Stratified, personalised or P4 medicine: a new direction...

Tuesday 12 May 2015
Heartbeat Education Centre, Southampton General Hospital

Session 3
Interdisciplinary approaches to stratified medicine

The next 14 minutes

- Global Challenges
- Gearing an entire country for stratified medicine
- Information science and “big data” as the catalyst for change
- With Big Data Goes Big Responsibilities

Convergence of Care with Research

Applications of Informatics to the study of Chronic Disease

14th May 2015
Andrew Morris
Professor of Medicine, University of Edinburgh

Chief Scientist
Scottish Government Health Directorate

Director of Farr Institute Scotland

Scotland’s Demographics 1911 - 2011
Population-based study 1.75M people in Scotland
More people have 2 or more CDs than one

“Management of patients with several chronic diseases is now the most important task facing health services in developed countries, which presents a fundamental challenge to the single-disease focus that pervades medicine”

Lancet May 15th 2012

Roles of informatics in translational medicine

1st gap in translation

Basic research  →  Prototype/Discovery

Bioinformatics
Medicinal Informatics
Text mining
Automated experimentation

2nd gap in translation

Preclin. Dev.  →  Late trials

Trial design & simulation tools
Trial recruitment & data man. tool
Guideline authoring tools
Decision support tools for Drs & pts.

Analysis of linked anonymised clinical datasets

HTA: Health Technology Assessment
HSR: Health Services Research

Adapted from Cooksey report Chart 7.1, page 105
The Revolution, Phase 2: How the UK Can Be The Winner

The digital revolution is entering a new phase.

First it was about connectivity, in new ways that hugely increased communications.

America was clearly the winner, enabled by a large single market, heavy investment in the required basic science and technical application, as well as an innovative and entrepreneurial culture.

Think of Google, eBay, Facebook, Amazon, PayPal, Yahoo, Microsoft, Twitter, Apple

This next phase of the digital revolution has PSI at the very foundation.

We enjoy significant advantages

We have the opportunity to be world leaders in the enlightened use of data.

Informatics to support patient care
Key Trends
- Population: 5.3 million
- Population Growth (2000-2011): +4.6%
- % aged 75+: 7.9%
- GDP Per Head in 2011: $42,124

Population Health
- Smoking Rate: Males 24%, Females 22%
- Alcohol Consumption per capita: 11.9 Litres
- % Overweight: Males 69%, Females 60%

Mortality (Deaths)
- Average Life Expectancy:
  - Males 76.1 years, Females 80.6 years
- Mortality per 100,000 Population (All Ages):
  - 701 in 2008, reduced to 641 by 2011
- Biggest Causes of Mortality:
  - Cancer (29%), Ischemic Heart Disease (14%), Stroke (9%), Mental (6%), Lower Respiratory (6%)

Illustrative Health Spend per Head
- Vast Majority Publicly Funded
- Per head 2010/11: $3,111
- Annual Growth 2000/01 to 2010/11: 4.5%

Inputs
- Acute Beds in 2011/12: 16,500 (NHS)
- Doctors in 2012: 12,000 (NHS WTE)
- Nurses / