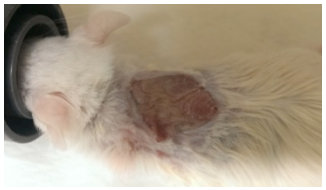


→ **CAR-Tregs**

MacDonald et al. *JCI*, 2016
Boardman et al. *AJT*, 2017
Noyan et al. *AJT*, 2017

Tregs can be detected in the human skin graft

BRG mouse transplanted with human skin



30 days

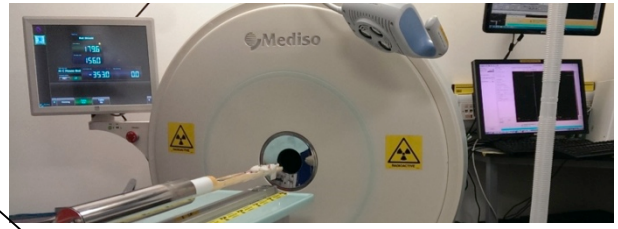
Day 0

Tregs

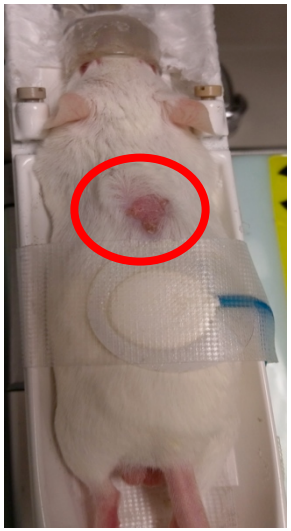
hNIS⁺Tregs

99mTc04

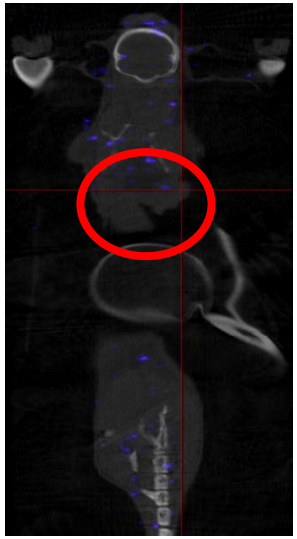
Micro SPECT/CT for small animal whole body imaging



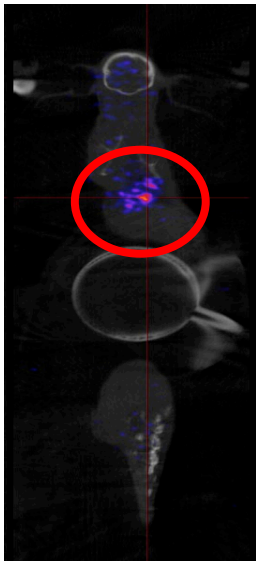
0, 3, 8, 16, 30, 40 days



SPECT/CT scan before injection of Treg cells



SPECT/CT scan day 40 after injection of Treg cells



Jacintha Jacob, Lesley Smyth and Gilbert Fruhwirth

Conclusions:

- Treg therapy is achievable and safe
- Treg therapy holds promise for inducing transplantation tolerance
- Clinical trials with CAR-expressing Tregs will be conducted in liver transplant patients
- A spin out company has attracted £35m investment to advance this therapeutic approach

The impact and contribution of AHSCs – life sciences and the long-term sustainability of healthcare

Guest speaker:

Rt Hon Professor Lord Kakkar

#KHP10Years

Mind & Body – how the nervous and immune systems interact and influence inflammatory and psychiatric disease

16 May 2019

Leonie Taams and Valeria Mondelli
(on behalf of many King's collaborators)

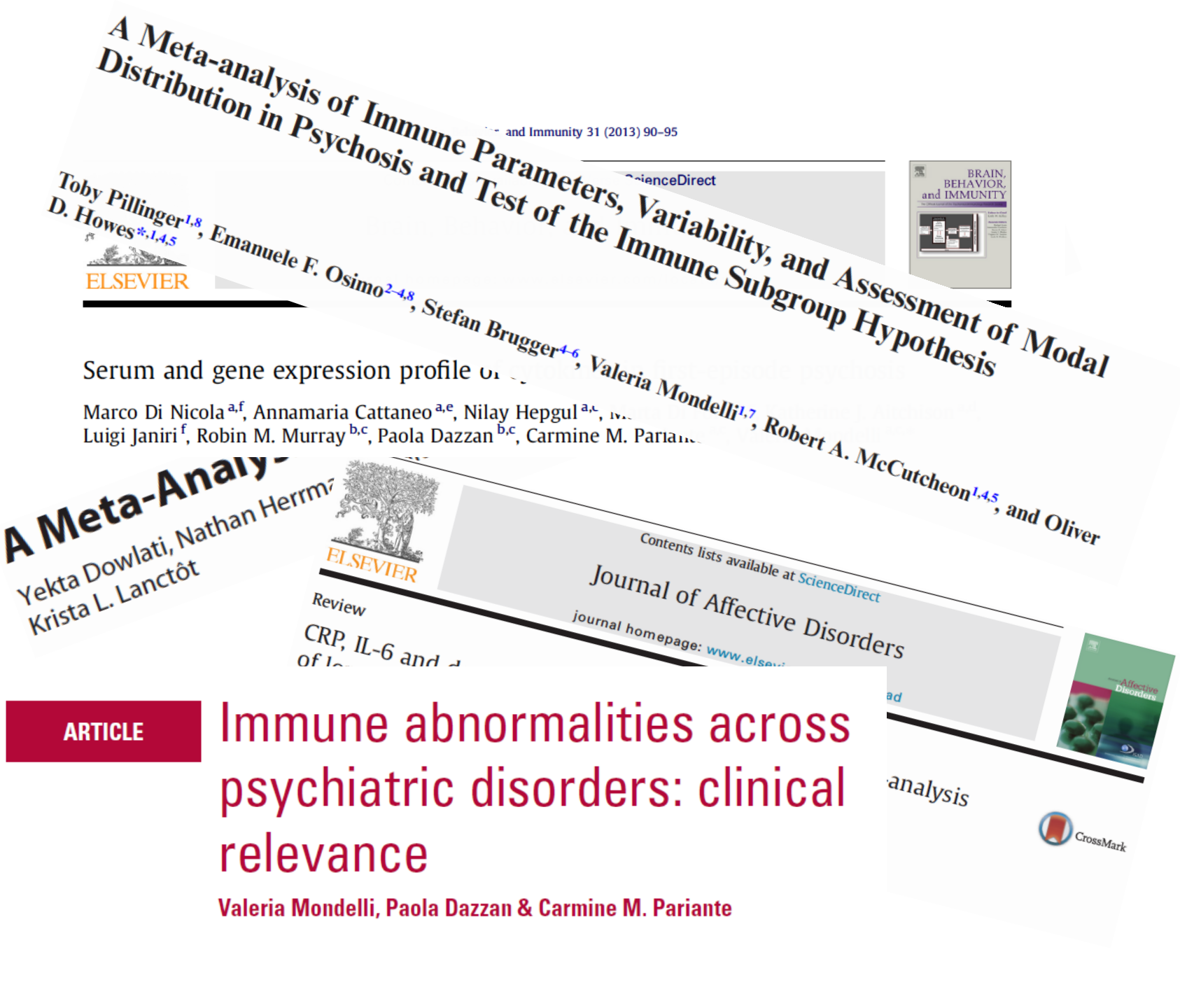
KING'S HEALTH PARTNERS

Pioneering better health for all

Faculty of Life Sciences & Medicine

Institute of Psychiatry, Psychology & Neuroscience

KING'S College LONDON

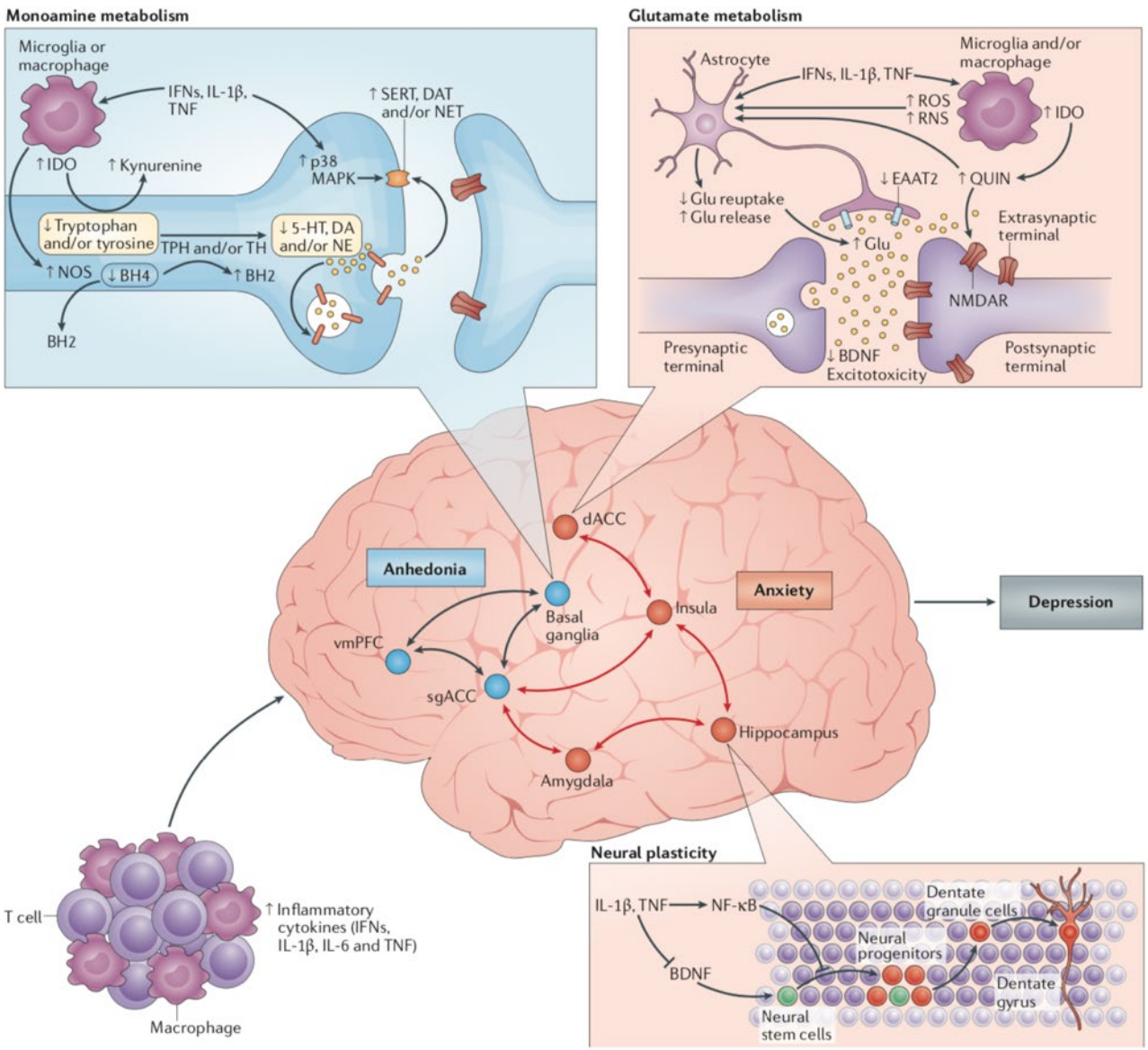


ARTICLE

Immune abnormalities across psychiatric disorders: clinical relevance

Valeria Mondelli, Paola Dazzan & Carmine M. Pariante

Central Nervous System and inflammation



Miller and Raison 2016

Childhood trauma and adulthood inflammation

Molecular Psychiatry (2016) 21, 642–649

www.nature.com/mp

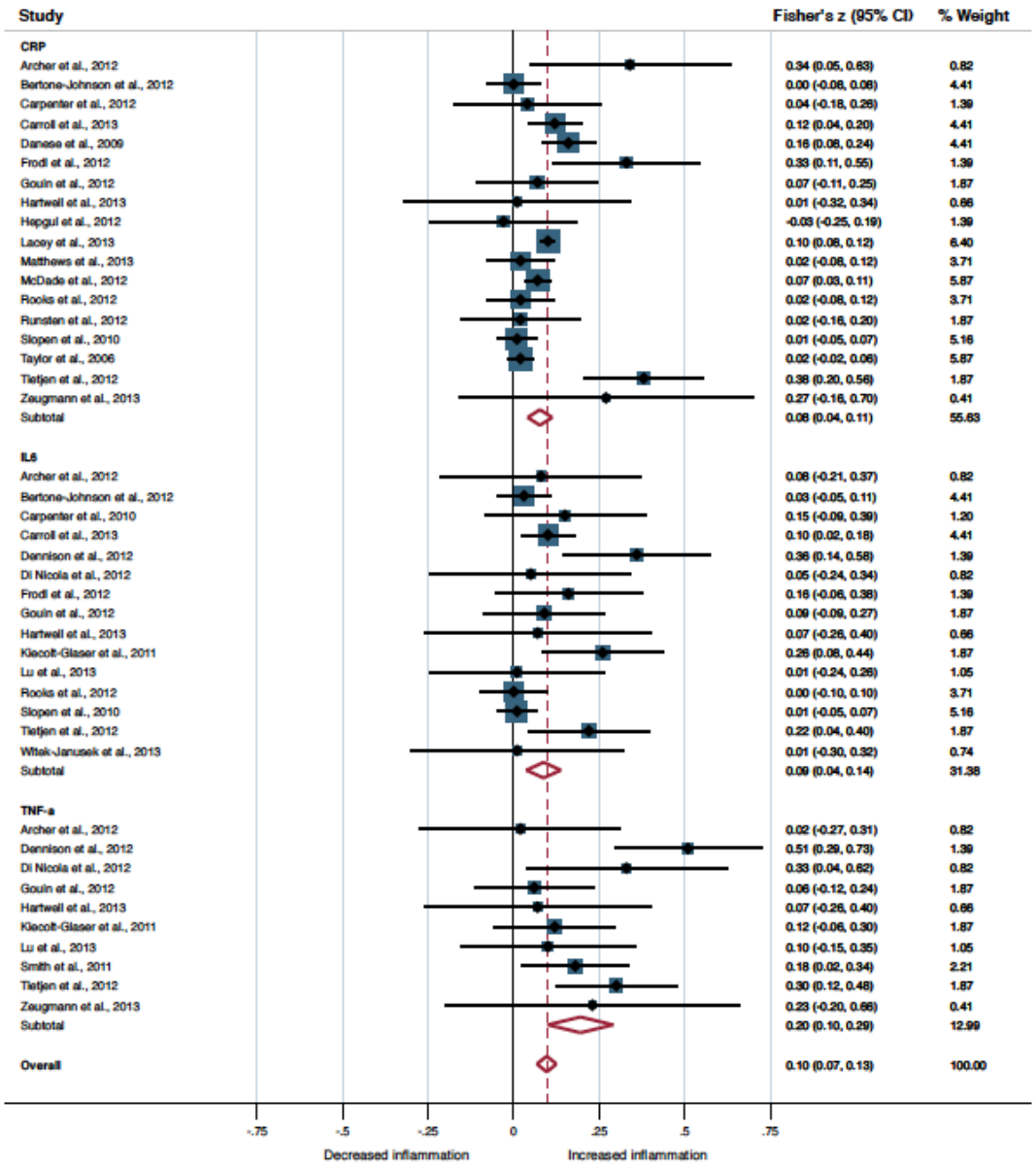
OPEN

ORIGINAL ARTICLE

Childhood trauma and adulthood inflammation: a meta-analysis of peripheral C-reactive protein, interleukin-6 and tumour necrosis factor-α

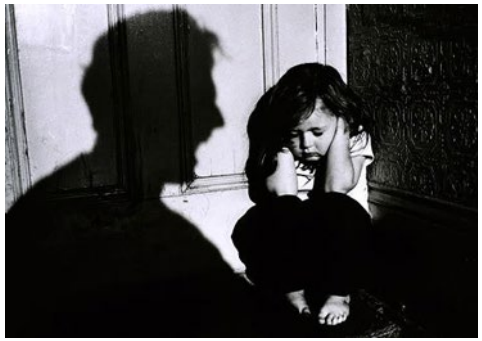
D Baumeister[1,2], R Akhtar[3], S Ciufolini[4,5], CM Pariante[1] and V Mondelli[1,5]

Childhood trauma and adulthood inflammation



Data from our meta-analysis show elevated levels of CRP, IL-6 and TNFα in adults with history of childhood trauma

Baumeister et al., Mol Psych 2016



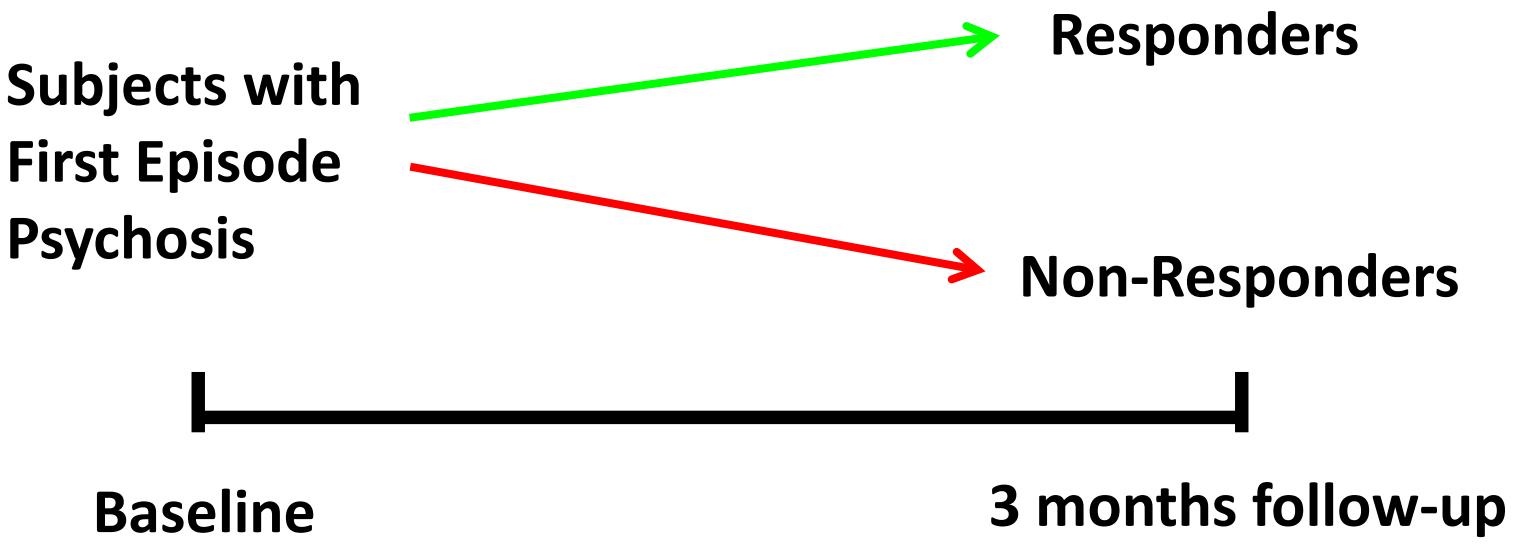
Inflammatory markers and clinical outcome in psychosis

Cortisol and Inflammatory Biomarkers Predict Poor Treatment Response in First Episode Psychosis

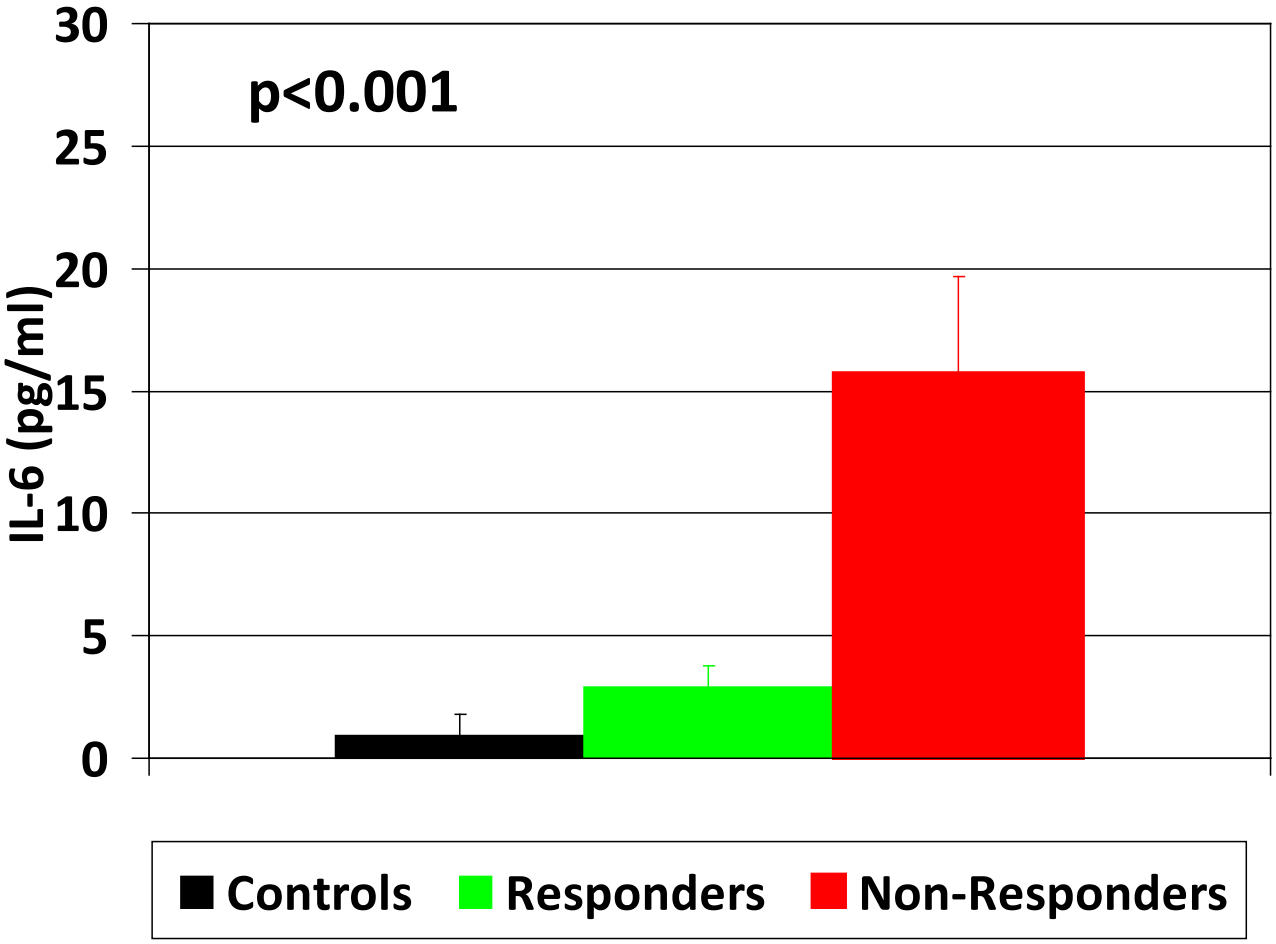
Valeria Mondelli[*,1,2], Simone Ciufolini[2,3], Martino Belvederi Murri[1], Stefania Bonaccorso[3], Marta Di Forti[3], Annalisa Giordano[3], Tiago R. Marques[3], Patricia A. Zunszain[1,2], Craig Morgan[4], Robin M. Murray[2,3], Carmine M. Pariante[1,2], and Paola Dazzan[2,3]

Schizophrenia Bulletin vol. 41 no. 5 pp. 1162–1170, 2015
doi:10.1093/schbul/sbv028
Advance Access publication March 31, 2015

Inflammatory markers and clinical outcome in psychosis

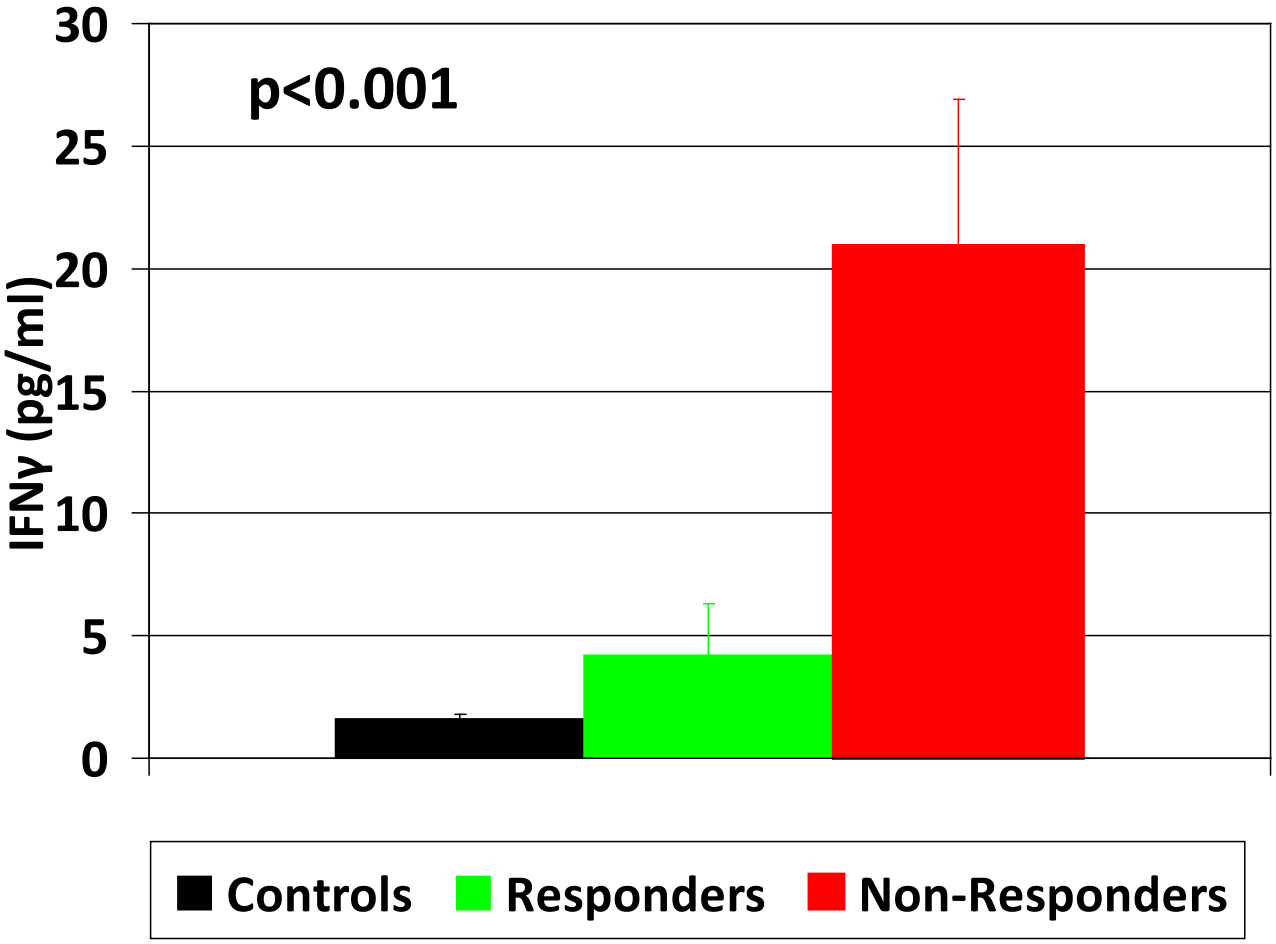


Interleukin-6 and clinical outcome



Mondelli et al., Schizophr Bull 2015

Interferon-γ and clinical outcome



Mondelli et al., Schizoph Bull, 2015

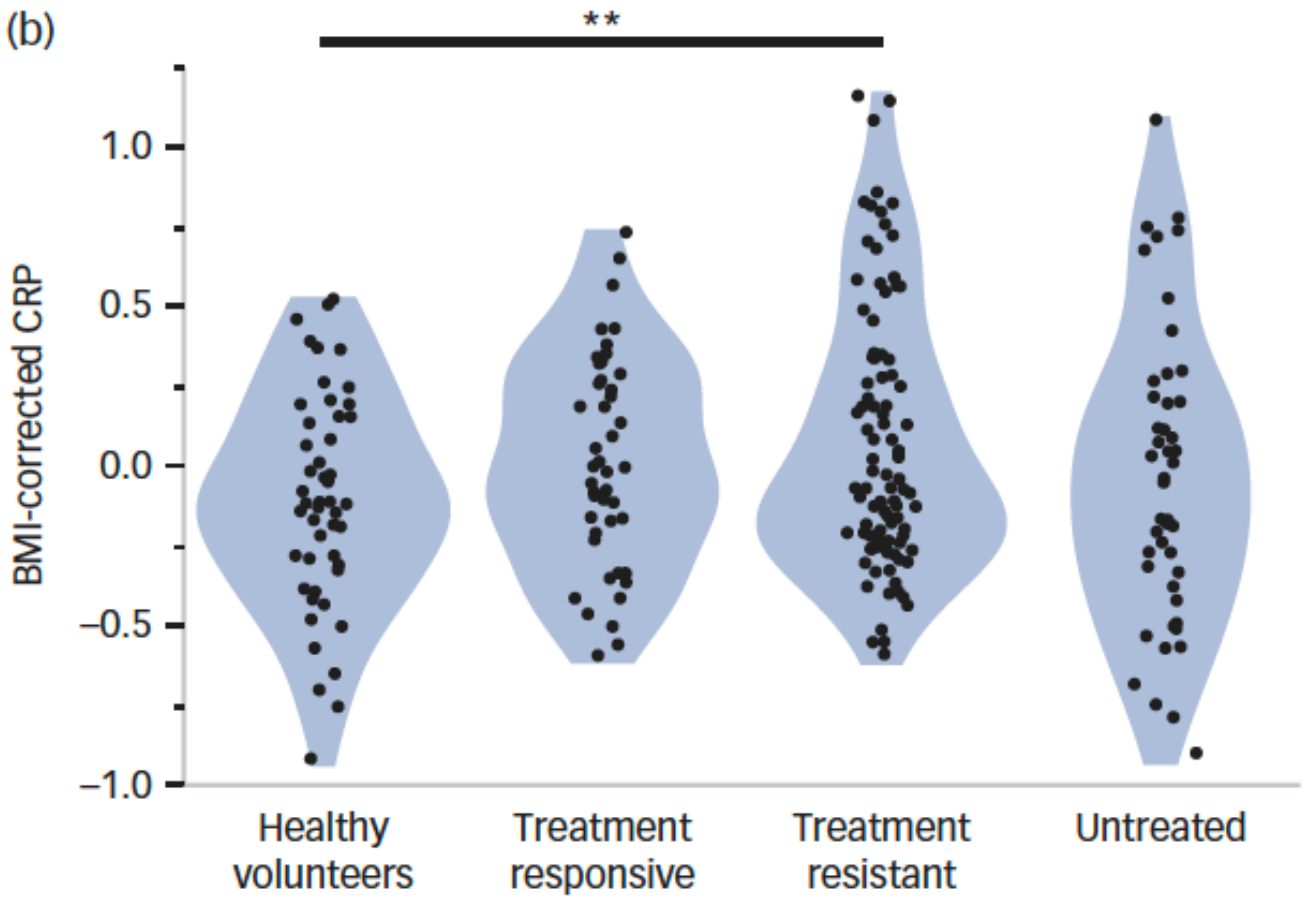
Depression and Inflammation: relevance for treatment?

BJPsych | The British Journal of Psychiatry (2018)
Page 1 of 9. doi: 10.1192/bjp.2018.66

Treatment-resistant depression and peripheral C-reactive protein

Samuel R. Chamberlain, Jonathan Cavanagh, Peter de Boer, Valeria Mondelli, Declan N.C. Jones, Wayne C. Drevets, Philip J. Cowen, Neil A. Harrison, Linda Pointon, Carmine M. Pariante* and Edward T. Bullmore*†

Depression and Inflammation: relevance for treatment?



wellcome trust

BIODEP STUDY

Chamberlain et al., 2018

Brain Microglia in Psychiatric Disorders

Brain microglia in psychiatric disorders

Valeria Mondelli, Anthony C Vernon, Federico Turkheimer, Paola Dazzan, Carmine M Pariante

The role of immune activation in psychiatric disorders has attracted considerable attention over the past two decades, contributing to the rise of a new era for psychiatry. Microglia, the macrophages of the brain, are progressively becoming the main focus of the research in this field. In this Review, we assess the literature on microglia activation across different psychiatric disorders, including post-mortem and in-vivo studies in humans and experimental studies in animals. Although microglia activation has been noted in all types of psychiatric disorder, no association was seen with specific diagnostic categories. Furthermore, the findings from these studies highlight that not all psychiatric patients have microglial activation. Therefore, the cause of the neuroinflammation in these cohorts and its implications are unclear. We discuss psychosocial stress as one of the main factors determining microglial activation in patients with psychiatric disorders, and explore the relevance of these findings for future treatment strategies.

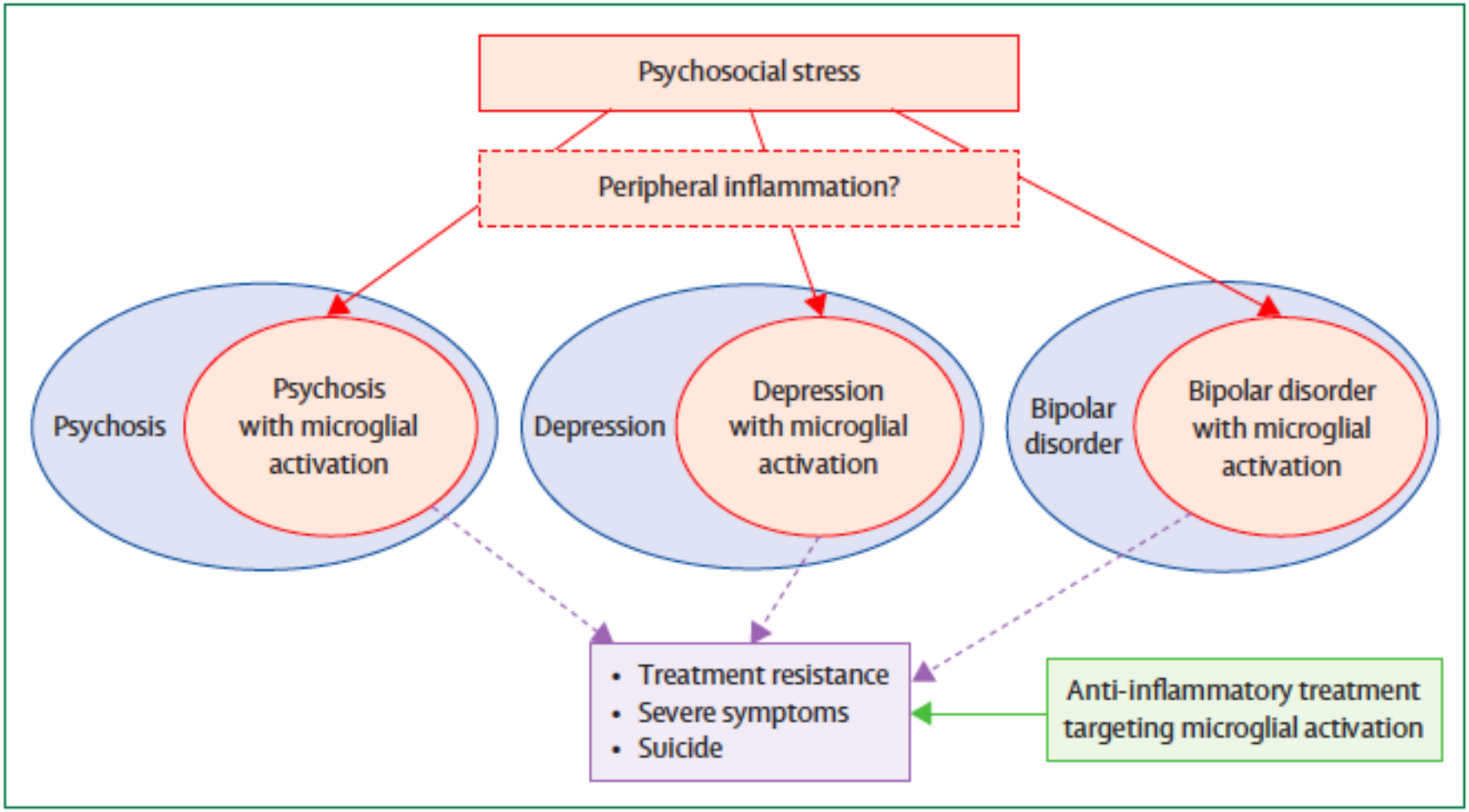
Lancet Psychiatry 2017

Published Online
April 25, 2017
http://dx.doi.org/10.1016/S2215-0366(17)30101-3

Department of Psychological Medicine (V Mondelli PhD, C M Pariante PhD), **Department of Basic and Clinical Neuroscience** (A C Vernon PhD), **Department of Neuroimaging**

Mondelli et al., Lancet Psychiatry 2017

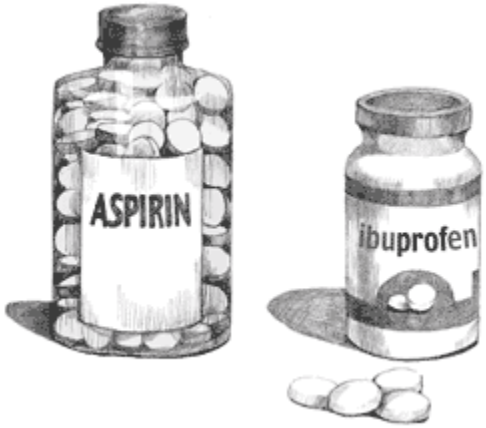
Microglia in Psychiatric Disorders



Mondelli et al., Lancet Psychiatry 2017

Anti-inflammatory treatments for depression and psychosis?

- If inflammation is increased in depression and psychosis, and it is contributing to lack of response to conventional psychotropic, can we use anti-inflammatory treatment to treat these patients?

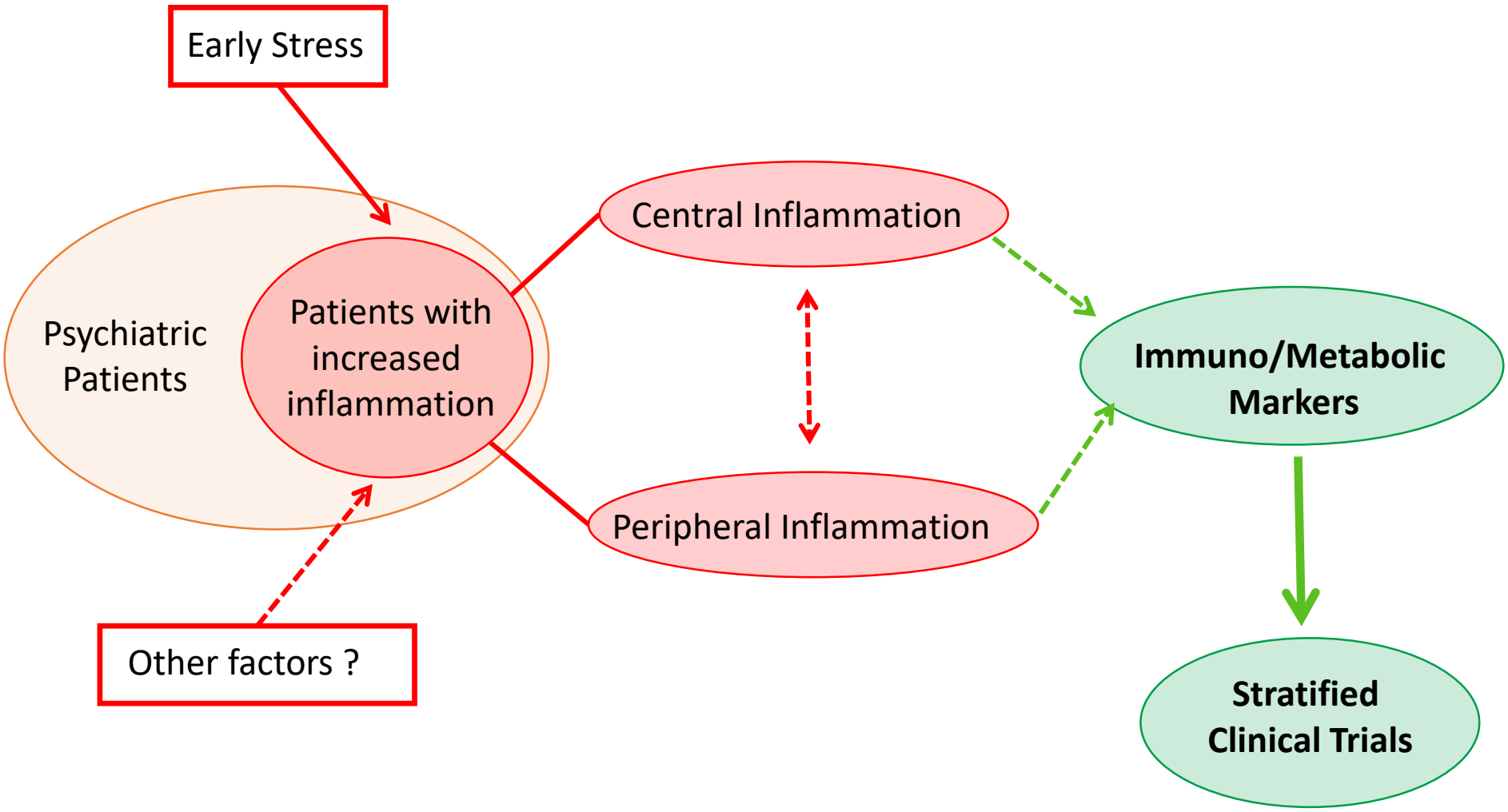


Minocycline trial

- We are conducting a randomized clinical trial using either minocycline or placebo in patients with treatment resistant depression and high levels of inflammation

- **MINDEP trial** funded by NIHR SLaM BRC

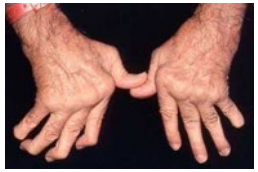
Proposed model and next steps




Body / inflammation biology
Mind / neuroscience

Inflammatory arthritis

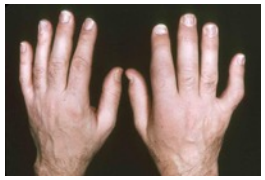
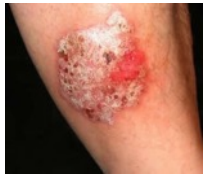
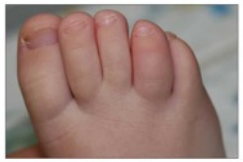
Rheumatoid arthritis



Chronic inflammation of the synovial lining

Affects ~400,000 patients in the UK

Psoriatic arthritis

Inflammatory disease of the joint and skin

Affects ~100,000 patients in the UK; ~30% of patients with psoriasis will develop PsA

Subtype of spondyloarthritis

RA and PsA are clinically, serologically and genetically distinct

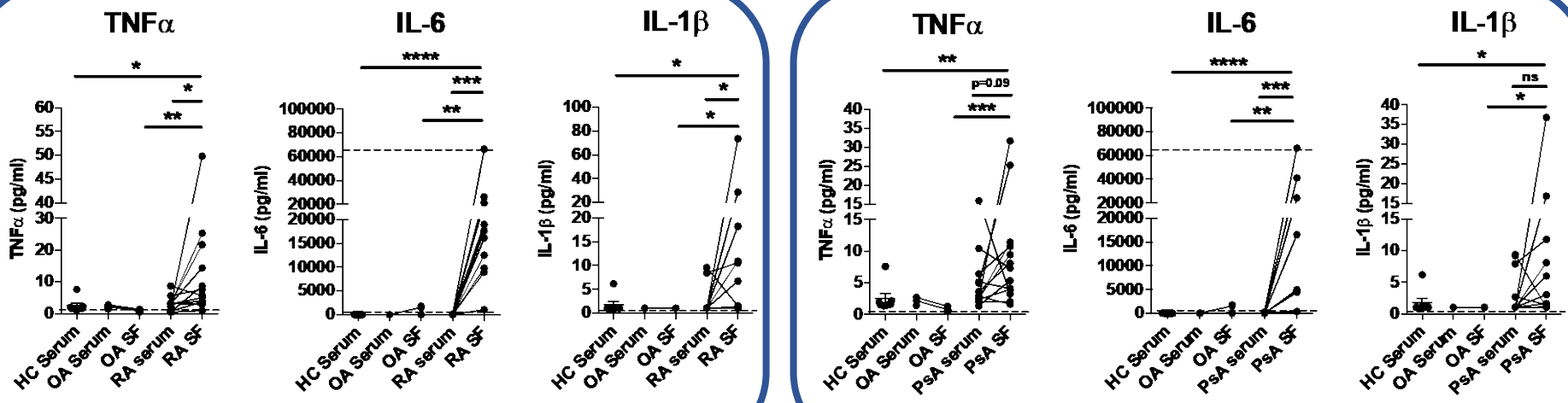
and immunologically

Inflammatory arthritis

Rheumatoid arthritis

Psoriatic arthritis

Inflammatory cytokines in the serum



Bommarito et al. Clin Exp Immunol 2017

Inflammatory Tc17 cells in the joint

Menon et al. Arthritis Rheumatol 2014; Steel et al. submitted

Chronic inflammatory disease and depression

- Psoriasis patients have an increased risk of depression, anxiety, and suicidality.
  - Estimated that in the UK, >10,400 diagnoses of depression, 7,100 diagnoses of anxiety, and 350 diagnoses of suicidality are attributable to psoriasis annually.

Kurd et al. Arch Dermatol. 2010 Aug; 146(8): 891–895
Cohen et al. JAMA Dermatol. 2016 Jan;152(1):73-9

- Individuals with immune-mediated inflammatory diseases, including IBD, MS and RA are at increased risk of psychiatric comorbidity. Increased risk seen for all three IMIDs and for all psychiatric disorders studied, implying a common underlying biology for psychiatric comorbidity in those with IMID.

Marrie et al. J Psychosom Res. 2017 Oct;101:17-23

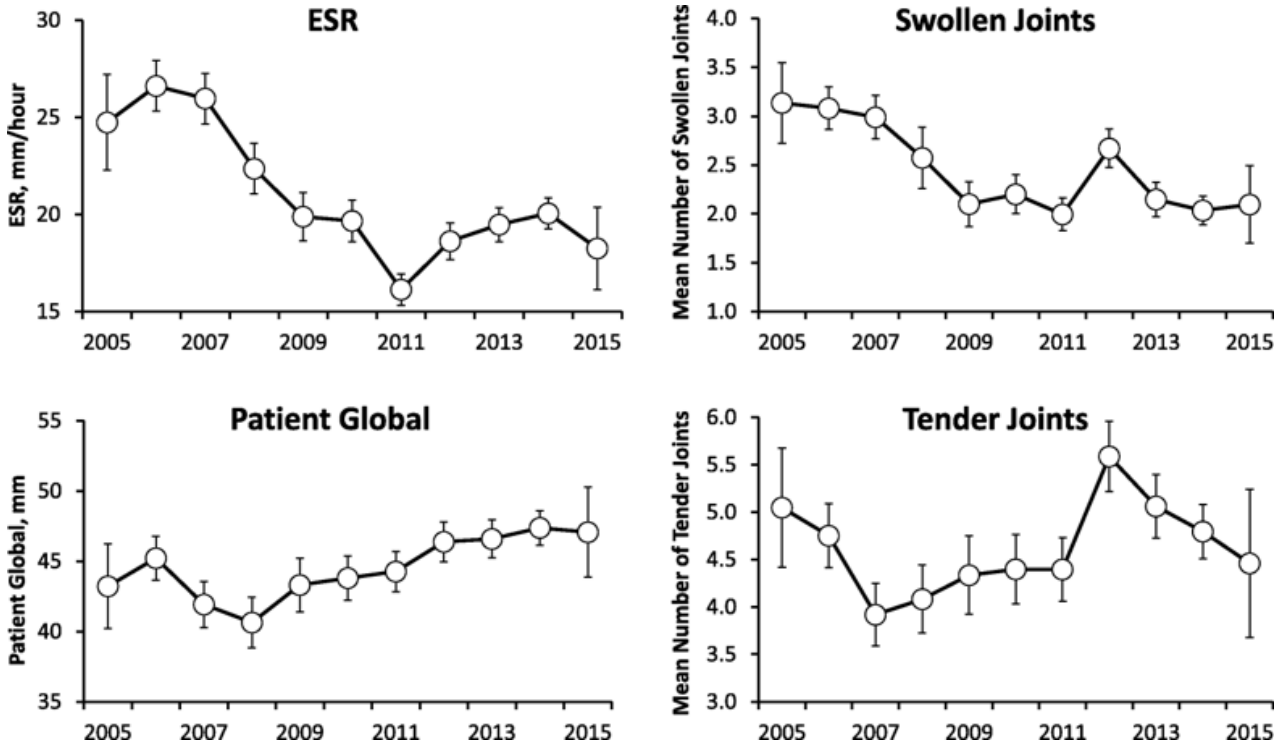
- 10% of people with ankylosing spondylitis have doctor–diagnosed depression compared to 6% of the general population seeking healthcare (13–year observation period).
- ~1 in 6 people (16.8%) with RA have major depressive disorder (UK average is 2.9%).
- Baseline and persistent symptoms of depression/anxiety are associated with poorer health outcomes in patients with RA over time, as well as reduced treatment response.
  - Persistent depression/anxiety: reduced odds of reaching RA remission at 2 years
  - Baseline depression/anxiety: 50% reduction in prednisolone treatment response in RA

Meesters et al. Arthritis Res Ther. 2014; 16: 418
Matcham et al. Rheumatology (Oxford). 2013;52:2136–48
Matcham et al. Rheumatology (Oxford). 2016;55(2):268-78

Inflammatory arthritis and pain

A longitudinal study of 1,693 patients with rheumatoid arthritis at Guy's Hospital showed that while anti-rheumatic treatment strategies reduced swollen joints over 10 years, measures of pain remained virtually unchanged over the same period.

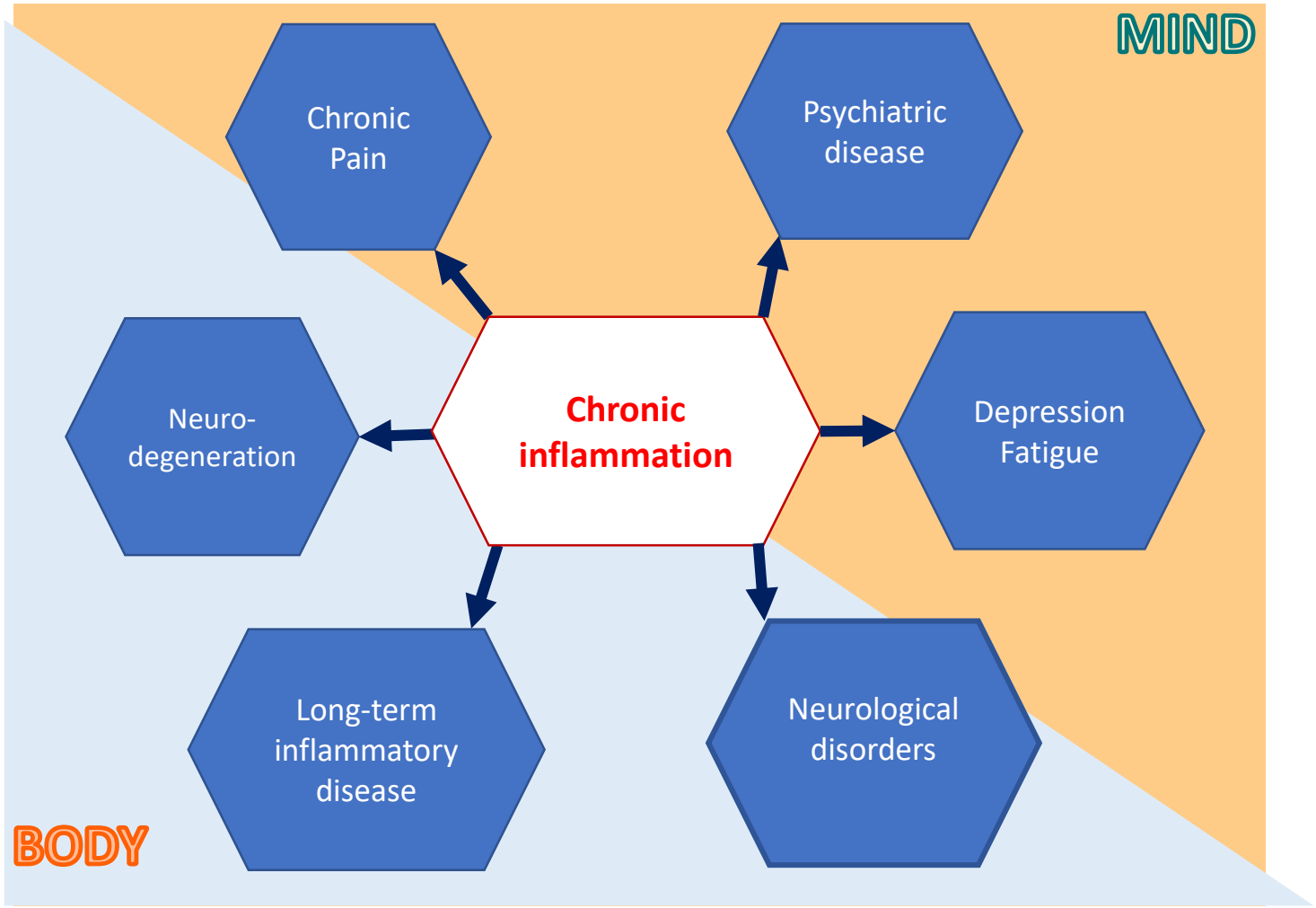
Gullick et al. BMC Rheumatology 2019



In ~3,000 patients recruited prospectively and a systematic review of 29 studies, markers of inflammation and DAS28 improved, but pain, fatigue, function and mental health were largely unchanged.

Matcham et al. Arthritis Rheumatol 2018

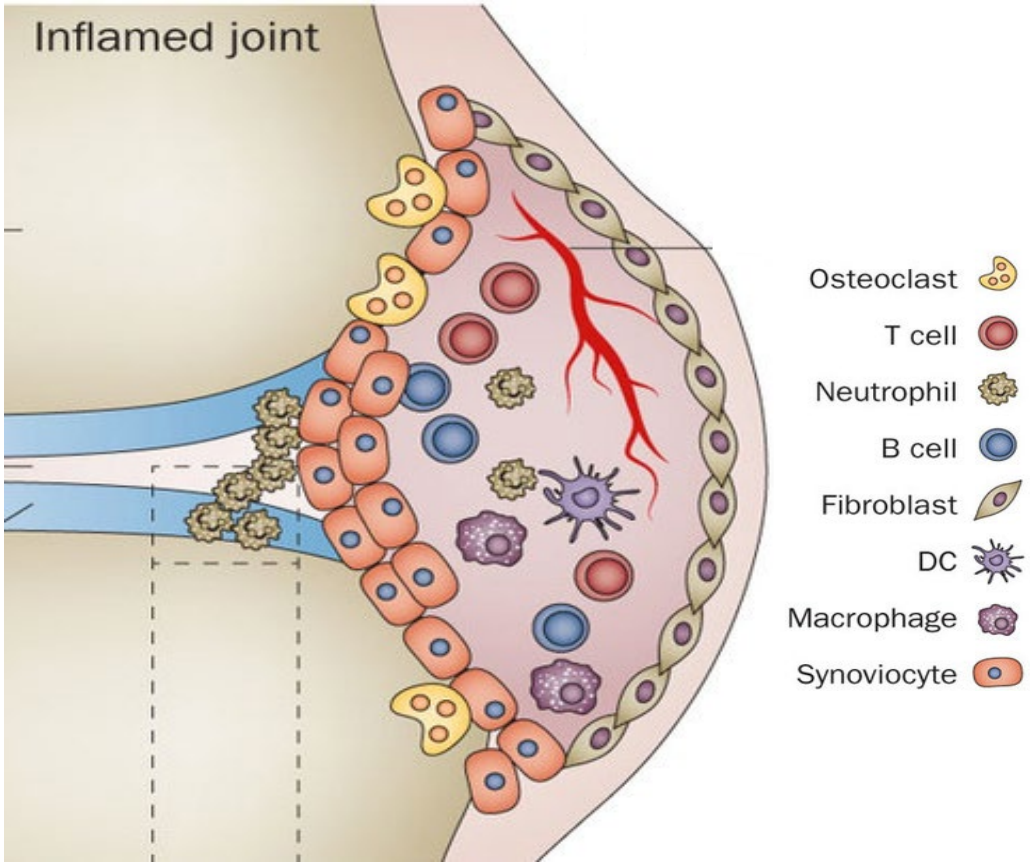
Inflammation underlies, or is associated with, many common pathologies



King's Together Strategic Award 'Body & Mind in Chronic Inflammation'

Leonie Taams, Franziska Denk, Carmine Pariante and many others

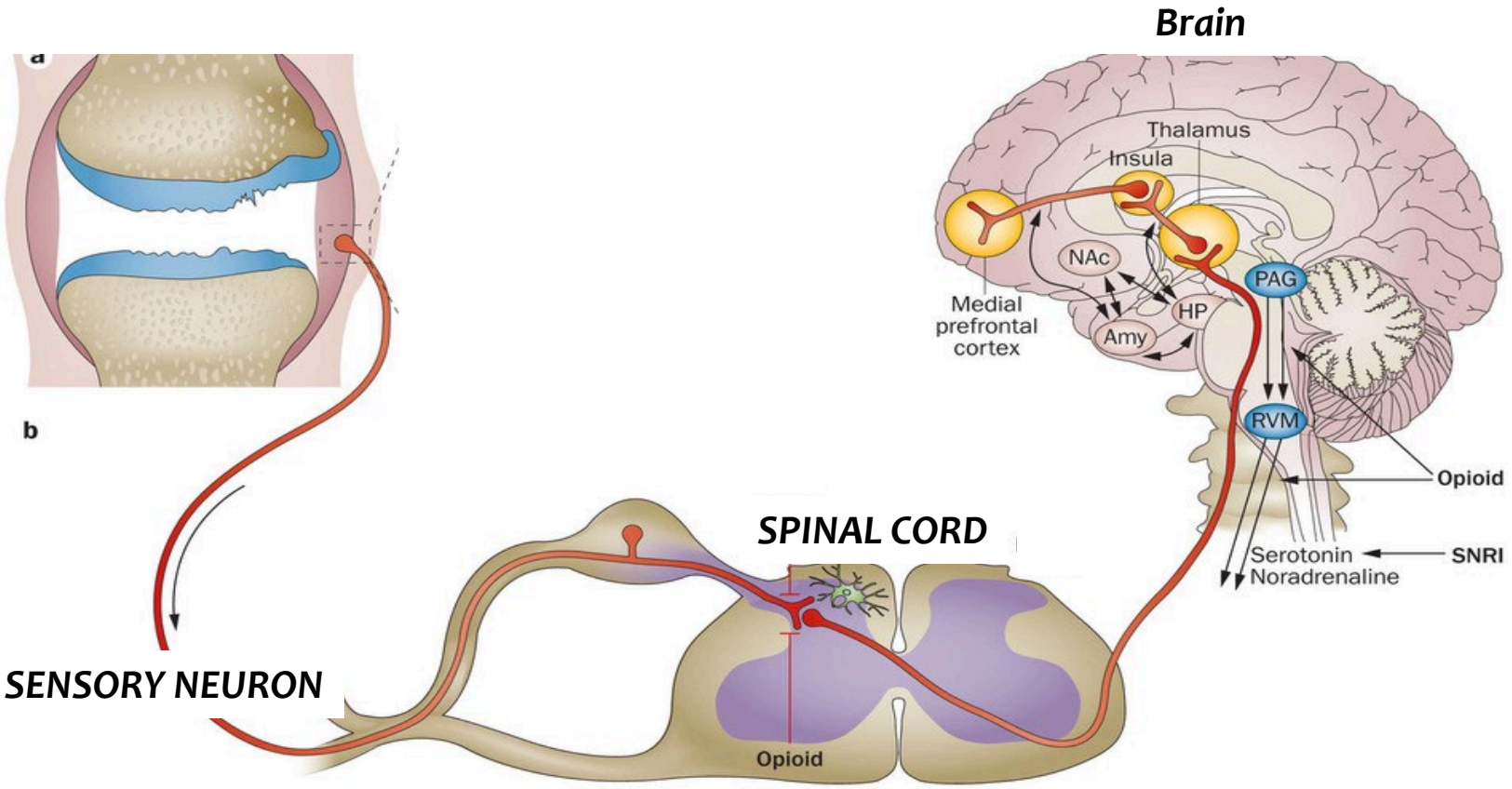
An immunologist's view of inflammatory arthritis



Courtesy of Franziska Denk

adapted from Wright et al, Nat Rev Rheumatol, 2014

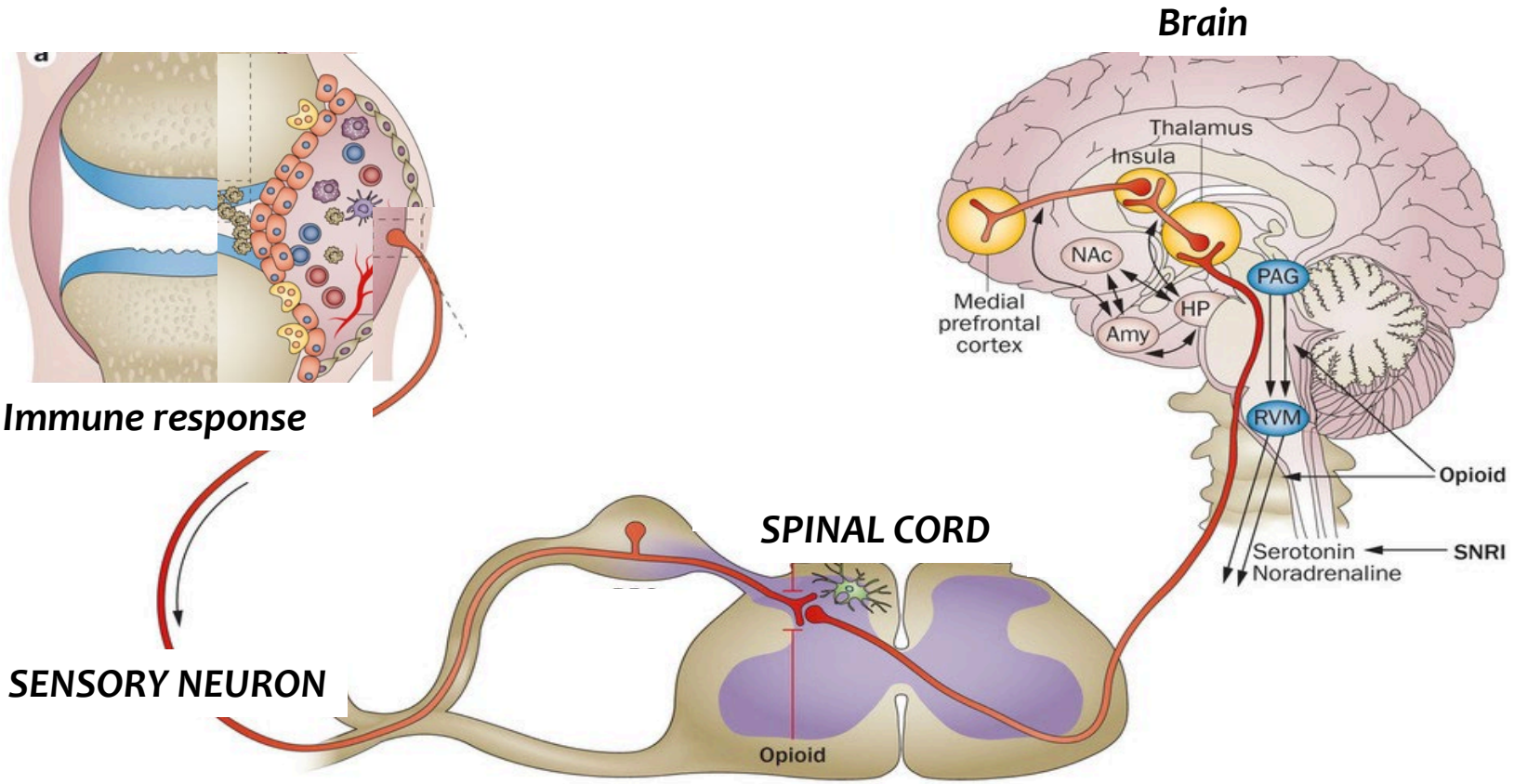
A neuroscientist's view of arthritis



Courtesy of Franziska Denk

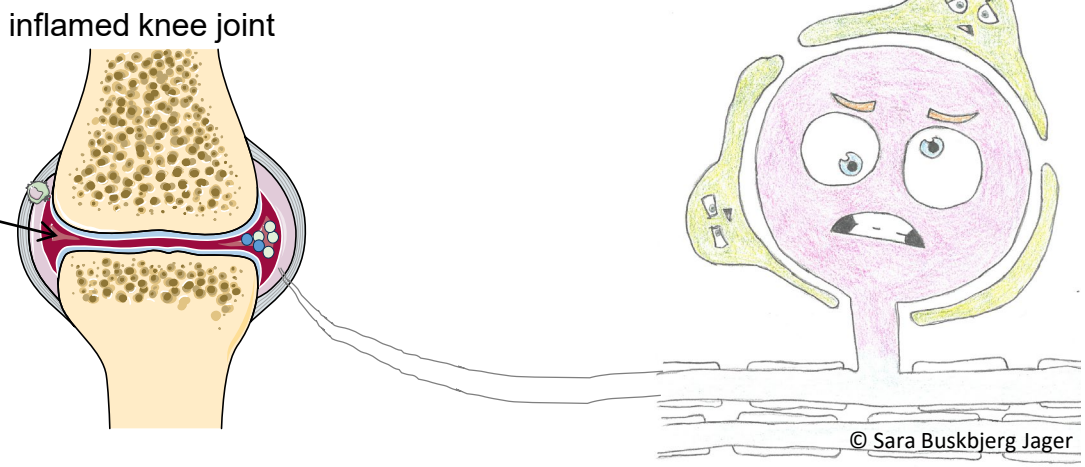
adapted from Malfait & Schnitzer, Nat Rev Rheumatol, 2014

Working together to capture the full complexity



Courtesy of Franziska Denk

How do immune cells & neurons communicate?



joint neuron made unhappy by some of these substances

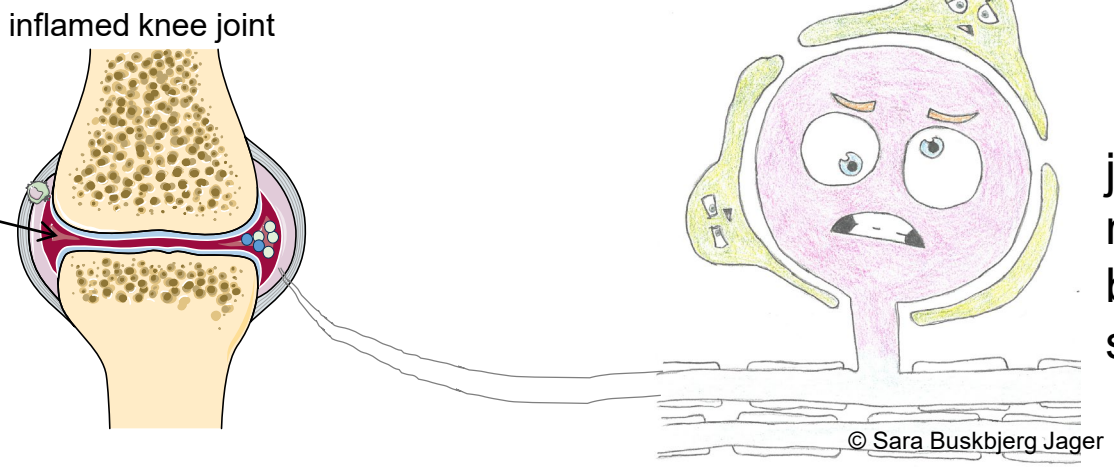
unhappy brain & chronic pain

So far we mainly asked: Which substances cause inflammation?

Now we should ask: Which inflammatory substances specifically talk to neurons?

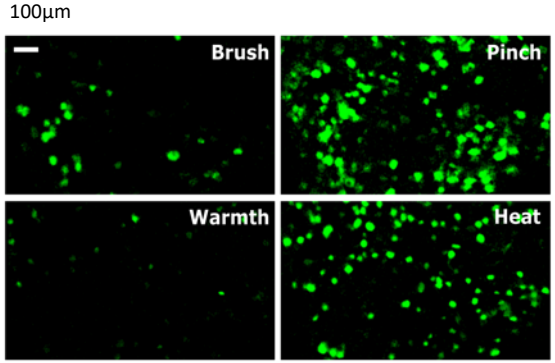
Courtesy of Franziska Denk

How do immune cells & neurons communicate?



joint neuron made unhappy by some of these substances

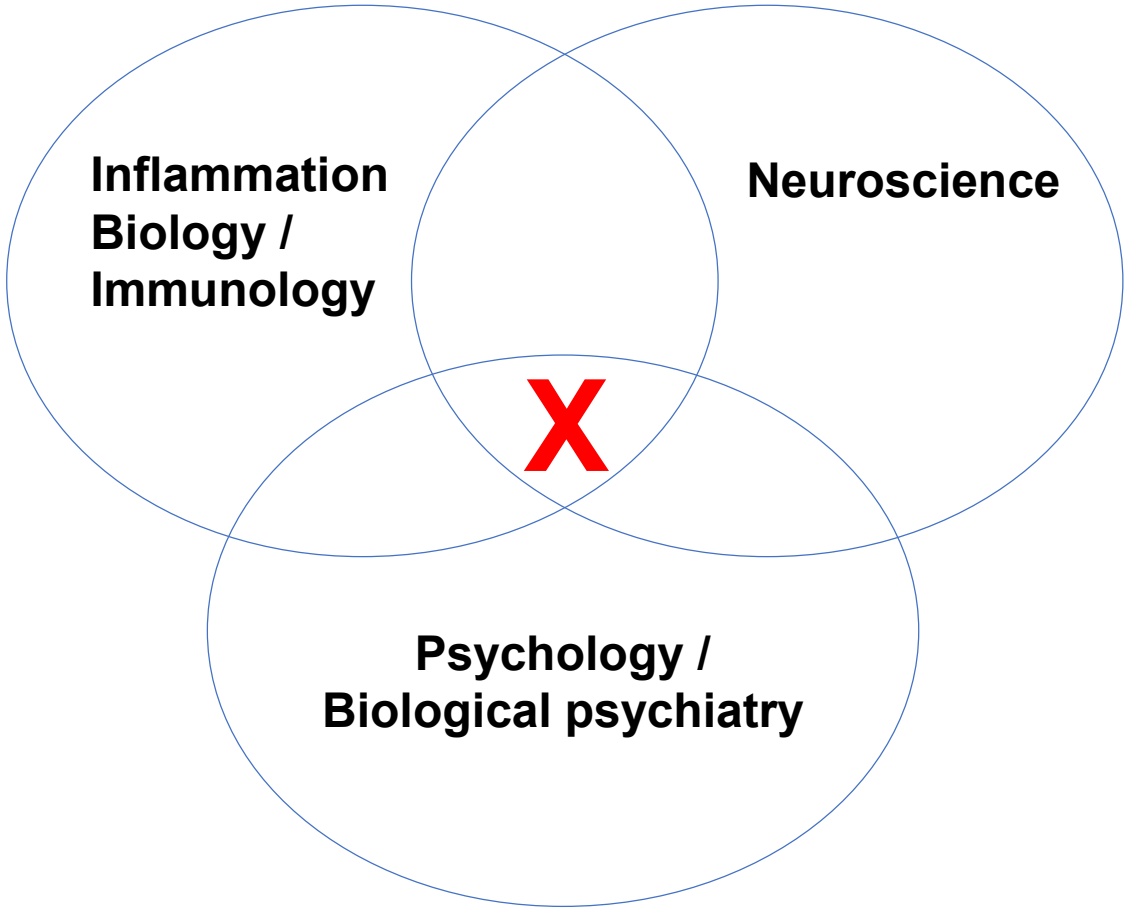
- ***Study neuro-immune interactions***
- ***Add inflammatory cells or substances from the inflamed joint to neurons***



Courtesy of Franziska Denk

Can we identify common molecular pathways?

RA
PsA
Psoriasis
IBD
Diabetes
…



Long-term pain
Spinal cord injury
Neurodegeneration
Schizophrenia
….

Depression, anxiety, psychosis, ….

Novel or re-purposed drugs for disease intervention….

Uniquely placed to address these questions

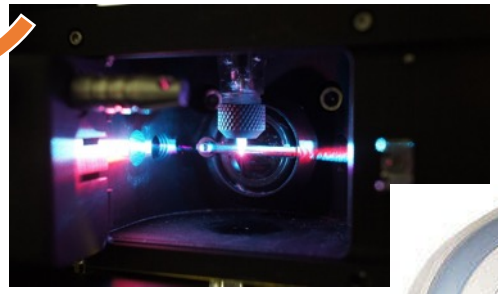
Internationally renowned Scientific Expertise

- Research Centres focused on Immunobiology of Inflammatory Disease
- Institute of Psychiatry, Psychology and Neuroscience
- UK Dementia Research Institute

Patient & Clinical Expertise

- Expert Patient groups
- King's Health Partners

Excellent infrastructure



- Our BRCs
- Imaging
- Flow core
- Genomics Core

Our ambitions

- To build a **strong network** to drive world-leading interdisciplinary research in “Neuro-Immune interactions in Health and Disease”

- To identify and lead on **important mechanistic research questions** at the interface of inflammation biology, neuroscience and mental health research

- To train a **new generation of research scientists** to perform integrated world-class research at the interface of neuroscience, immunology/inflammation biology and psychology/psychiatry.

Thank you

Q&A

Coffee break

Second session at 11:35

#KHP10Years

Public Health England

Protecting and improving the nation's health

AHSCs, preventive challenges and the NHS going forward

Yvonne Doyle CB MD.
Regional Director, Public Health England London
Statutory Adviser to the Mayor of London

Prepared for King's Health Partners Annual Conference, 16th May 2019

Public Health England

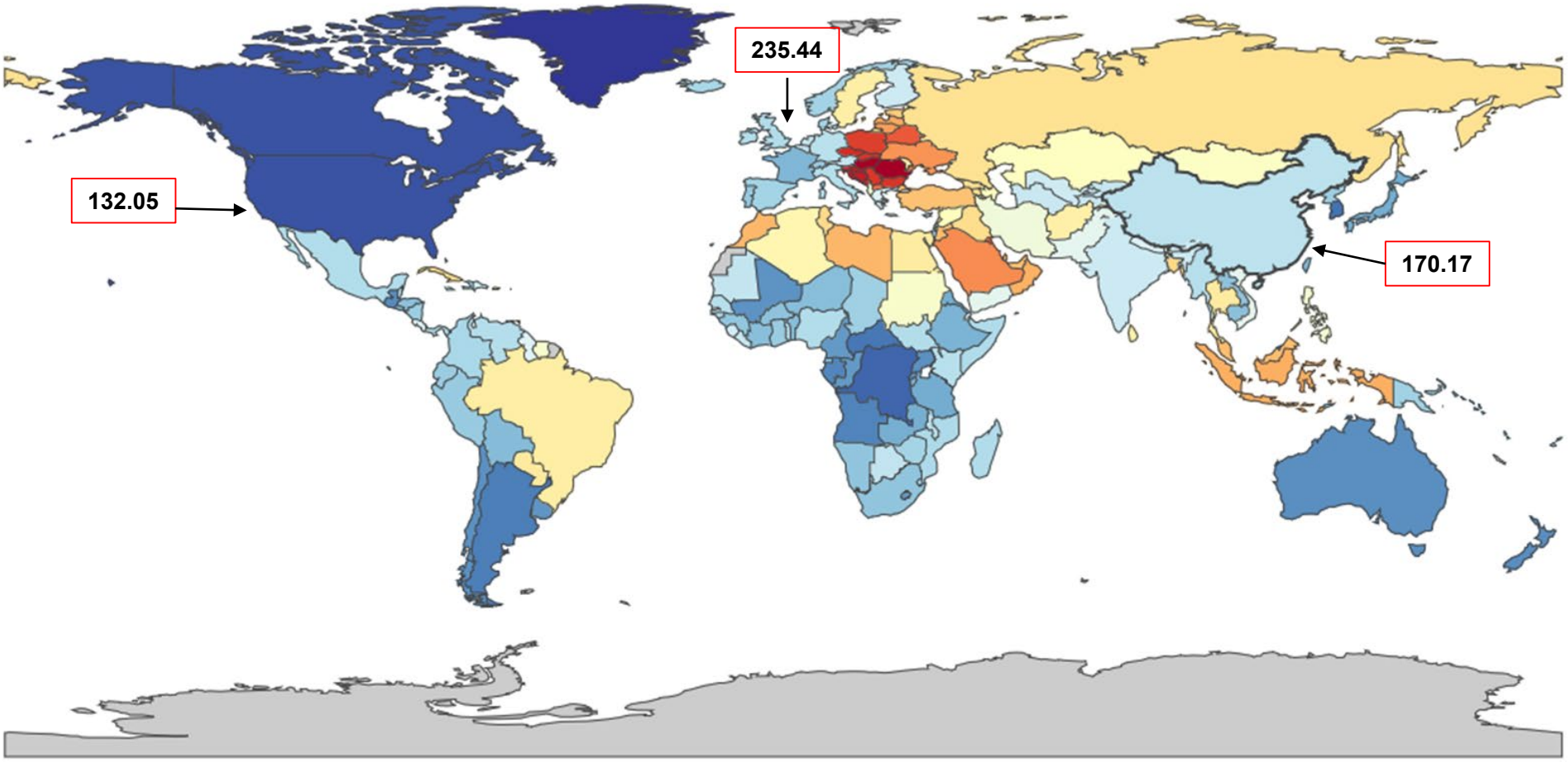
Protecting and improving the nation's health

We have a great variety of ways to describe problems in the UK and international populations

Solutions are less often taught, researched or practiced

Global Burden of Disease

Years of life in disability from ischemic heart disease for individuals aged 15-49 years in China, UK and USA . Rate per 100,000 population, 2016

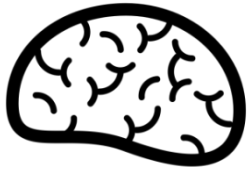


Top killers and health risks in London

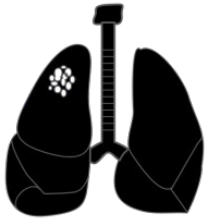
The Top 5 Killers

Ischaemic heart disease
12.7%

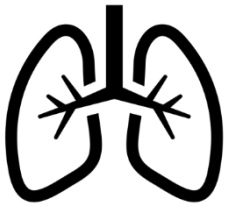
Dementia and Alzheimer's disease
8.3%



Cerebrovascular disease
6.5%



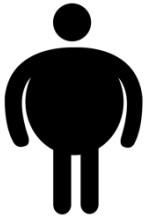
Malignant neoplasm of trachea, bronchus and lung
6.2%



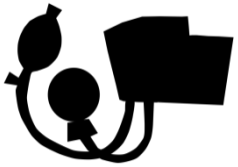
Chronic lower respiratory disease
5.8%

The Top 5 Risks

Smoking



Obesity



High Blood Pressure

Pre-diabetes

Alcohol

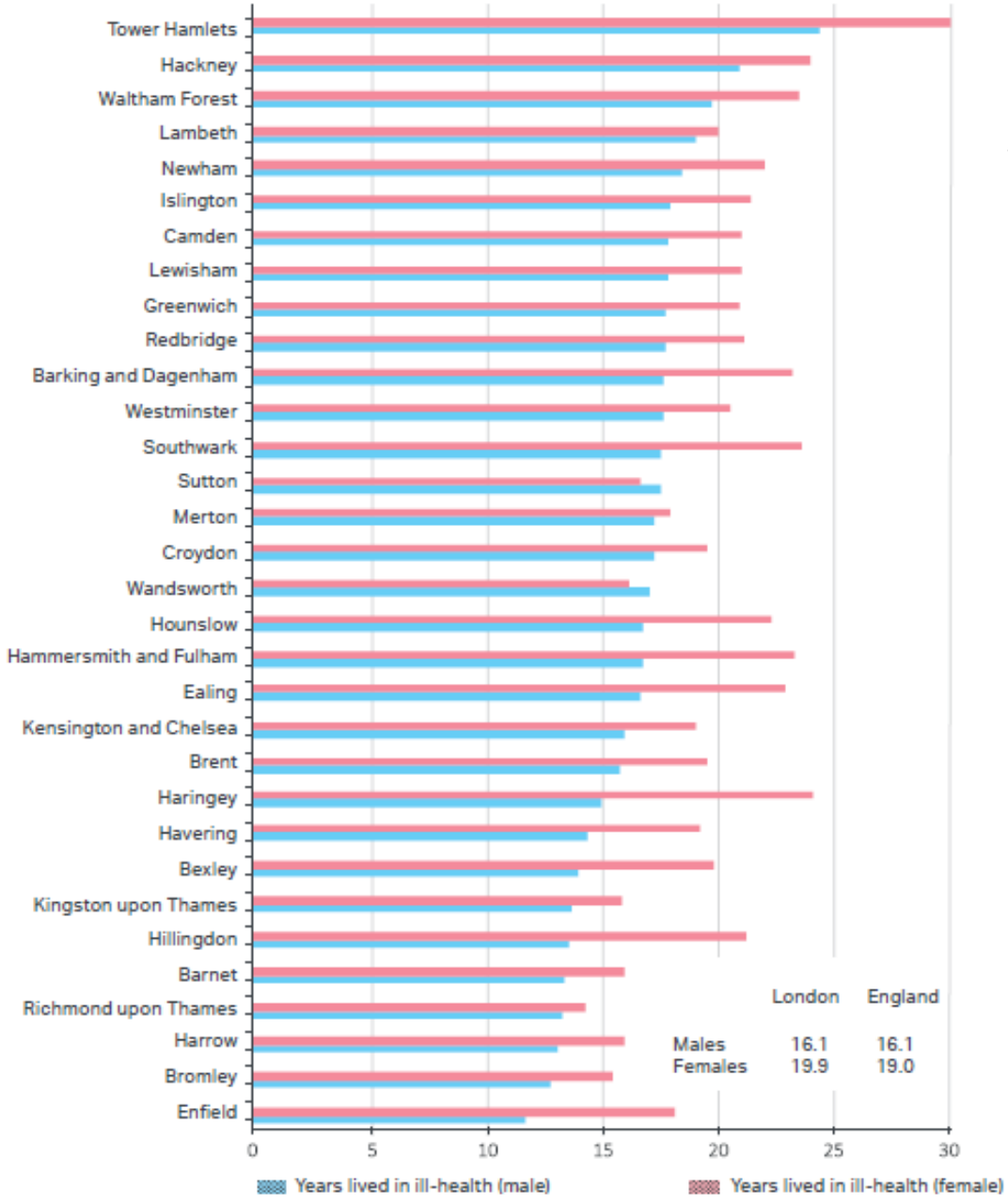
Top 5 leading causes of morbidity* (level 3 disease groups) by age, females, England, 2016

Age	1st	2nd	3rd	4th	5th
15 to 49 year olds	Low back and neck pain	Migraine	Skin diseases	Depressive disorders	Anxiety disorders
50 to 69 year olds	Low back and neck pain	Sense organ diseases	Depressive disorders	Migraine	Skin diseases
70 or older	Low back and neck pain	Sense organ diseases	Alzheimer's disease and other dementias	Falls	Oral disorders
All ages (age-standardised)	Low back and neck pain	Skin diseases	Migraine	Depressive disorders	Sense organ diseases

Top 5 leading causes of morbidity* (level 3 disease groups) by age, males, England, 2016

Age	1st	2nd	3rd	4th	5th
15 to 49 year olds	Low back and neck pain	Skin diseases	Depressive disorders	Migraine	Drug use disorders
50 to 69 year olds	Low back and neck pain	Sense organ diseases	Oral disorders	Skin diseases	Depressive disorders
70 or older	Sense organ diseases	Low back and neck pain	Stroke	Oral disorders	Alzheimer's disease and other dementias
All ages (age-standardised)	Low back and neck pain	Skin diseases	Sense organ diseases	Depressive disorders	Migraine

Figure 1: Years of life lived in ill-health by borough, male and female



Reference: Public Health England, Public Health Outcomes Framework, calculated as the difference between life expectancy at birth indicator 0.1i and healthy life expectancy at birth indicator 0.1ii, 2013-15
Note: Calculated by taking Healthy Life Expectancy 2013-15 from Life expectancy at birth 2013-15

Years lived in ill-health, London boroughs, 2013-15.

2 x

The rate of early deaths from preventable causes is twice as high in Tower Hamlets as it is in the City of London

Public Health England

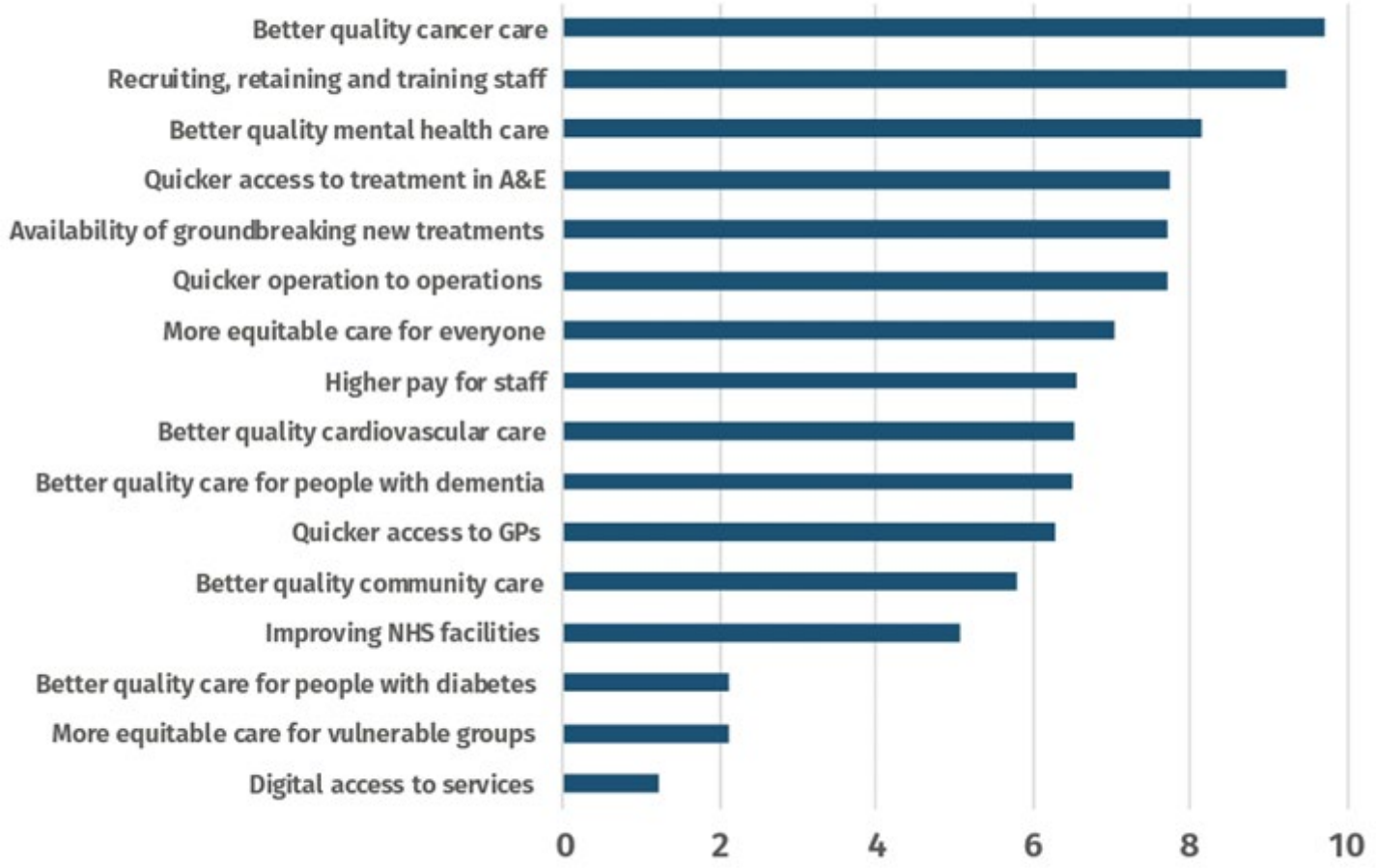
Protecting and improving the nation's health

Despite manifest inequalities in health and imbalance in health care solutions to major risks in England, the voting public have very clear ideas as to where funding should go.

And it s not always where it is needed.

FIGURE S1

Relative importance placed on spending priorities as determined by the MaxDiff score



Source: ComRes Polling

Public Health England

Protecting and improving the nation's health

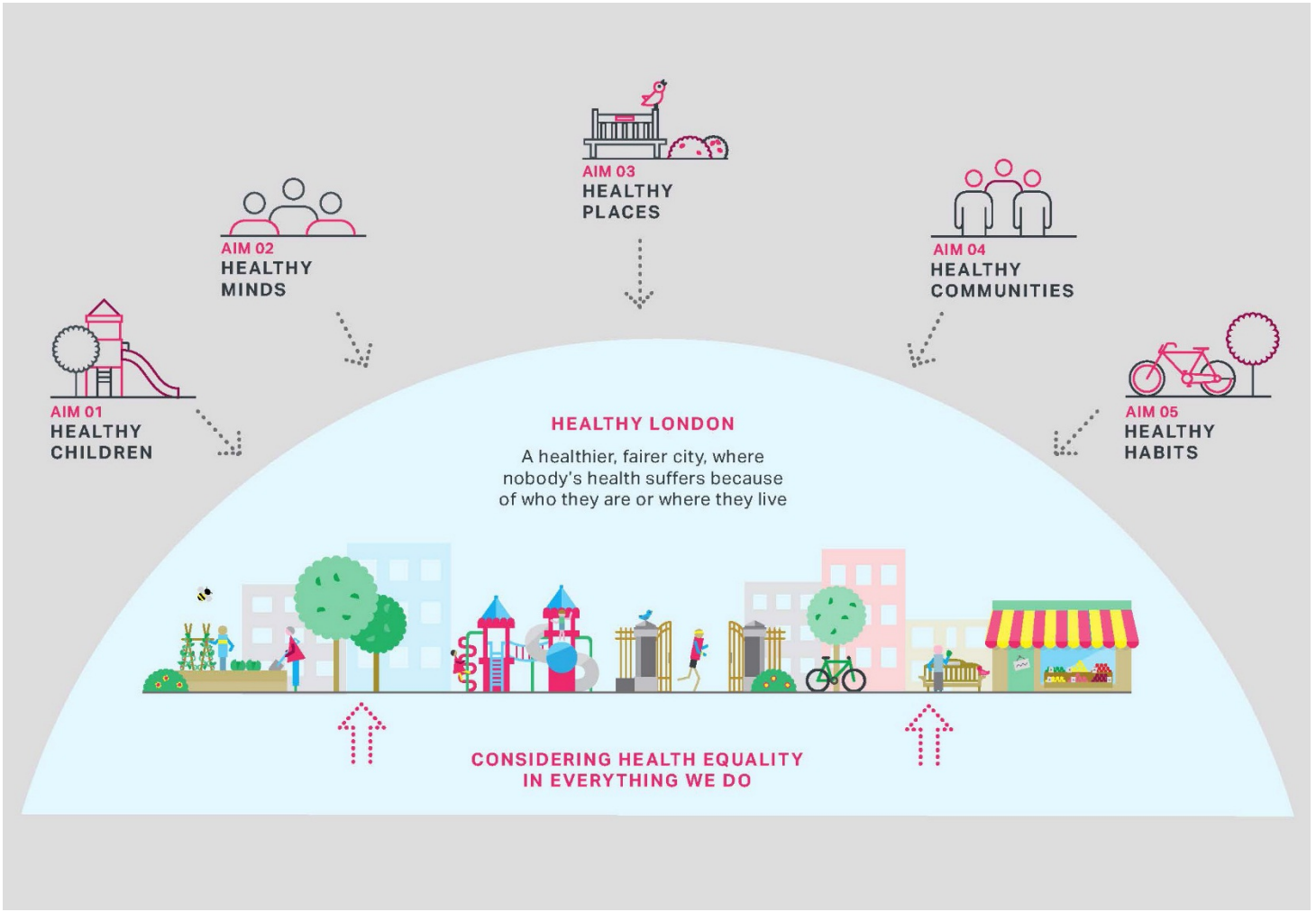
However practice is changing and experienced practitioners are making use of new opportunities – for instance working at city level and learning internationally.

Example:
Work to get health in all policies at city level.

Public Health England

Protecting and improving the nation's health

London's Response to Inequalities in Health: London Mayor's Health Inequalities Strategy and Programmes, 2018



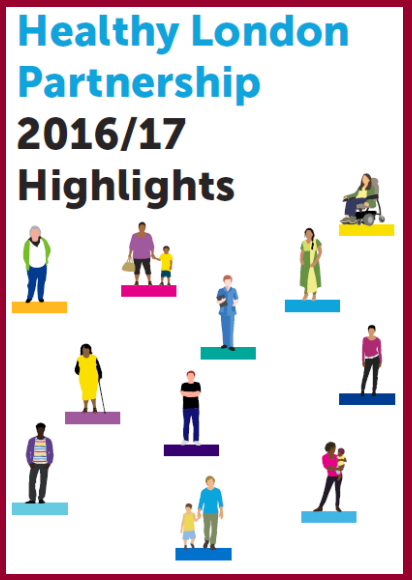
Implementation of a ‘health in all policies’ approach

Public Health England

Protecting and improving the nation’s health

1. Health in All Policies Approach – The Mayor’s Seven Statutory Strategies

2. Partnership across the city



3. Learning from other cities

Public Health England

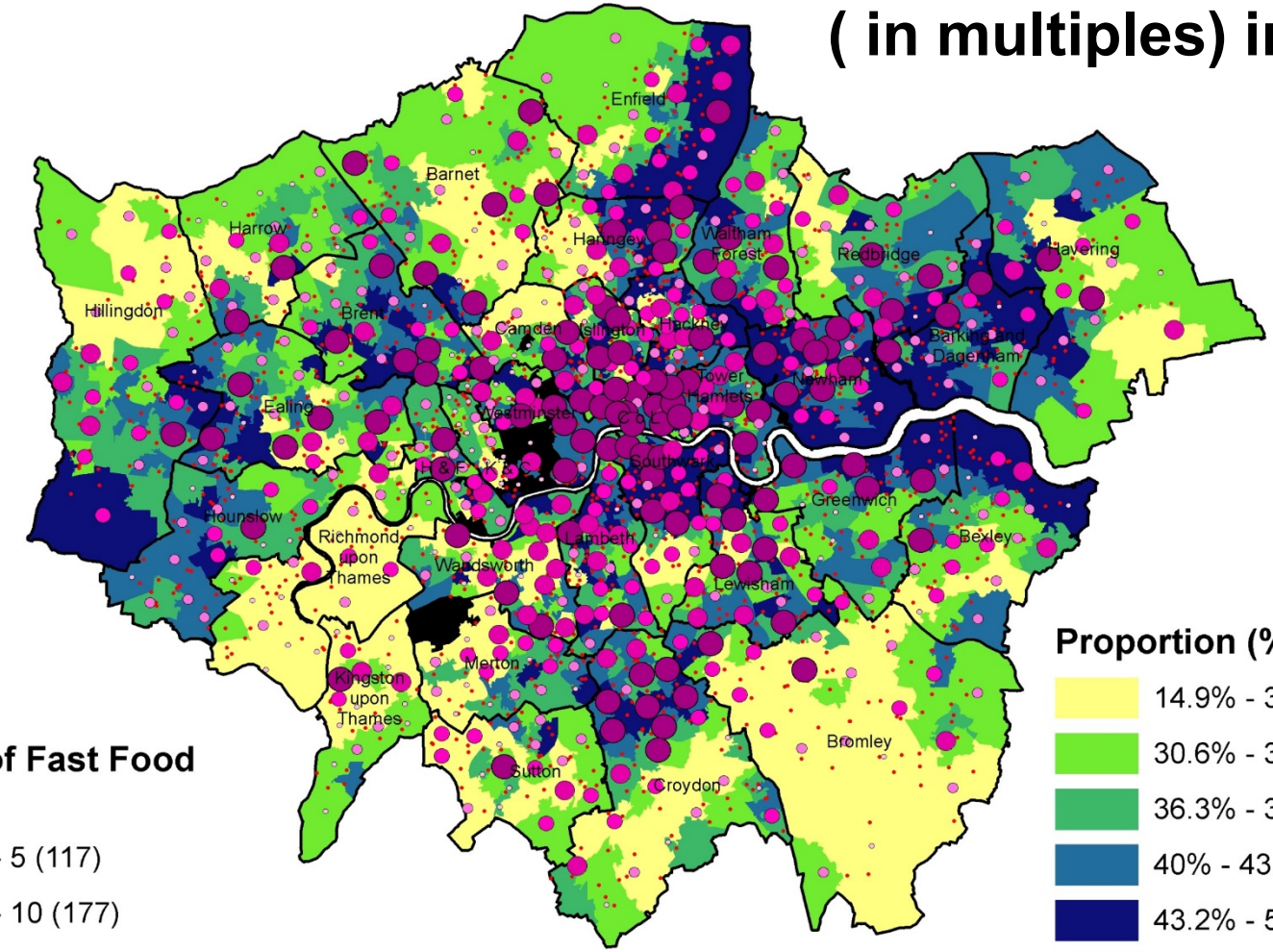
Protecting and improving the nation's health

When practitioners do act, they do so on best information – which may not be far removed from intuition. Research on preventive interventions lags behind the need to take action.

Examples are:

(i)child obesity - a major problem in London.
(ii) How to address environmental concerns when the science points in a different direction

Fast Food outlets (in multiples) in London



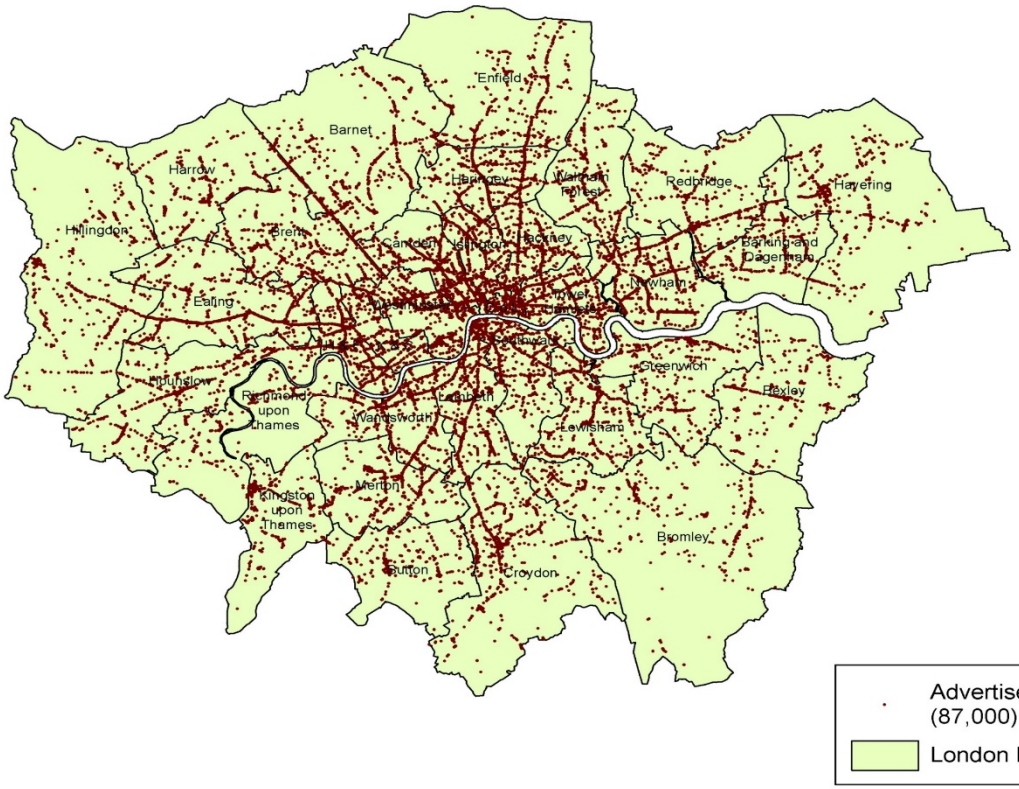
Count of Fast Food Outlets

- 1 - 5 (117)
- 6 - 10 (177)
- 11 - 15 (136)
- 16 - 20 (86)
- 21 - 147 (113)

Proportion (%)

- 14.9% - 30.5% (194)
- 30.6% - 36.2% (194)
- 36.3% - 39.9% (194)
- 40% - 43.1% (194)
- 43.2% - 52.2% (193)
- Not available (14)
- Primary Schools (1,860)
- London Boroughs (33)

Junk food reminders everywhere



Tube 'junk food' advert ban announced by London mayor

23 November 2018 | 178

PA

"Junk food" adverts will be banned on the Underground, Overground and bus network

A ban on junk food advertising across London's entire public transport network will be introduced next year.

LIVE BBC London Live: Latest updates

1 hour ago

Surrey begin title defence against Essex

Top Stories

Brexit deal is 'doomed' warns Fallon

Ex-cabinet minister says agreement is the "worst of all worlds" as PM visits Wales and Northern Ireland.

1 hour ago

May challenges Corbyn to Brexit TV debate

3 hours ago

Hedges praises 'brave and strong' wife

2 hours ago

Features

This was not a simple exercise. We used national expertise to support our actions.

Sun.maid Raisins

High energy and sugar product but high fibre and fruit.

NPM classifies the product as non-HFSS.

This product would be allowed to advertise on TFL.

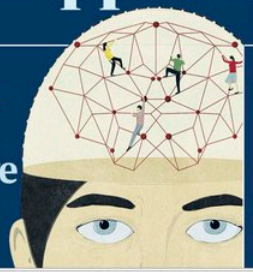
Nutrition

Typical Values	Typical Values Per 100g
Energy	1,322 kJ
-	316 kcal
Fat	0.7 g
of which saturates	0.0 g
Carbohydrates	76.9 g
of which sugars	71.4 g
Fibre	5.8 g
Protein	3.0 g
Salt	0.02 g

Section:GDN 1N PaGe:1 Edition Date:181013 Edition:01 Zone:S Sent at 12/10/2018 18:55

Free supplement **Train your brain**

Top tips, exercises and tests to improve your memory



The Guardian

Saturday
13 October 2018
Issue № 53,539
£2.90

Revealed: 'huge concentration' of toxins around Grenfell site

Exclusive
Assess the risks to those nearby, says expert, after early results of study

Nick Hopkins

Toxins that may have long-term health implications for the survivors of the Grenfell Tower fire, and thousands of people who live and work nearby, have been identified in the preliminary findings of a study led by one of the world's leading toxicology experts, the Guardian can reveal.

Early results of Prof Anna Stec's analysis led her to privately urge Public Health England (PHE), the Department of Health, the police and Kensington and Chelsea council to organise tests to ensure potential health risks could be assessed.

In briefings to senior health agency staff, Stec warned she had found "huge concentrations" of potential carcinogens in the dust and soil around the tower, and in burnt debris that had fallen from the tower. High levels of hydrogen cyanide were also present in the soil she analysed.

She suggested the health authorities should consider taking samples of blood and saliva from survivors, firefighters and those who live in the area to monitor any damage to their DNA.

But PHE decided against committing to the action she suggested until publication of her full report, which is likely to be early next year - 18 months after the fire that killed 72 people in June 2017.

The Guardian has been told this decision caused widespread concern among other health agencies, which had supported the idea of a mass health-surveillance programme, and a PR campaign to inform people about the potential risks.

Stec is an acknowledged expert in toxicology and leads a fire chemistry team at the University of Central Lancashire. She was recently appointed as an expert witness to the Grenfell Tower inquiry. She began an independent study late last year after hearing the concerns of survivors, who have long feared there may be hidden health consequences from the devastating blaze that engulfed the tower.

While PHE has monitored the air quality around the tower and has repeatedly said it has found nothing to cause concern, Stec has been focusing on soil, dust and residue.

Taking samples from eight sites up to a mile away from Grenfell Tower, the professor told the Guardian she had been investigating what might be present in the general area to help identify any potential health risks to survivors and firefighters.

In a statement to the Guardian, Stec said: "I have taken a high number of samples from a number of locations in the area - some were taken close to Grenfell Tower, others were taken from almost a mile away.

"As a result of this work, 2

▲ *The fire, which killed 72 people, may affect local people's health for years to come* PHOTOGRAPH: DANIEL LEAL-OLIVAS/AFP/GETTY

Stars come out for yet another royal wedding
Page 8

Easy bento boxes
Feast

Help! It's almost half term!
Travel

The emergence of social movements around the environment

Public Health England

Protecting and improving the nation's health

Opportunities:

The direction of healthcare: return of the NHS into population health and the importance of a place based approach

(Some) new methods in prediction

Technology innovations

The NHS Opportunities : The NHS Long Term Plan: areas of important action.

1. Leadership for high value, preventive healthcare in a place including experimentation using new methods e.g. digital access

2. Partner to other agencies in delivering an integrated approach to population needs

3. Employer and provider of opportunities to those most in need of acquiring basic skills

4. Addressing equity of access to care that is systematically good- most importantly where disadvantage is high

5. Provider of data, skills and funding for research that addresses questions on prevention that need an answer

Good Thinking
London's Digital Mental Wellbeing Service

- There is an acknowledged unmet need for people in mental distress in London and people are discussing and searching for support online.
- *Good Thinking*, London's digital mental wellbeing service, is an exemplar of digital service innovation.
- *Good Thinking* supports prevention and early help at scale, by giving all adult Londoners access to a quality assured 24hr /7 days a week online service.
- *Good Thinking* is aimed at finding those without formal diagnosis who may not see themselves as having a mental health problem and guiding them to self-help tools including NHS-endorsed apps and local resources using state-of-the-art digital marketing techniques.

Who Is Using The Service

Dec 2017 – September 2018

100,000 +	31%	Anxious	£
No. of Users (Total no. visits 400,000)	**Returning Users**	**Most Visited Topic**	***Good Thinking* currently costs less than 50p per service user.**

Website: https://www.good-thinking.uk/

Good Thinking is being evaluated by Kings College London (due 2019)

Evaluation feedback from King's College London has provided invaluable insight into the value of *Good Thinking* and it's unique approach to support people with their mental wellbeing:

"I liked how immediate it was as well. So, if you are feeling bad, you can go on it in a second instead of having to, in the real world, wait for an appointment or wait for a GP appointment and a referral, for example." – Female, 18-24.

"I think the biggest help it gives you is that you are not alone, and you can see that other people are feeling similar to what I am." – Male, 45-54.

Public Health England · NHS · Healthy London Partnership · SUPPORTED BY MAYOR OF LONDON · LONDON COUNCILS

Emerging methods with potential to benefit a preventive approach –

but not all deliver the expected results

- Social innovations:

  Accelerators, incubation, new financing methods, innovation mapping, people powered results (100 day challenges); expert by experience led programmes

- The derivation and faster control of outbreaks of disease through whole genome sequencing

- Modelling techniques to predict adverse health risk for instance type of stroke; and clinical outcomes for example patient deterioration in ITU, using deep learning

- The use of artificial intelligence to pattern environmental profiles of a place and link with known risks of poor outcomes (for instance traffic profiling via imaging and air pollution, or accident risks)

- However there are questions over the utility of polygenetic disease risk prediction and also the communication of risk to individuals in order that they change behaviours

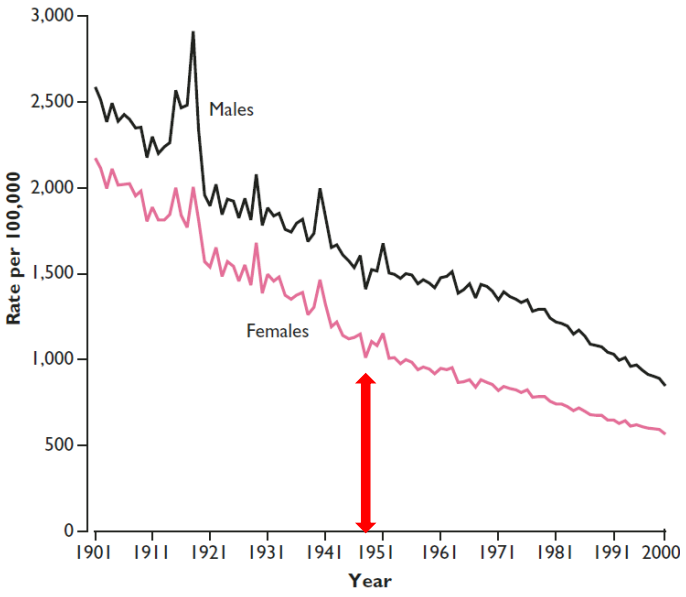
Public Health England

Protecting and improving the nation's health

Research and the role of AHSCs in supporting implementation of evidence based interventions

Mortality in England & Wales 1901 – 2000

Age-standardised annual mortality rate, all causes of death combined, by sex

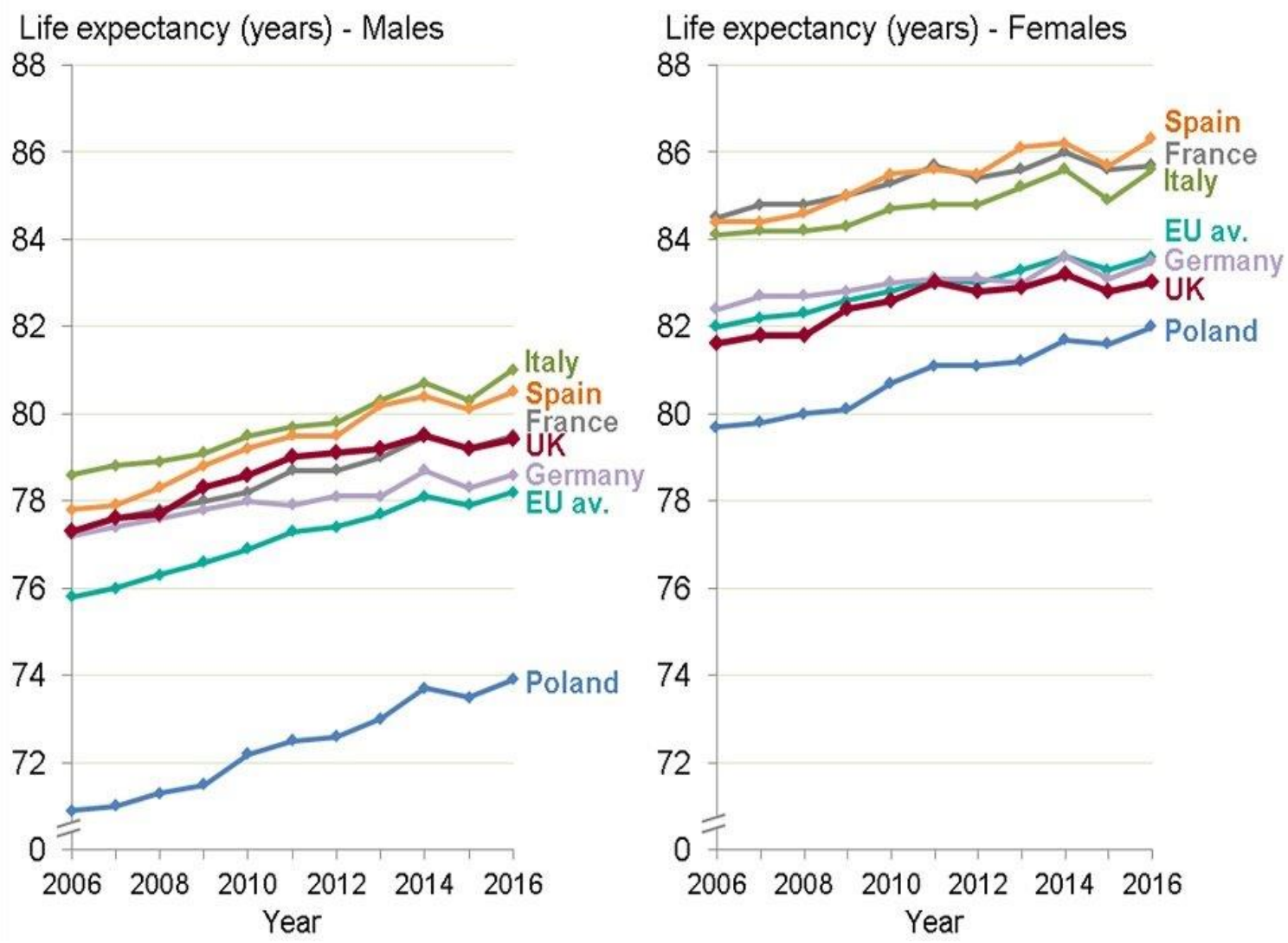


1948

2015

"By 2035 we will enjoy five more years of healthy, independent life whilst closing the gap between richest and poorest"

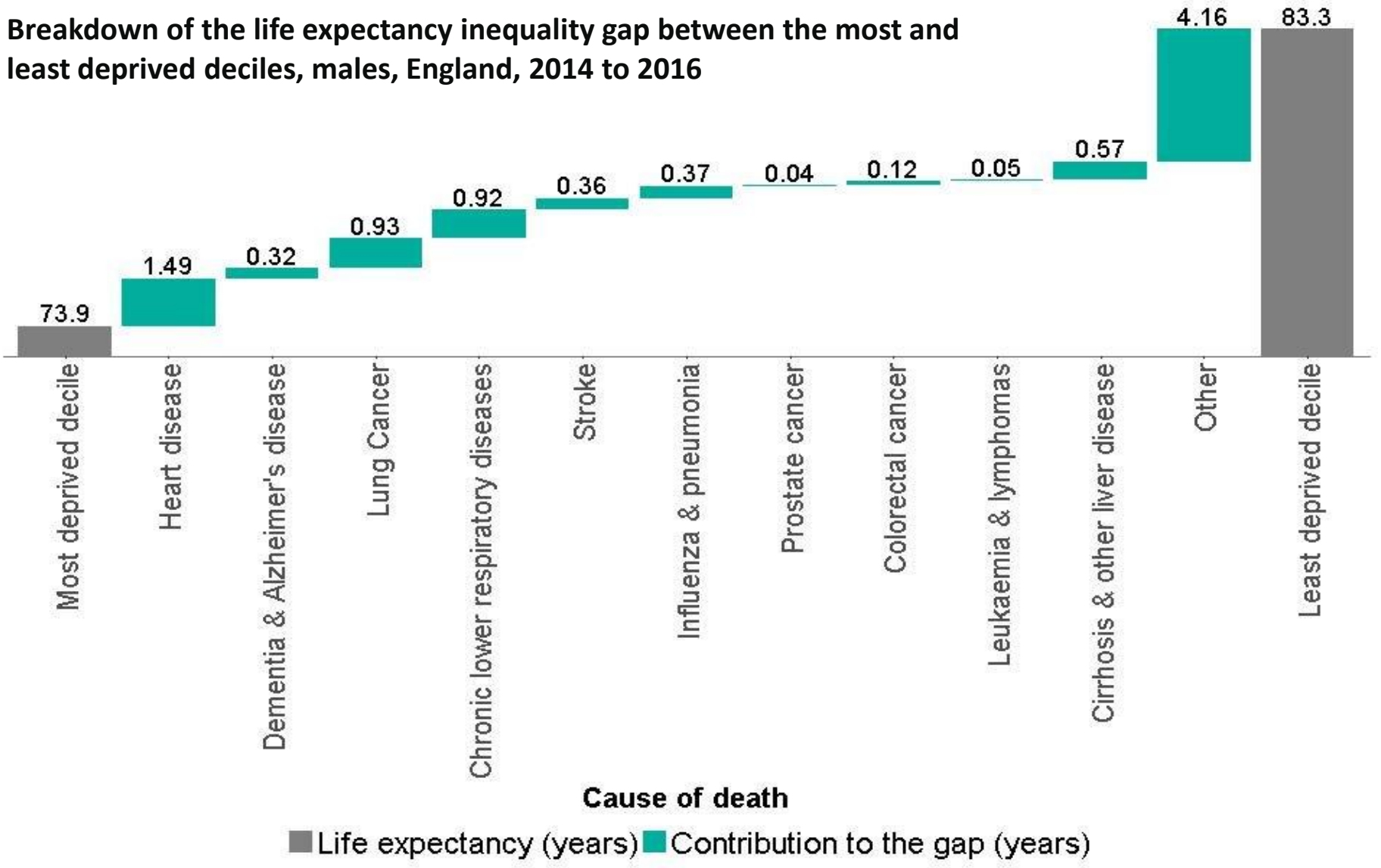
Challenge: What is happening here and why?



Source: Public Health England analysis based on mortality and population data. Health Profile for England, 2018

What have we learnt about interventions that make a difference?

Breakdown of the life expectancy inequality gap between the most and least deprived deciles, males, England, 2014 to 2016



Source: Public Health England analysis based on mortality and population data from ONS and Index of Multiple Deprivation 2015 from Ministry of Housing, Communities and Local Government

A selection of questions from PHE divisions relating to challenges in practice

- How to mitigate the impacts of anti-microbial resistance through better practices
- What behaviour change interventions will improve infection prevention and control?
- How can we enhance our better understanding of the risk to the public from vector-borne diseases including Lyme disease in England?
- What concepts of good health are now highly regards by the population?
- Is ‘digital health’ widening or narrowing health inequalities?
- What is effective and safe for maternal weight management during pregnancy?
- How feasible is surveillance of synthetic opioids through voluntary testing of users in contact with treatment services?
- What are the true impacts of welfare reform on health?
- What are the factors underlying the slowdown in population health at either end of life/

Public Health England

Protecting and improving the nation's health

Conclusions

We do understand in increasingly elegant ways, what the health challenges in England are

Practice in public health has changed, from description of problems only, to an expectation that solutions will be offered too

Taking the right approach, using the best methods, and linking cause and effect during implementation is not informed enough by evidence because research has not kept apace with practice

There are new opportunities from policy proposals; the NHS Long Term Plan requires thinking beyond the sections labelled 'prevention'.

There are also enablers coming from method development, some of the most interesting of which have come from outside the health sector

Public Health England

Protecting and improving the nation's health

Conclusions

This poses challenges to researchers in public health who may need to think differently and form new alliances to provide much needed knowledge

There are also challenges for funders in deciding what constitutes acceptable methods and approaches

BUT that is not a request to bypass high quality epidemiological approaches where these are appropriate!

Observation: there are still major gaps in knowledge as to why major changes in population health profiles have occurred both in England and globally.

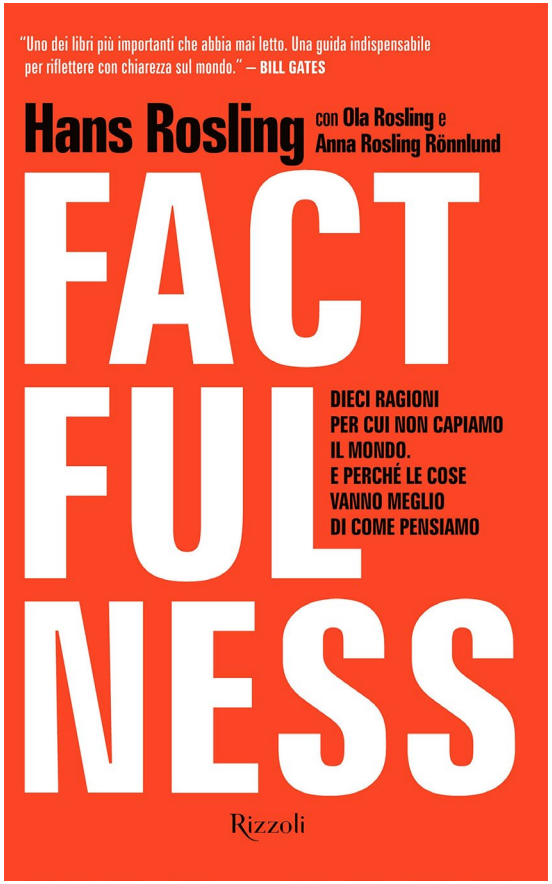
The future of population health

Kenji Shibuya, MD, DrPH
Director, University Institute for Population Health

King's Health Partners Annual Conference
May 2019

Outline

1. From health care to social system
2. Local-global interactions
3. Toward the future of health systems

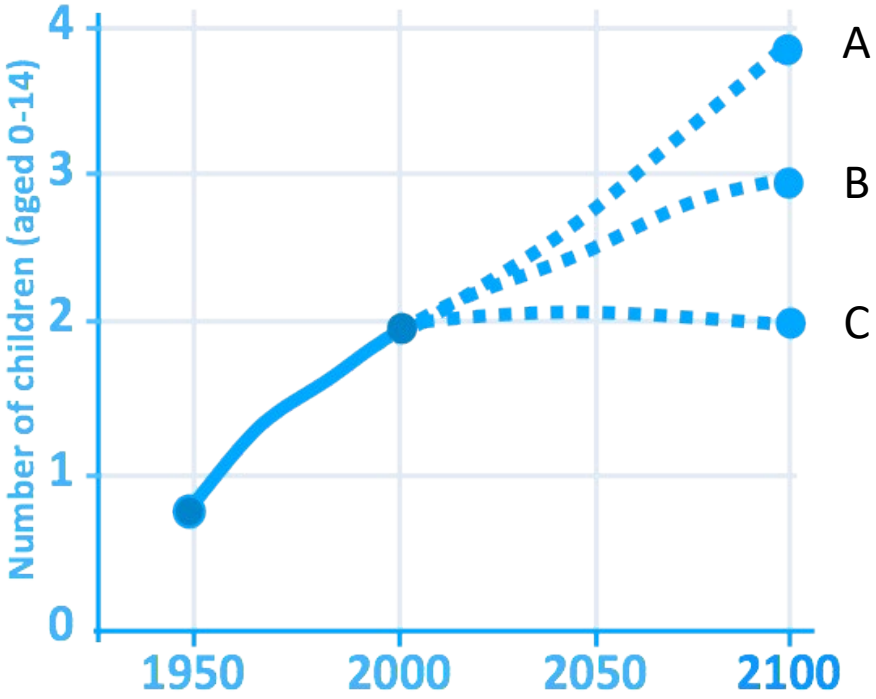


Source: Hans Rosling

What is the average life expectancy of the world's population?

1. 55 years
2. 65 years
3. 75 years

How many children does the UN estimate there will be globally by the year 2100?



Source: UN Population Division

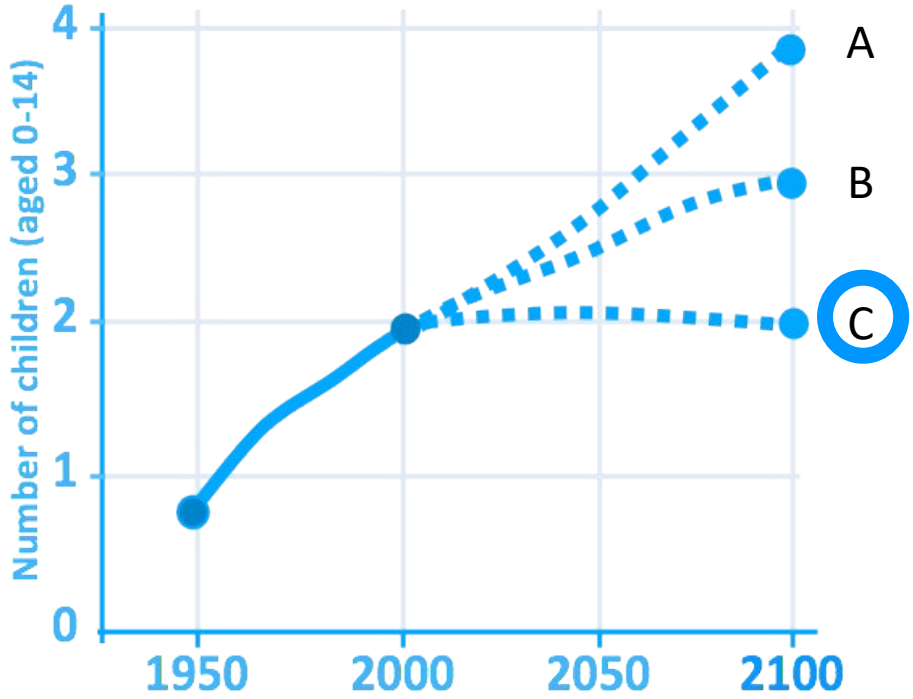
What is the average life expectancy of the world's population?

1.55 years

2.65 years

3.75 years

How many children does the UN estimate there will be globally by the year 2100?



Source: UN Population Division

Four tsunamis in health systems

1. Population ageing
2. Chronic diseases
3. Explosion of health technologies
4. Globalization

Source: Tedros Adhanom/Suwit Wibulpolprasert

“Japan: a mirror for our future”

“The success of Japan’s health system matters not only because of its importance to Japanese citizens, but also because Japan is a barometer of western health.” - Richard Horton

Source: Lancet 2011

Stagnated healthy life expectancy and widening gaps in Japanese population

Articles

Population health and regional variations of disease burden in Japan, 1990–2015: a systematic subnational analysis for the Global Burden of Disease Study 2015

Shuhei Nomura, Haruka Sakamoto, Scott Glenn, Yusuke Tsugawa, Sarah K Abe, Md M Rahman, Jonathan C Brown, Satoshi Ezoe*, Christina Fitzmaurice*, Tsuyoshi Inokuchi*, Nicholas J Kassebaum*, Norito Kawakami*, Yosuke Kita, Naoki Kondo*, Stephen S Lim*, Satoshi Maruyama*, Hiroaki Miyata*, Meghan D Mooney*, Mohsen Naghavi*, Tomoko Onoda*, Erika Ota*, Yuji Otake*, Gregory A Roth*, Eiko Saito*, Takahiro Tabuchi*, Yohsuke Takasaki*, Tadayuki Tanimura*, Manami Uechi*, Theo Vos*, Haidong Wang*, Manami Inoue, Christopher J L Murray, Kenji Shibuya†*

Summary

Background Japan has entered the era of super-ageing and advanced health transition, which is increasingly putting pressure on the sustainability of its health system. The level and pace of this health transition might vary across regions within Japan and concern is growing about increasing regional variations in disease burden. The Global Burden of Diseases, Injuries, and Risk Factors Study 2015 (GBD 2015) provides a comprehensive, comparable framework. We used data from GBD 2015 with the aim to quantify the burden of disease and injuries, and to attribute risk factors in Japan at a subnational, prefecture-level.

Methods We used data from GBD 2015 for 315 causes and 79 risk factors of death, disease, and injury incidence and prevalence to measure the burden of diseases and injuries in Japan and in the 47 Japanese prefectures from 1990 to 2015. We extracted data from GBD 2015 to assess mortality, causes of death, years of life lost (YLLs), years lived with disability (YLDs), disability-adjusted life-years (DALYs), life expectancy, and healthy life expectancy (HALE) in Japan and its 47 prefectures. We split extracted data by prefecture and applied GBD methods to generate estimates of burden, and attributable burden due to known risk factors. We examined the prefecture-level relationships of common health system inputs (eg, health expenditure and workforces) to the GBD outputs in 2015 to address underlying determinants of regional health variations.

Findings Life expectancy at birth in Japan increased by 4·2 years from 79·0 years (95% uncertainty interval [UI] 79·0 to 79·0) to 83·2 years (83·1 to 83·2) between 1990 and 2015. However, the gaps between prefectures with the lowest and highest life expectancies and HALE have widened, from 2·5 to 3·1 years and from 2·3 to 2·7 years, respectively, from 1990 to 2015. Although overall age-standardised death rates decreased by 29·0% (28·7 to 29·3) from 1990 to 2015, the rates of mortality decline in this period substantially varied across the prefectures, ranging from –32·4% (–34·8 to –30·0) to –22·0% (–20·4 to –20·1). During the same time period, the rate of age-standardised DALYs was reduced overall by 19·8% (17·9 to 22·0). The reduction in rates of age-standardised YLDs was very small by 3·5% (2·6 to 4·3). The pace of reduction in mortality and DALYs in many leading causes has largely levelled off since 2005. Known risk factors accounted for 34·5% (32·4 to 36·9) of DALYs; the two leading behavioural risk factors were unhealthy diets and tobacco smoking in 2015. The common health system inputs were not associated with age-standardised death and DALY rates in 2015.

Interpretation Japan has been successful overall in reducing mortality and disability from most major diseases. However, progress has slowed down and health variations between prefectures is growing. In view of the limited

Published Online July 19, 2017 http://dx.doi.org/10.1016/S0140-6736(17)31544-1

See Online/Comment http://dx.doi.org/10.1016/S0140-6736(17)31792-0

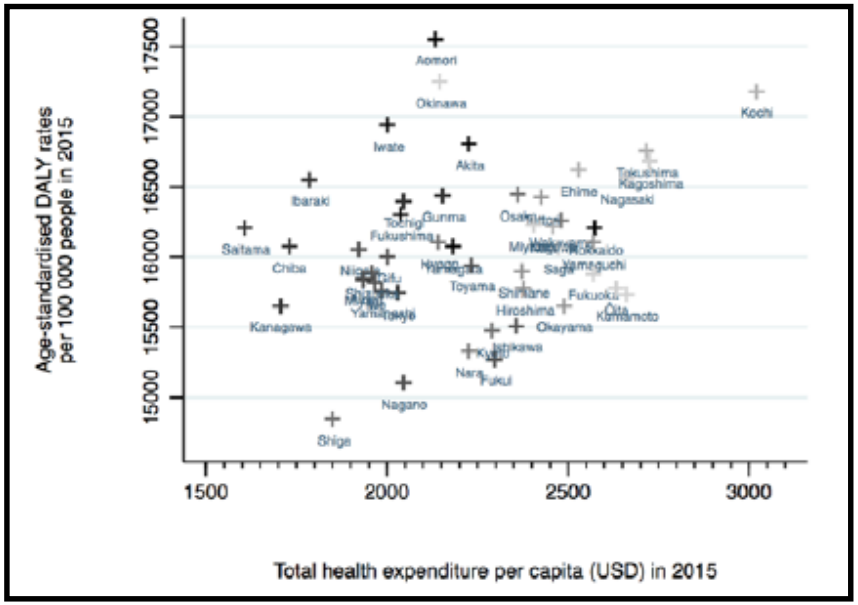
*Authors listed alphabetically

†Corresponding author

Department of Global Health Policy, Graduate School of Medicine (S Nomura MSc, H Sakamoto MD, S K Abe PhD, M M Rahman PhD, S Ezoe MD, E Saito PhD, Prof M Inoue MD, Prof K Shibuya MD), **Department of Mental Health** (Prof N Kawakami MD), **and Department of Health and Social Behaviour** (N Kondo MD), **School of Public Health, The University of Tokyo, Tokyo, Japan; Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA, USA** (S Glenn MSc, J C Brown MAIS, C Fitzmaurice MD, N J Kassebaum MD, Prof S S Lim PhD, M D Mooney BS, Prof M Naghavi PhD, G A Roth MD, Prof T Vos PhD, H Wang PhD, Prof C J L Murray DPhil); **Division of General Internal Medicine and Health Services Research, David Geffen School of**

Source: Nomura et al. 2017

No correlation between inputs and health outcomes



Grand convergence in population health policy, research and practice

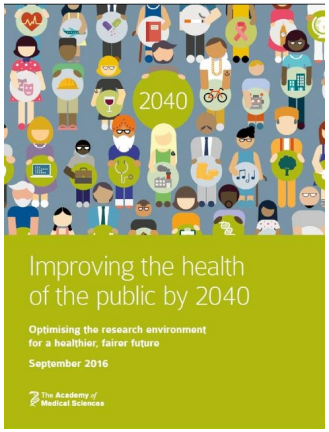
Health Care 2035: Japan Vision

Source: Ministry of Health, Labour and Welfare, 2015

The current health care system must be rebuilt as a new sort of "social system."

A paradigm shift is needed from public health to health of the public.

Improving the Health of the Public by 2040



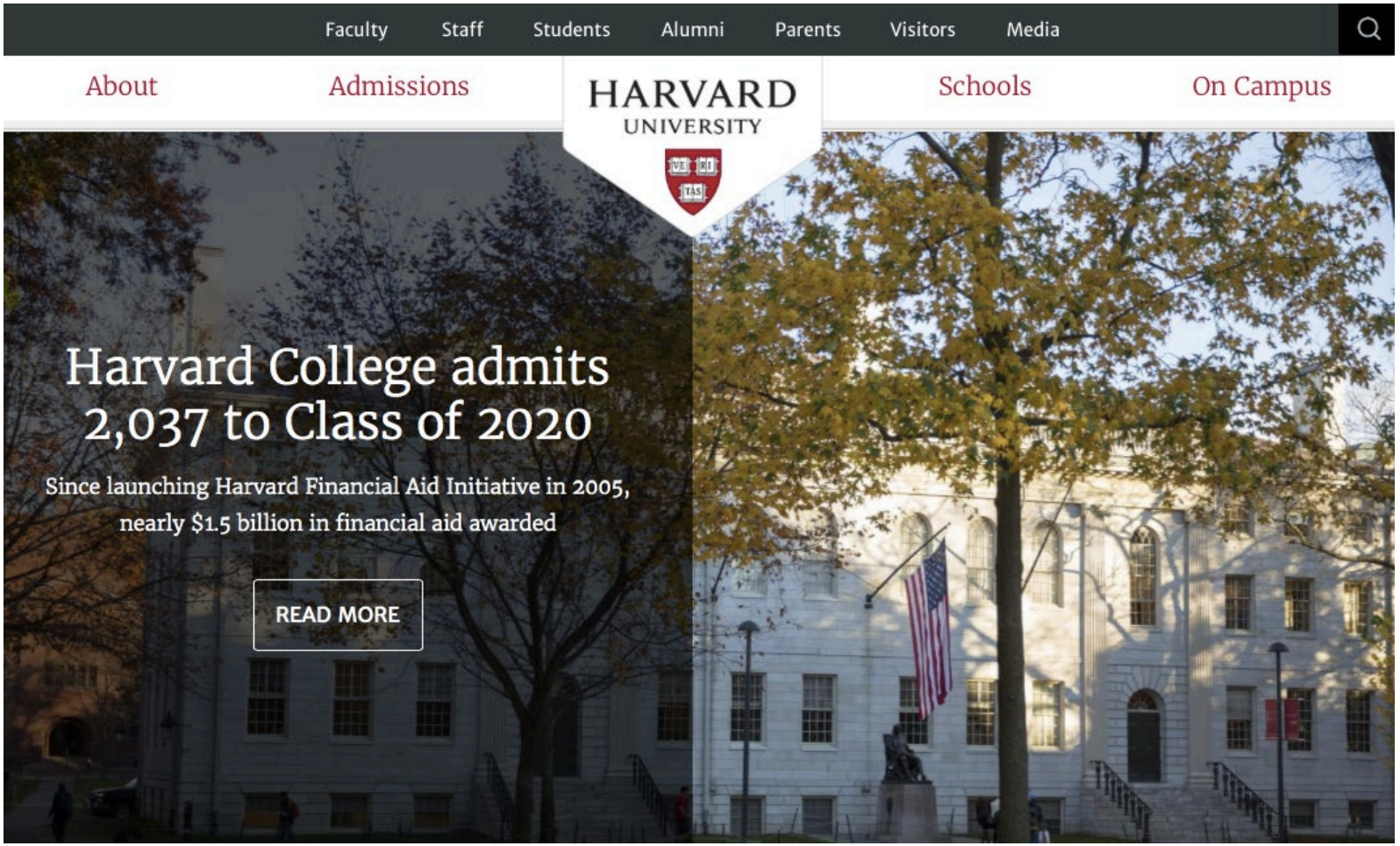
Five supporting ambitions

Environments	Empowerment	Values	Sustainability	Resilience
All elements of the UK environment support healthy living for everybody.	People are empowered to actively contribute to their own and other people's health.	All sectors of society value health and health equity, and they are indicators of societal success.	Improvements to UK health are gained in ways that are economically, environmentally and socially sustainable.	The UK has developed resilience to potential health crises and is a major contributor to global health security.

Source: Academy of Medical Sciences, 2016

Outline

1. From health care to social system
2. Local-global interactions
3. Toward the future of health systems



Source: www.harvard.edu

Beyond universal health coverage (UHC)

Systems, local-global interactions, inter-disciplinary approaches, human security, life design,,,,

Series

Japan: Universal Health Care at 50 Years 6

Future of Japan's system of good health at low cost with equity: beyond universal coverage

Kenji Shibuya, Hideki Hashimoto, Naoki Ikegami, Akihiro Nishi, Tetsuya Tanimoto, Hiroaki Miyata, Keizo Takemi, Michael R Reich

Japan's premier health accomplishment in the past 50 years has been the achievement of good population health at low cost and increased equity between different population groups. The development of Japan's policies for universal coverage are similar to the policy debates that many countries are having in their own contexts. The financial sustainability of Japan's universal coverage is under threat from demographic, economic, and political factors. Furthermore, a series of crises—both natural and nuclear—after the magnitude 9·0 Great East Japan Earthquake on March 11, 2011, has shaken up the entire Japanese social system that was developed and built after World War 2, and shown existing structural problems in the Japanese health system. Here, we propose four major reforms to assure the sustainability and equity of Japan's health accomplishments in the past 50 years—implement a human-security value-based reform; redefine the role of the central and local governments; improve the quality of health care; and commit to global health. Now is the time for rebirth of Japan and its health system.

Lancet 2011; 378: 1265–73
Published Online September 1, 2011
DOI:10.1016/S0140-6736(11)61098-2
See Comment page 1205
See Comment Lancet 2011; 378: 1051
See Series Lancet 2011; 378: 1094, 1105, 1124, and 1181
See Online/Comment DOI:10.1016/S0140-6736(11)61148-3 and DOI:10.1016/S0140-6736(11)60820-9
This is the sixth in a Series of six papers about Japan's universal health care at 50 years

Department of Global Health Policy, Graduate School of Medicine, University of Tokyo, Tokyo, Japan (Prof K Shibuya MD); Department of Health Economics and Epidemiology Research, University of Tokyo, Tokyo, Japan (Prof H Hashimoto MD); Department of Health Policy and Management, Keio University School of Medicine, Tokyo, Japan (Prof N Ikegami MD); Department of Society, Human Development, and Health, Harvard School of Public Health, Boston, MA, USA (A Nishi MD); Department of Public Health, Graduate School of Medicine, University of Tokyo, Tokyo, Japan (A Nishi); Cancer Institute, Japanese Foundation for Cancer Research, Tokyo, Japan (T Tanimoto MD); Department of Healthcare Quality Assessment, University of Tokyo, Tokyo, Japan (H Miyata PhD); School of Political Science and Economics, Tokai University, Kanagawa, Japan (Prof K Takemi MA); and Department of Global Health and Population, Harvard School of Public Health, Boston, MA, USA (Prof M R Reich PhD)

Introduction

The global health community is quickening its efforts aimed at ensuring health coverage for all.[1–3] The 58th session of the World Health Assembly in 2005 endorsed a resolution, urging its member countries to work towards sustainable health financing, defining universal health coverage as access for all to appropriate health services at an affordable cost. The World Health Assembly also urged countries to strive for the achievement of universal coverage by using, in accord with their specific contexts, a mix of prepayment systems that include tax-based financing and social health insurance.[4] In the past decade, low-income countries such as Ghana and Rwanda have introduced national health insurance schemes designed to achieve universal coverage at an affordable cost.[5–7]

The definition of universal coverage is still debated, but generally it is access to key promotive, preventive, curative, and rehabilitative health interventions for all at an affordable cost. The principle of financial risk protection ensures that the cost of care does not put people at risk of financial catastrophe.[4,8,9] The social health insurance approach allows the gradual expansion of the population covered and solidarity among the individuals enrolled in each plan.[7] Japan achieved universal health insurance coverage in 1961 when virtually the entire population became covered by plans for social health insurance.[10]

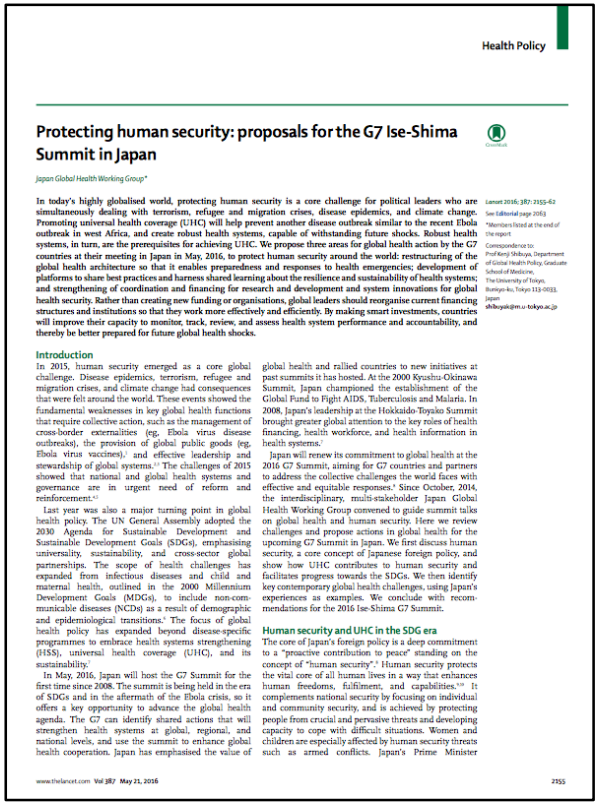
Achievement of universal coverage is, however, not an end, but the beginning of new challenges. Universal

Search strategy and selection criteria

We searched PubMed, Medline, Embase, Jamas, and Jstor databases, government reports, and unpublished literature from domestic sources. Once a source was identified, it was used to generate additional material (eg, by searching the reference lists of reports obtained while using this search strategy). The first section of this work is based on the earlier reports in this Lancet Series in which health and its associated factors are assessed in Japan 50 years after the introduction of universal health care coverage in the country. To discuss the effects of the Great East Japan Earthquake and the accident at the Fukushima nuclear power plant that followed, we used reports identified and retrieved using the above-mentioned method and documents issued by the International Atomic Energy Agency, Japanese Government, and other sources including those produced by the domestic media.

Key messages

- Although Japan achieved universal coverage in 1961 and other health-care policies and programmes have led to excellent population health at low cost with equity, the nation now has many challenges.
- Three common challenges to the health system of Japan—economic sustainability, political governance, and responsiveness to patients—were identified in the other reports in this Lancet Series.
- The Great East Japan Earthquake in March, 2011, showed the underlying structural problems in the health system but made the three challenges much more difficult to resolve fiscally.
- To address these challenges, we propose four major reforms for Japan's health-care system: implement human-security value-based reform; redefine the role of the central and local governments; improve the quality of health care; and commit to global health.
- There are promising signs that Japan will be able to achieve both structural health reform and disaster reconstruction. This domestic experience could be the basis for Japan to take an increased proactive role in promoting global health.



Health Policy

Protecting human security: proposals for the G7 Ise-Shima Summit in Japan

Japan Global Health Working Group*

In today's highly globalised world, protecting human security is a core challenge for political leaders who are simultaneously dealing with terrorism, refugee and migration crises, disease epidemics, and climate change. Promoting universal health coverage (UHC) will help prevent another disease outbreak similar to the recent Ebola outbreak in west Africa, and create robust health systems, capable of withstanding future shocks. Robust health systems, in turn, are the prerequisites for achieving UHC. We propose three areas for global health action by the G7 countries at their meeting in Japan in May, 2016, to protect human security around the world: restructuring of the global health architecture so that it enables preparedness and responses to health emergencies; development of platforms to share best practices and harness shared learning about the resilience and sustainability of health systems; and strengthening of coordination and financing for research and development and system innovations for global health security. Rather than creating new funding or organisations, global leaders should reorganise current financing structures and institutions so that they work more effectively and efficiently. By making smart investments, countries will improve their capacity to monitor, track, review, and assess health system performance and accountability, and thereby be better prepared for future global health shocks.

Lancet 2016; 387: 2155–62
See Editorial page 2063

*Members listed at the end of the report
Correspondence to: Prof Kenji Shibuya, Department of Global Health Policy, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Tokyo 113-0033, Japan
shibuyak@m.u-tokyo.ac.jp

Introduction

In 2015, human security emerged as a core global challenge. Disease epidemics, terrorism, refugee and migration crises, and climate change had consequences that were felt around the world. These events showed the fundamental weaknesses in key global health functions that require collective action, such as the management of cross-border externalities (eg, Ebola virus disease outbreaks), the provision of global public goods (eg, Ebola virus vaccines),[1] and effective leadership and stewardship of global systems.[2,3] The challenges of 2015 showed that national and global health systems and governance are in urgent need of reform and reinforcement.[4,5]

Last year was also a major turning point in global health policy. The UN General Assembly adopted the 2030 Agenda for Sustainable Development and Sustainable Development Goals (SDGs), emphasising universality, sustainability, and cross-sector global partnerships. The scope of health challenges has expanded from infectious diseases and child and maternal health, outlined in the 2000 Millennium Development Goals (MDGs), to include non-communicable diseases (NCDs) as a result of demographic and epidemiological transitions.[6] The focus of global health policy has expanded beyond disease-specific programmes to embrace health systems strengthening (HSS), universal health coverage (UHC), and its sustainability.[7]

In May, 2016, Japan will host the G7 Summit for the first time since 2008. The summit is being held in the era of SDGs and in the aftermath of the Ebola crisis, so it offers a key opportunity to advance the global health agenda. The G7 can identify shared actions that will strengthen health systems at global, regional, and national levels, and use the summit to enhance global health cooperation. Japan has emphasised the value of global health and rallied countries to new initiatives at past summits it has hosted. At the 2000 Kyushu-Okinawa Summit, Japan championed the establishment of the Global Fund to Fight AIDS, Tuberculosis and Malaria. In 2008, Japan's leadership at the Hokkaido-Toyako Summit brought greater global attention to the key roles of health financing, health workforce, and health information in health systems.[7]

Japan will renew its commitment to global health at the 2016 G7 Summit, aiming for G7 countries and partners to address the collective challenges the world faces with effective and equitable responses.[8] Since October, 2014, the interdisciplinary, multi-stakeholder Japan Global Health Working Group convened to guide summit talks on global health and human security. Here we review challenges and propose actions in global health for the upcoming G7 Summit in Japan. We first discuss human security, a core concept of Japanese foreign policy, and show how UHC contributes to human security and facilitates progress towards the SDGs. We then identify key contemporary global health challenges, using Japan's experiences as examples. We conclude with recommendations for the 2016 Ise-Shima G7 Summit.

Human security and UHC in the SDG era

The core of Japan's foreign policy is a deep commitment to a "proactive contribution to peace" standing on the concept of "human security".[9] Human security protects the vital core of all human lives in a way that enhances human freedoms, fulfilment, and capabilities.[9,10] It complements national security by focusing on individual and community security, and is achieved by protecting people from crucial and pervasive threats and developing capacity to cope with difficult situations. Women and children are especially affected by human security threats such as armed conflicts. Japan's Prime Minister

Integrating global health into domestic health policy

Prime Minister Abe's commentary in The Lancet

Japan's vision for a peaceful and healthier world

Health is fundamentally a global issue. Recent outbreaks of Ebola virus disease and Middle East respiratory syndrome have reminded us that global health issues require collective action. The world must unite and countries must establish resilient and sustainable health systems, ensuring that each individual is secure and receives the highest attainable standard of health. Japan has been a longstanding advocate of human security[1] and has taken concrete action on the ground in support of this principle. Human security protects the vital core of all human lives in a way that enhances freedom, fulfilment, and capabilities[1,2] and underlies Japan's policy of Proactive Contribution to Peace. Japan regards health as an indispensable element of human security.[1]

In September, 2015, the United Nations General Assembly adopted the 2030 agenda for sustainable development, which includes universal health coverage

First, in preparation for the G7 Summit, we will discuss how to address the challenges of public health emergencies. The existing global health architecture must be restructured to ensure prompt and effective responses to public health emergencies. Public and private partners, government, and civil society—at global, regional, country, and community levels—should reach agreement on their respective roles in advance of emergencies. Japan expects WHO to have the lead role in prompt detection and containment, especially in the early stages of a public health emergency, while acknowledging WHO's need for further reform and capacity strengthening. Japan is ready to support this reform process, including the launch of the Contingency Fund for Emergencies.[6] Japan also fully supports the efforts of the World Bank's Pandemic Emergency Facility, and calls for coordination between WHO and the World

"Japan's global health priorities are to construct a global health architecture that can respond to public health crises."

"Japan is pioneering the response to the challenge of ageing while maintaining a sustainable health system. Japan will contribute further to UHC."

"Japan is all the more responsible for addressing the threat of antimicrobial resistance as countries develop their own national action plans."

Source: Abe S. Lancet 2015;386:2367-69

Outline

1. From health care to social system
2. Local-global interactions
3. Toward the future of health systems

New players

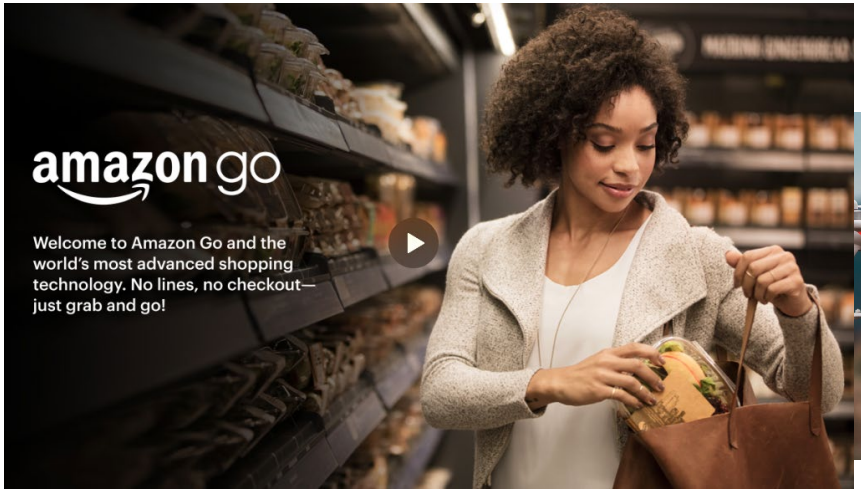
Amazon-Berkshire-JP Morgan health

Source: qz.com/1192693/amazon-jp-morgan-and-berkshire-hathaway-are-starting-a-healthcare-company/

Space X

Source: thenewsrecorder.com/news/space/spacex-will-build-new-next-gen-mars-bound-falcon-rocket-los-angeles-35727.html

Technologies



Source: https://www.amazon.com/b?ie=UTF8&node=16008589011

Source: https://medium.com/@maciejkranz/ai-is-the-brain-iot-is-the-body-85af8f36fc55

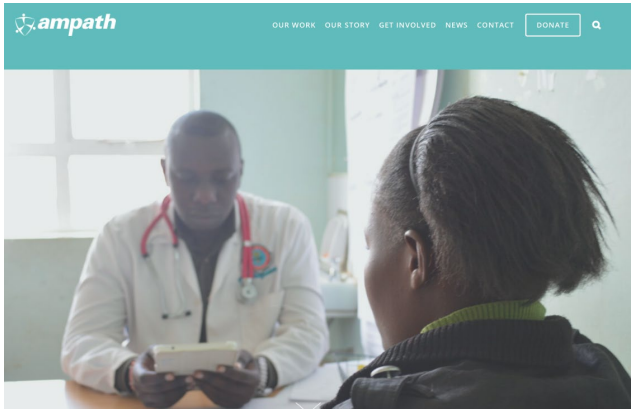
Transforming deliveries

India: Home-based care x Uber

PORTEA
HEAL AT HOME

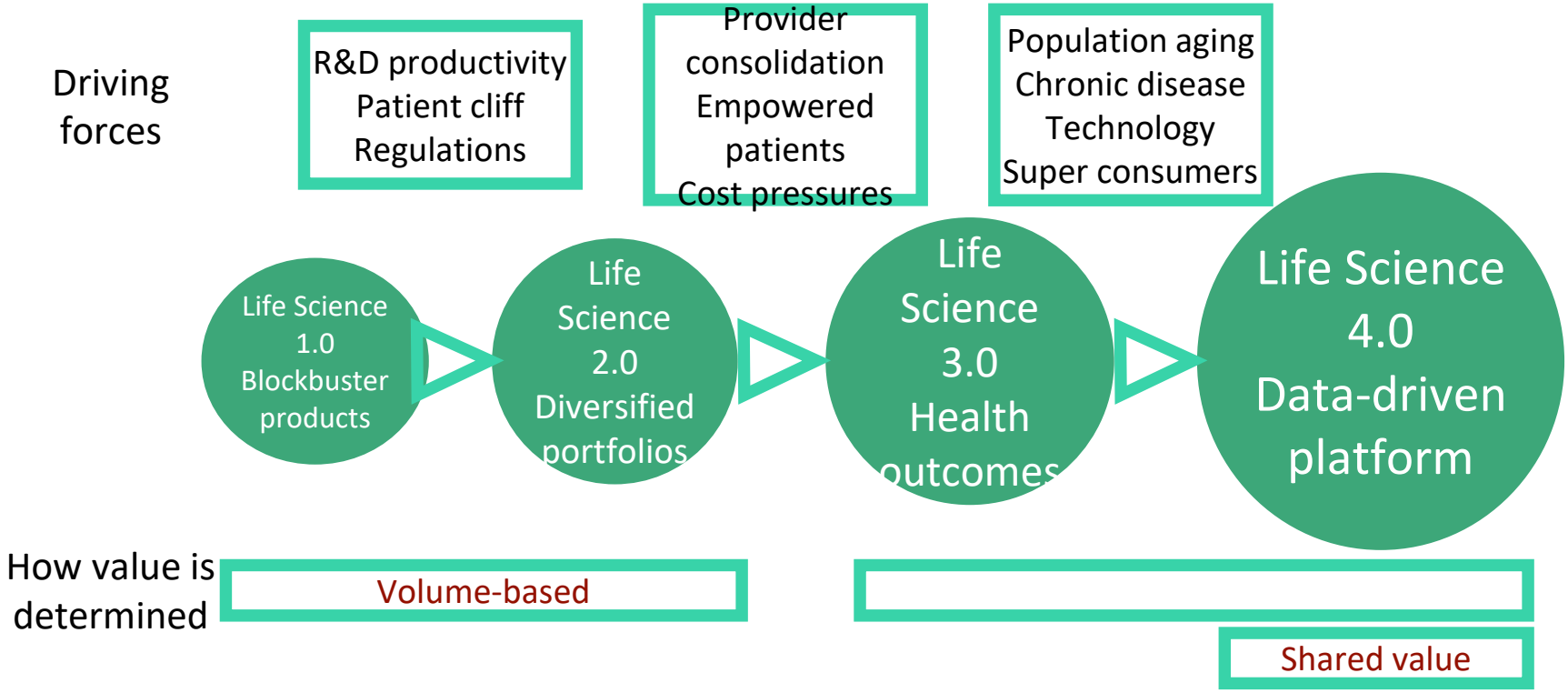
Source: www.portea.com

Kenya: Integrated primary care x life design



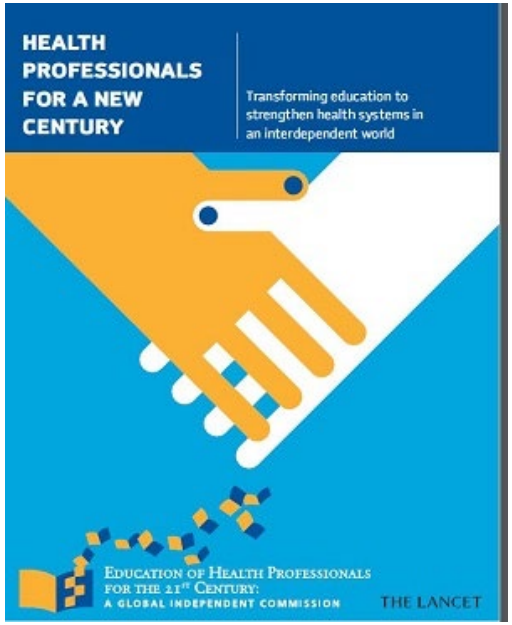
Source: https://www.ampathkenya.org/care-programs

Transforming life sciences



Source: EYGM Life Science 4.0 https://assets.ey.com/content/dam/ey-sites/ey-com/global/topics/digital/ey-when-the-human-body-is-the-biggest-data-platform-who-will-capture-value.pdf

Transformative education for health professionals

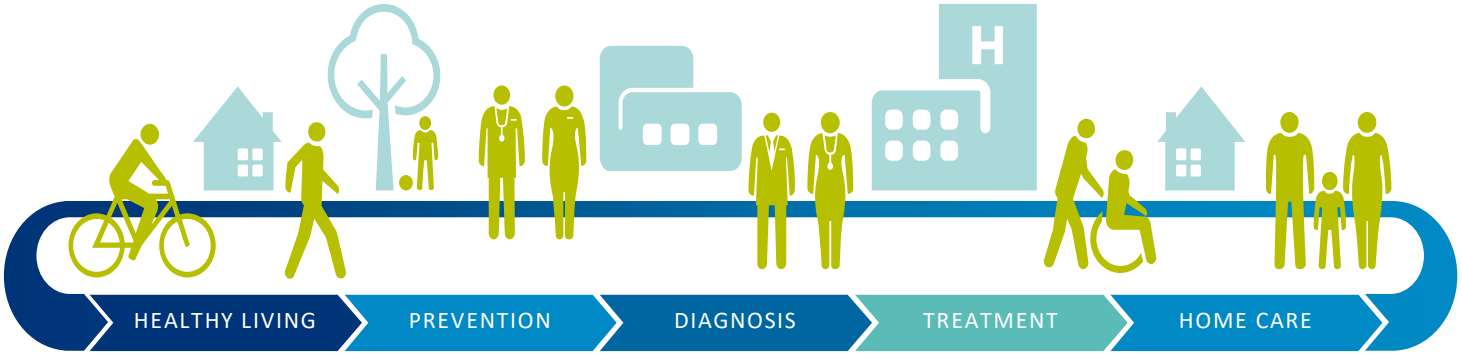


1900 → 2000

	Science-based education	Problem-based education	System-based education
Instructional	Scientific curriculum	Problem-based learning	• Competency -driven • Local-global
Institutional	Universities	Academic centers	Health systems

Source: Frenk, Chen et al. Lancet 2011

Our Institute = Person-Centered Open Platform for Wellbeing (PeOPLe)



LEAN HEALTHCARE 1

Implement value-based health care

LIFE DESIGN 2

Empower society and support personal choice

GLOBAL HEALTH LEADER 3

Lead and contribute to global health

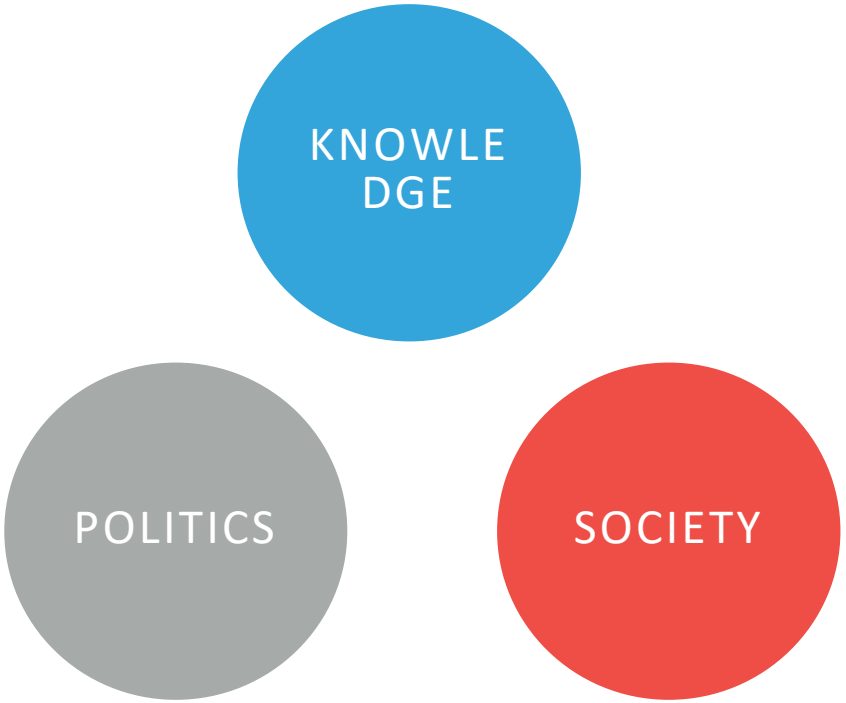
A future health system in the era of "precision health" and "no one left behind"

Why King’s?

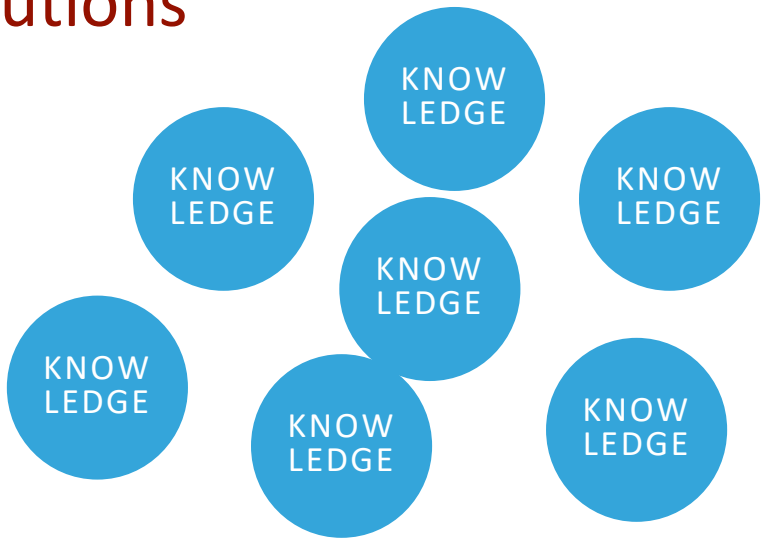
“Triangles that move the mountain”

Dr. Suwit Wibulpolprasert

Source:
www.who.int/workforcealliance/about/governance/board/wibulpolprasert/en/



Academic institutions



Body

Individual

Local

Disease

Mind

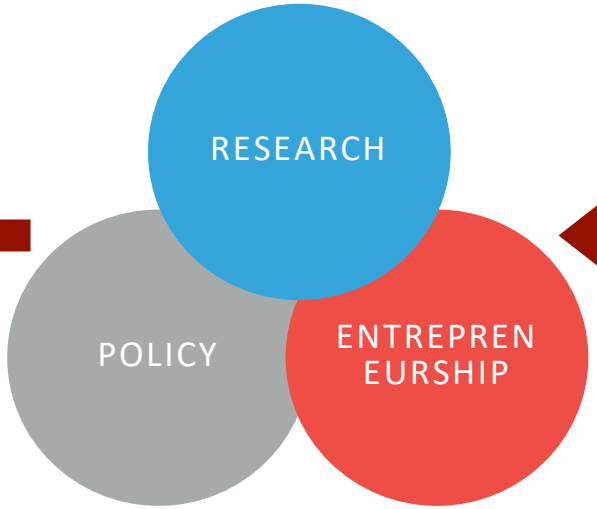
Society

Global

System

Why population health at King's?

King's asset = South London, a mirror for the world's future



Four "tsunamis" in health systems:

1. Population ageing
2. Chronic diseases
3. Health technologies
4. Globalization

Body and Mind
Individual and Society
Local and Global
Disease and System

Appointed as a Special Advisor to the WHO Director-General

Summary

1. From health care to social system
2. Local-global interactions
3. Toward the future of health systems

Institute of Women and Children's Health

King's Health Partners Annual Conference

May 2019

Institute of Women and Children's Health

- The Institute will coordinate a strategic advance in knowledge and healthcare, creating an academic focus to optimise the health of the population we serve, locally and worldwide.
- The Institute will have:
  - A focus on diseases that cause significant distress to large numbers of patients.
  - A combined approach to mind and body health- working closely with the Centre for Children's and Young People's Mental Health.
  - A life-course approach engaging with mothers and children from pre-conception to adolescence.
  - A vision that includes both local and global health, and the intent to create change at the population level.

The Institute will facilitate collaboration between NHS and University

What the Institute is built from:

- Strong institutional support
  - FoLSM created Department of Women and Children's Health
  - Evelina London has tangible desire to develop academic paediatrics
  - KHP supported a physical hub for Institute activity
  - Understanding with IoPPN that we are stronger together
- A critical mass of the leading researchers in Women and Children's Health Unique opportunities to combine mental and physical health
- Gaps in the market
  - Lifecourse approaches to women's and children's health research
  - Collaborations within the Institute and KHP to create new opportunitie
  - Clinical trials management

Papers in Nature, New England Journal, Lancet 2016-19

1. Placental growth factor testing to assess women with suspected pre-eclampsia: a multicentre, pragmatic, stepped-wedge cluster-randomised controlled trial. Duhig KE, et al. **Lancet**. 2019. pii: S0140-6736(18): 33212-4.
2. Three-dimensional visualisation of the fetal heart using prenatal MRI with motion-corrected slice-volume registration: a prospective, single-centre cohort study. Lloyd DFA, et al **Lancet**. 2019 ;393(10181):1619-1627.
3. Randomized Trial of Platelet-Transfusion Thresholds in Neonates. Curley A et al. **N Engl J Med**. 2019;380(3):242-251.
4. Association of adverse perinatal outcomes of intrahepatic cholestasis of pregnancy with biochemical markers: results of aggregate and individual patient data meta-analyses. Ovadia C, et al. **Lancet**. 2019;393(10174):899-909.
5. F … ntre, double-blind, randomised,
6. F … o-group,randomised trial. Miller D,
7. E … wedge, cluster-randomised
8. M … le-blind trial. Sharp A. STRIDER
9. S … 2018;392(10155):1349-1357.
10. Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health. Stephenson J et al. **Lancet**. 2018;391(10132):1830-1841.
11. Segregation of mitochondrial DNA heteroplasmy through a developmental genetic bottleneck in human embryos. Floros VI et al; **Nat Cell Biol**. 2018; 20(2):144-151.
12. Integrative genomics of microglia implicates DLG4 (PSD95) in the white matter development of preterm infants. Krishan et al. **Nature Commun**. 2017 Sep 5;8(1):428.
13. Pluripotent state transitions coordinate morphogenesis in mouse and human embryos. Shahbazi et al **Nature.** 2017;552(7684):239-243.
14. Human pluripotent stem cells recurrently acquire and expand dominant negative P53 mutations. Merkle FT et al. **Nature**. 2017;545(7653):229-233.
15. Pre-eclampsia. Mol BWJ, et al. **Lancet.** 2016 Mar 5;387(10022):999-1011.
16. Hysteroscopy in recurrent in-vitro fertilisation failure (TROPHY): a multicentre, randomised controlled trial. El-Toukhy T et al. **Lancet.** 2016; 387(10038):2614-2621.
17. Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia. Rolnik DL et al. **N Engl J Med.** 2017;377(7):613-622
18. A Randomized Trial of a Cervical Pessary to Prevent Preterm Singleton Birth. Nicolaides KH et al. **N Engl J Med.** 2016;374(11):1044-52
19. Randomized Trial of Introduction of Allergenic Foods in Breast-Fed Infants. Perkin et al. **N Engl J Med**. 2016;374(18):1733-43.
20. Effect of Avoidance on Peanut Allergy after Early Peanut Consumption. Du Toit G, et al **N Engl J Med.** 2016;374(15):1435-43.
21. Metformin versus Placebo in Obese Pregnant Women without Diabetes Mellitus. Syngelaki A, et al **N Engl J Med.** 2016;374(5):434-43

Randomized Trial of Platelet-Transfusion Thresholds in Neonates. Curley A et al. **N Engl J Med**. 2019;380(3):242-251.

Current grants over £2 million

- AIMS-2-TRIALS. European Commission. Murphy et al. **£117 million**.
- The Developing Human Connectome Project. European Commission. Edwards et al **€15 million**
- A computer-guided imaging system for prenatal screening and comprehensive diagnosis of fetal abnormalities. Wellcome Trust. Razavi et al. **£10 million**
- Biomarkers in Atopic Dermatitis and Psoriasis. European Commission. Flohr et al. **£8.7 million**
- The Developing Brain. MRC. Edwards et al. **£7.2 million**
- GCRF: The PRECISE Trial. MRC. Von Dadelszen et al **£7.9 million**
- ASSET. NIHR. Prince et al. NIHR. **£6.9 million**
- Driving next generation autophagy researchers towards translation. European Commission. Jungbluth et al. **£2.9 million**
- Sleep, Treatment and Learning in Childhood Epilepsy. NIHR. Gringras, et al £ **£2.3 million**
- Improving Maternal and Perinatal Outcomes. NIHR. Chappell et al **£2.2 million**
- Structure and function of the placenta from implantation to delivery: a next generation MRI approach. Rutherford et al National Institutes of Health USA. **£2 million**

Key initiatives

- Appointment of a new Professor of Paediatrics
- Development of appropriate Paediatric Clinical Research Facilities
- Support for research active clinicians
  - 19 new Honorary KCL appointments
- Support for collaborative external funding applications
  - MRC ELIXIR programme
  - Clinical Academic Research Partnerships
- Support for teaching
  - Administrative support to develop teaching and training
- The creation of a 'Women and Children's spoke' Clinical Trials Unit
- Developing novel collaborations across King's Health Partners.
  - *King's Together* Grants
  - Bioengineering, Imaging and Technology Development on the St Thomas' Campus
  - PhD Programme
  - Population and Global Health Initiatives

Cross-fertilizing PhD Programme

- Aliya Amin supervised by Prof Cath Williamson (Maternal Medicine), Prof Anil Dhawan and Dr Emer Fitzpatrick (Paediatric Liver).
  - **'Impact of intermittent cold exposure on progression of non-alcoholic fatty liver diseases in children and young people'**
- Fiona Rattray supervised by Dr Michael Absoud (Neurodisability) F Happe (Centre for Social, Developmental and Genetic Psychiatry).
  - **Ocular biomarkers in childhood neurodevelopmental disorders**'
- Arti Mistry supervised by Prof Rachael Tribe (Women's Health) and Prof Heinz Jungbluth (Paediatrics).
  - **'The impact of mutations in the type 1 ryanodine receptor (*RYR1*) gene on uterine and vascular smooth muscle function in pregnancy'.**

- Inaugural symposium June 10th, Bush House.
- Speakers include:
  - Chris Whitty. Chief Scientific Advisor to the Department of Health and Social Care
  - Anthony Costello, Ex Head, Maternal and Child Health, World Health Authority
  - Karen Edmond, Professor of Paediatrics, King's College London.

Improving health service delivery for newborns and children, especially the most disadvantaged

Karen Edmond

May 2019

Target groups

In both high and low income countries

- Children living in poverty
- Children living in families with mental health and substance use disorders
- Children living in humanitarian conflict settings

- Especially, young infants

Domains

- Delivery channels – ambulatory and outreach
- Tools – epidemiological and interventional

- ‘On the ground’ proximal care provider, programs and policies
- Unacceptable not to focus at scale on low cost easily implementable health services and not to provide outreach care

Tools and delivery channels

Interventional tools

- Nutrition - early infant feeding, micronutrient supplementation
- Neurodevelopment and mental health - CQI, ages and stages, postnatal depression, brief interventions
- Preterm - early infant feeding, kangaroo mother care, neurodevelopment

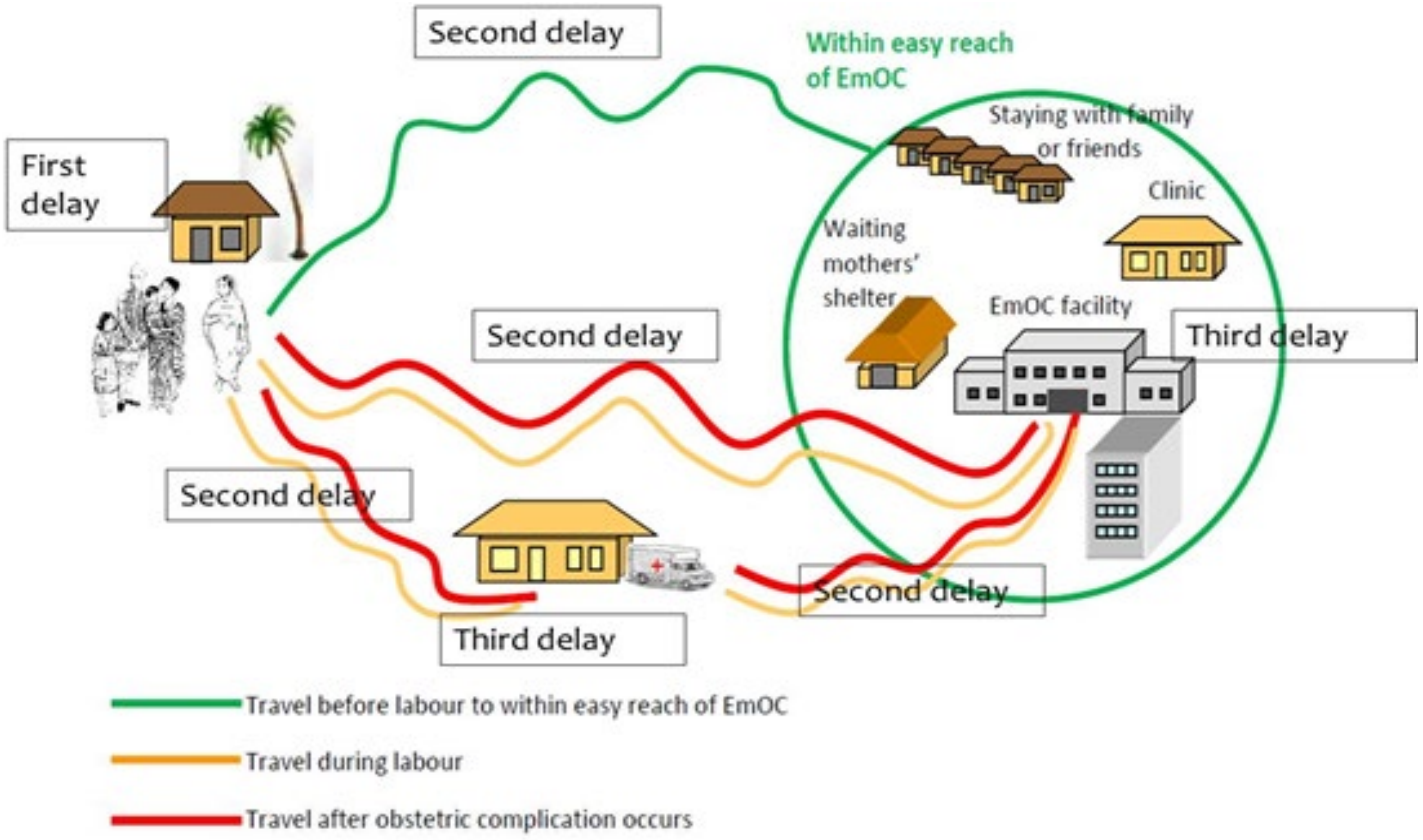
Epidemiological tools

- Front end systems – personal health records, electronic front ends and CQI
- Routinely collected data - HMIS, Demographic Health Surveys (DHS), Demographic Surveillance Systems (DSS), verbal autopsies, **data linkage**
- Analysis - RCTs, difference in difference (DiD), meta-analysis

Delivery channels

- Interface - hospital to primary care - ambulatory care, care coordination
- Outreach - **home visiting, mobile health teams**
- Referral systems - **conditional cash transfers**, mini ambulances, maternity waiting rooms
- Health care providers - interpersonal communication (IPC), QoC, **CQI, personal health records,** electronic health records

Basic framework – the three delays model



Practicalities

- Working across a number of sites
- Testing - tools and delivery channels
- Strengthening - delivery of services from laboratory to the community - workforce, technologies, hardware, resourcing, partnerships, monitoring

Unicef - Afghanistan

Maternal, newborn, and child health strategies

Financial incentives

Maternity waiting homes

Community ambulances

Mothers and children

Skilled health providers

Community midwifery training

Community outreach teams

Community health workers

Key points

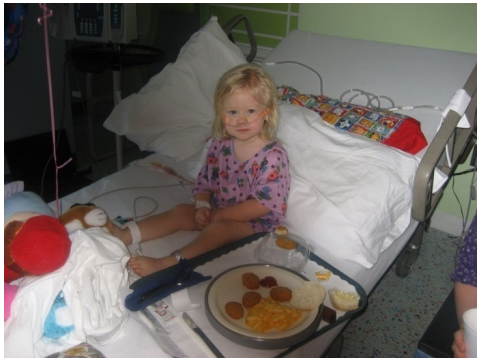
- Is possible to improve access and service delivery at scale using low cost interventions for most disadvantaged mothers and children; including services to improve morbidity, mortality and neurodevelopment
- Locally focused delivery channels and tools for the front line health care providers, especially primary care are essential
- It is unacceptable not to focus at scale on low cost easily implementable health services and not to provide outreach care
- Can strengthen delivery of services from laboratory to the community - workforce, technologies, hardware, resources, partnerships, monitoring

Delivery of child health services moving forward

- Inclusive - of mothers and children, of providers, from primary to tertiary care, from laboratory to community, from clinical to educative to academic
- Multisite - committed to outreach, most disadvantaged
- Quality – technical, specialist services nested in population data linkage, providing services to the community and informing global policy
- Building - on the hardwork that has gone before
- Categorised into - workforce, technologies, hardware, resourcing, partnerships, monitoring

Conclusions

- Health services research is at an exciting phase – especially primary care
- All the component parts are here at KHP – vision, structure, geography, commitment, energy, methodologies
- Potential to be a game changer, deal breaker, leader in both population and specialist service delivery
- Clear way forward
- Building on hard work
- Using skills and defined methods
- Together we can achieve so much for our children



The Vital 5

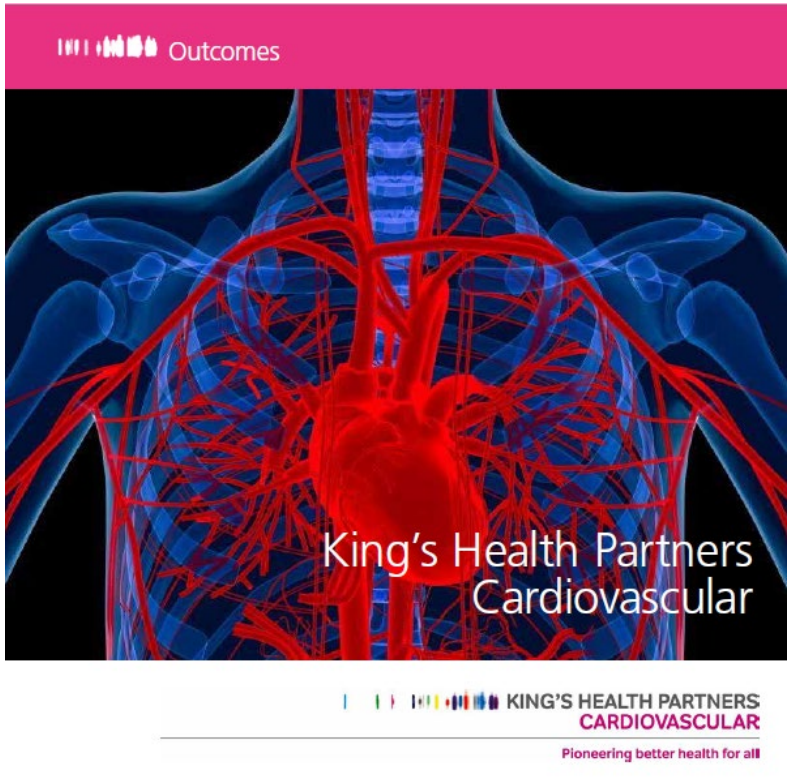
King's Health Partners Annual Conference

Prof John Moxham | 16 May 2019

Value remains a central theme of our Academic Health Sciences Centre

$$\text{Value} = \frac{\text{Outcomes that matter to patients, service users and carers}}{\text{Costs of achieving those outcomes Over the complete pathway of care}}$$

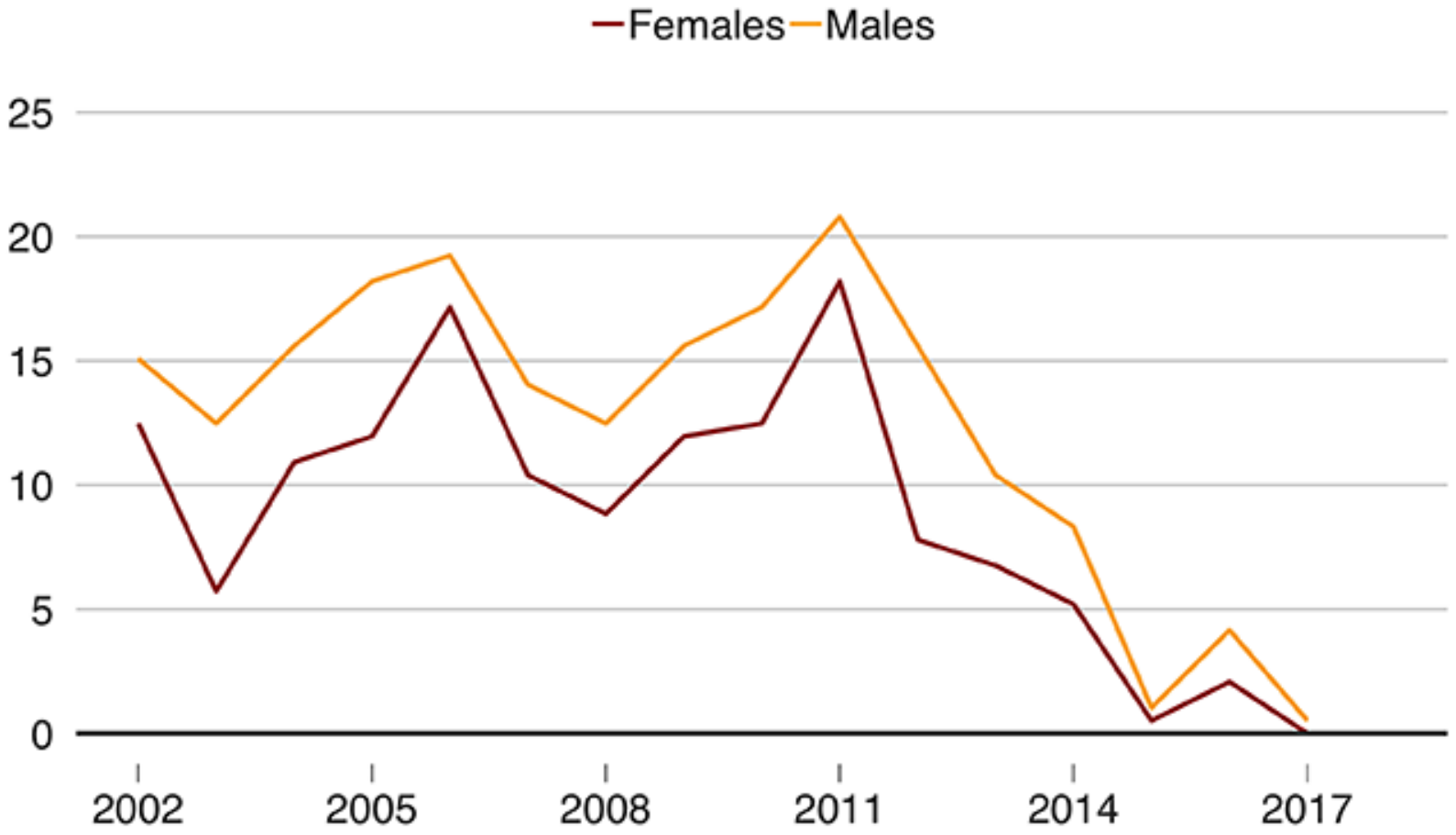
We continue to share outcomes across our clinical academic groups



We have now published 17 outcomes books and have started to develop outcomes scorecards with Palliative Care and Pharmaceutical Sciences.

Focus on outcomes and value is more important than ever – *life expectancy is stalling*

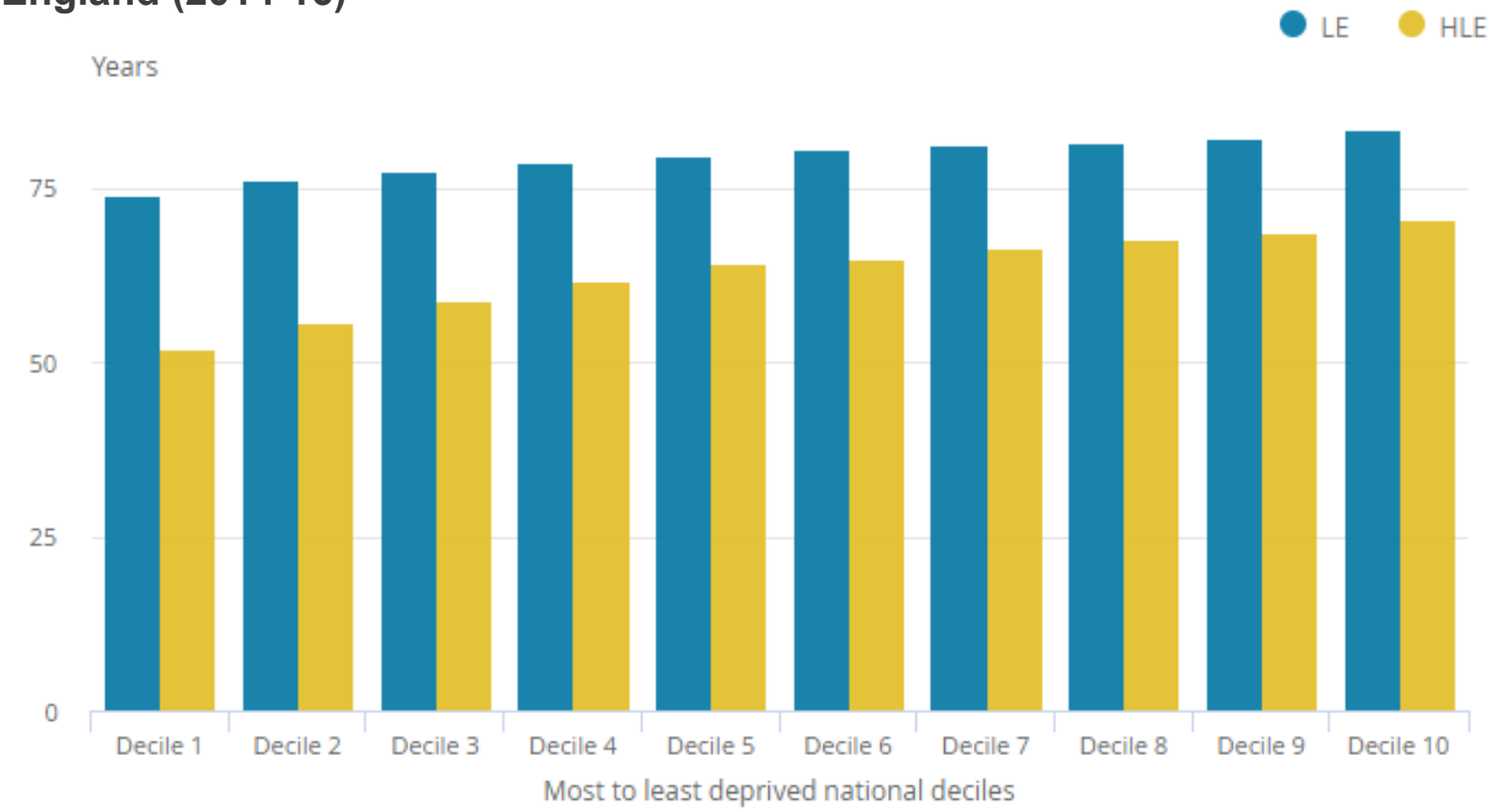
Changes in life expectancy (UK, annual changes in weeks)



Source: Office for National Statistics: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/lifeexpectancies/datasets/nationallifetablesenglandreferencetables
Image from related BBC News website article: https://www.bbc.co.uk/news/health-45638646

Focus on outcomes and value is more important than ever – *wide and persisting health inequalities*

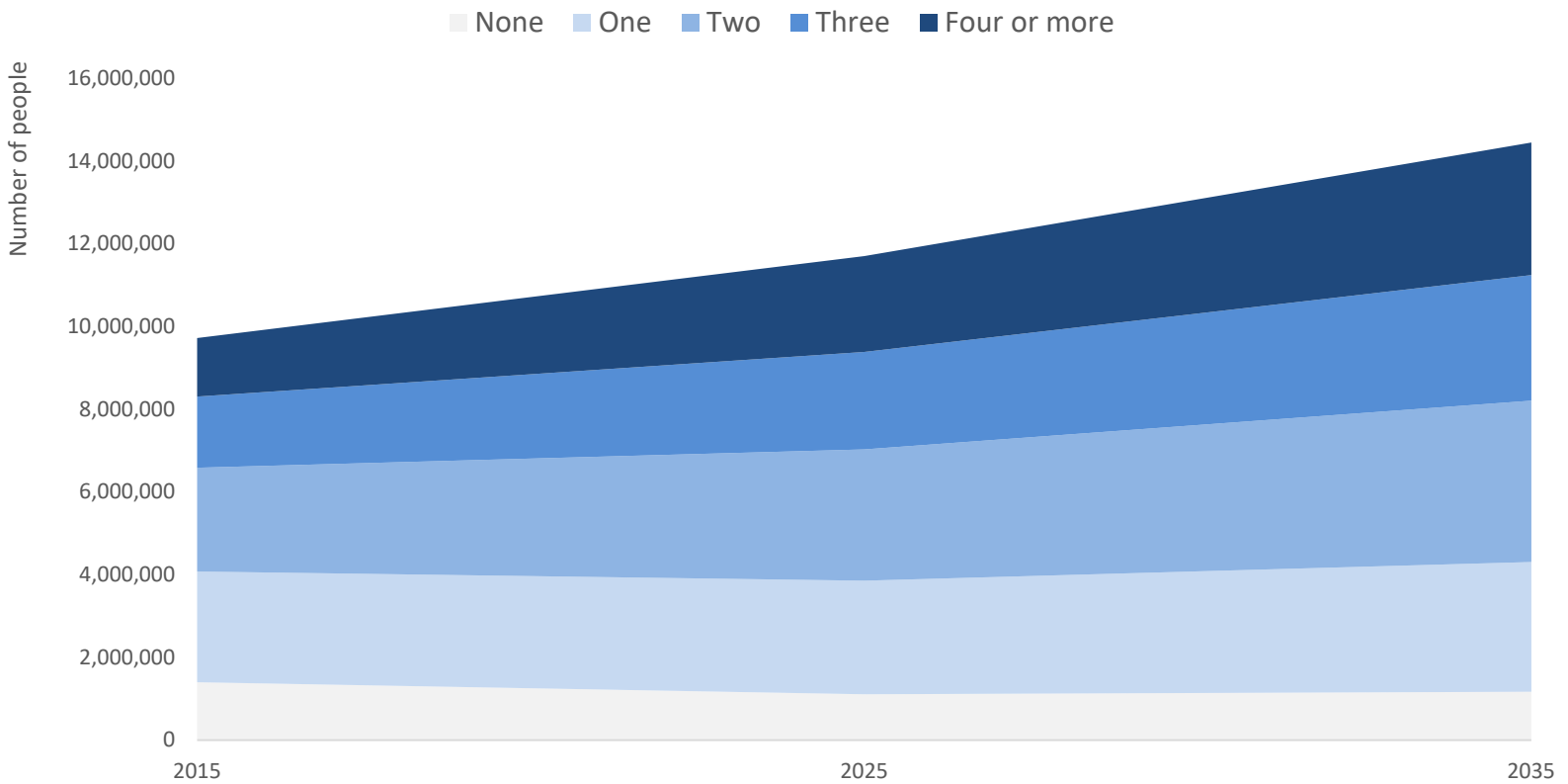
Healthy life expectancy (HLE) and life expectancy (LE) for males at birth in England (2014-16)



Source: Office for National Statistics, March 2018, "Health state life expectancies by national deprivation deciles, England and Wales: 2014 to 2016" https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/healthinequalities/bulletins/healthstatelifeexpectanciesbyindexofmultipledeprivationimd/englandandwales2014to2016

Focus on outcomes and value is more important than ever – *increasing ill health*

Projected number of people aged 65 and over with multi-morbidity in 2015, 2025, and 2035 in England

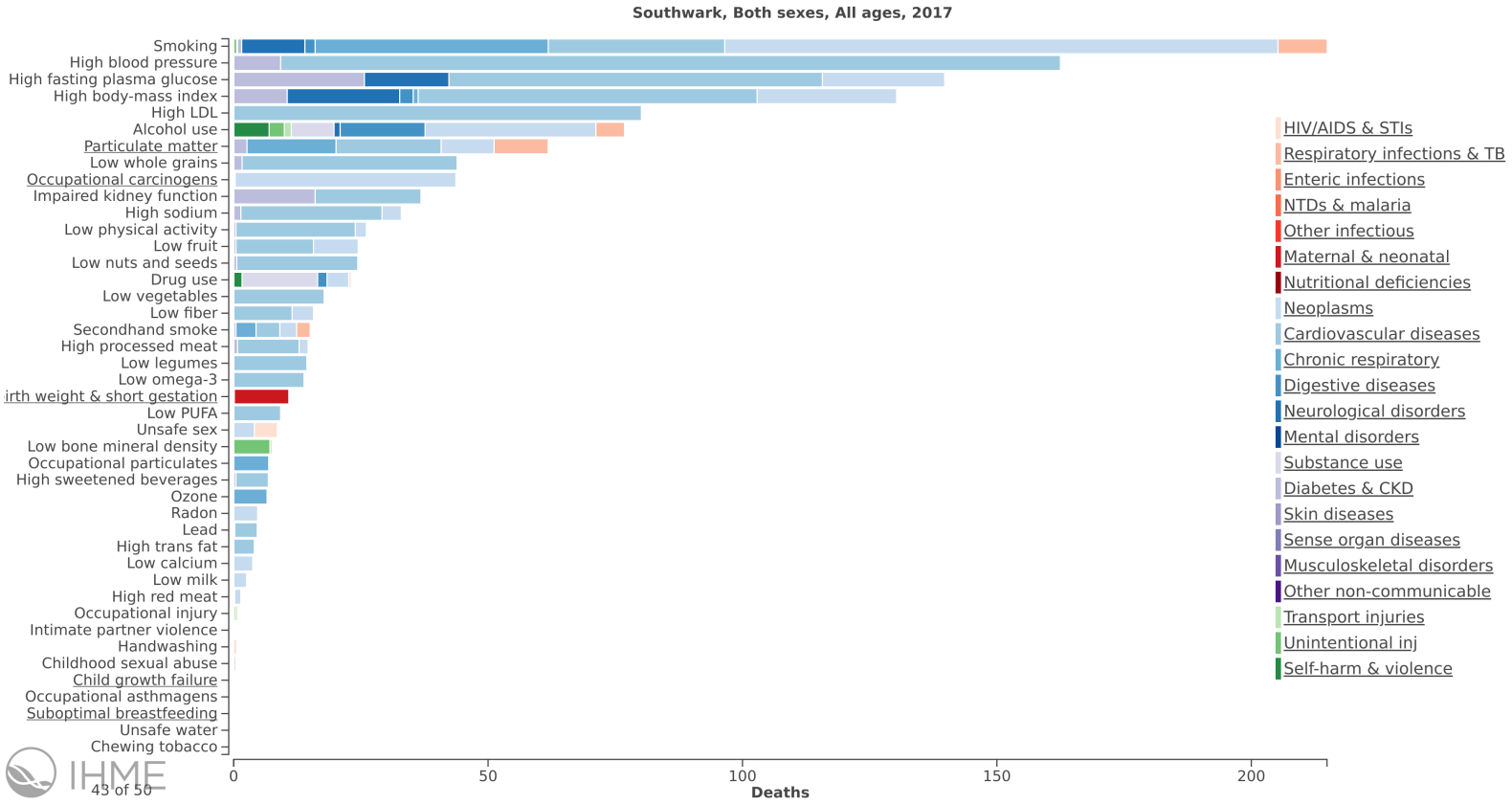


Source: Kingston et al, *Age and Ageing*, Volume 47, Issue 3, 1 May 2018, Pages 374–380, "Projections of multi-morbidity in the older population in England to 2035: estimates from the Population Ageing and Care Simulation (PACSim) model", https://academic.oup.com/ageing/article/47/3/374/4815738

Improving health and addressing the known major causes of death is a massive value proposition

Burden of disease – Southwark

(number of deaths by cause and risk factor; both sexes, all ages, 2017)

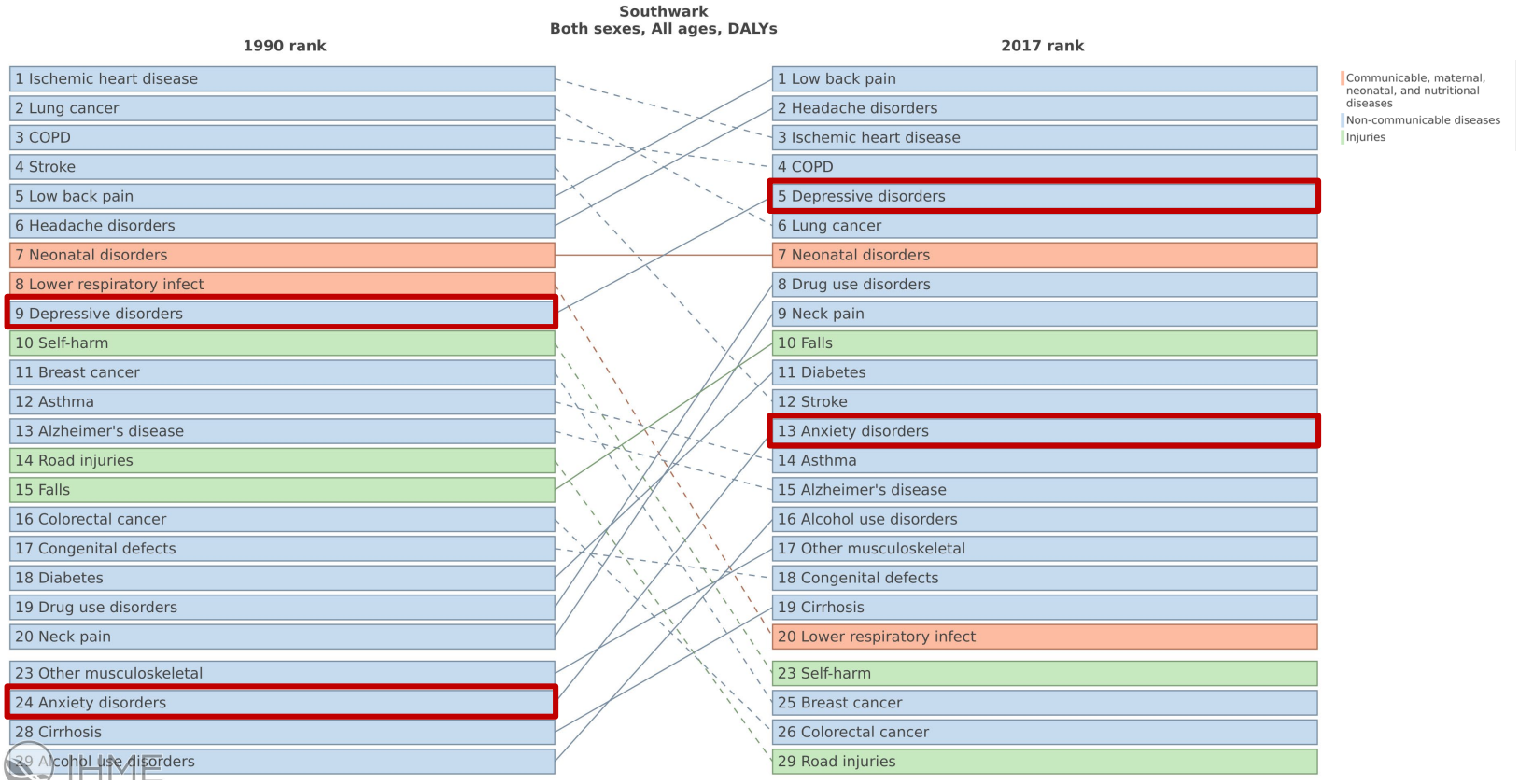


Source: Institute of Health Metrics and Evaluation [online]: https://vizhub.healthdata.org/gbd-compare/. Accessed 08/03/2019.

Focusing on both physical and mental health and wellbeing

Burden of disease – Southwark

(disability adjusted life years by cause; both sexes, all ages, 1990 and 2017)



Source: Institute of Health Metrics and Evaluation [online]: https://vizhub.healthdata.org/gbd-compare/. Accessed 08/03/2019.

The Vital 5 – improving outcomes and reducing health inequalities – responding to the Burden of Disease

Overall Aim: Improve the population's health and reduce health inequalities by focusing on the Vital 5 to support prevention, detection, health promotion, management and treatment wherever there is an opportunity to do so.

1	2	3	4	5
Blood pressure	**Obesity**	**Mental health**	**Smoking status**	**Alcohol intake**

Standardised and routine recording and clinical management of these 5 key scores for all our patients is a vital component to delivering consistent high quality equitable care.

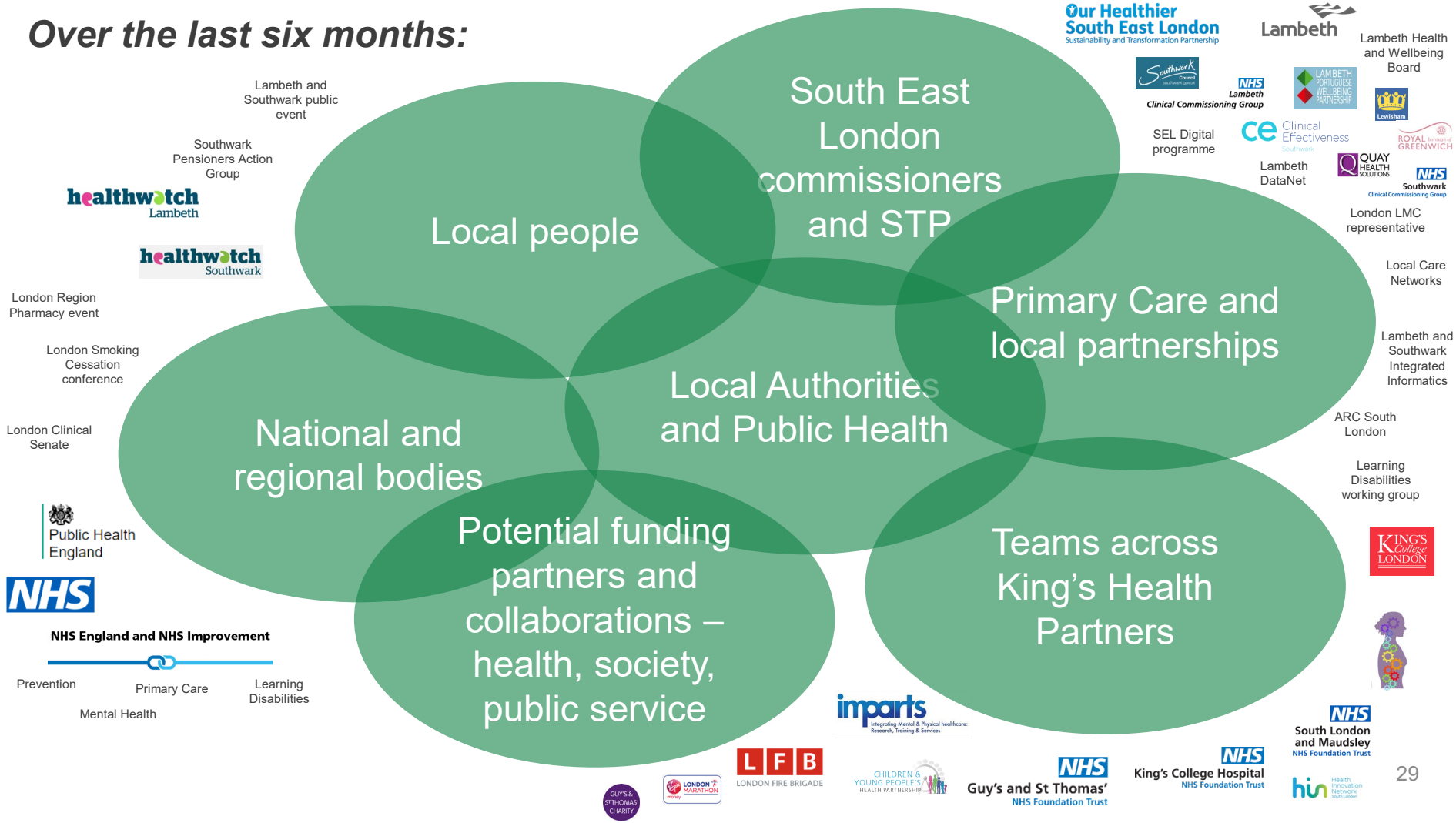
The challenge and opportunity – The Vital 5 for Life

Our vision is for the ***Vital 5 for life***, including a dedicated focus on known inequalities in learning disabilities and severe mental illness.

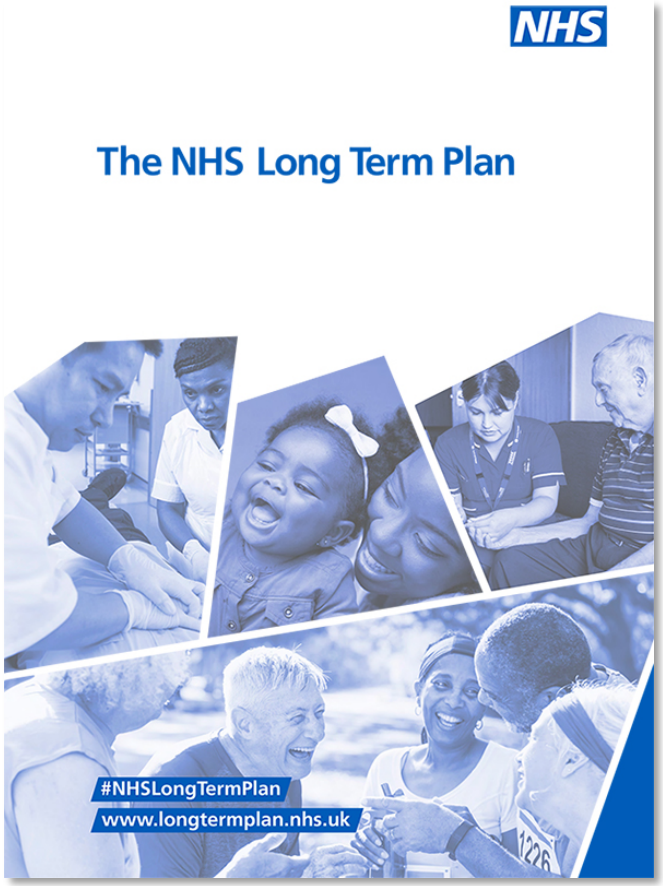
- Enabling people to *know your Vital 5,* including when you are well
- Supporting people to improve their Vital 5
- Building a population-wide conversation
- Implementing system-wide approaches to improve Vital 5 for a population

Working together with people across health and care

Over the last six months:



Outcomes that matter to people – *improving health and wellbeing and reducing inequalities*



Our mission together for the next ten years…

Q & A

Lunch at 13.15pm

Workshops begin at 2pm

#KHP10Years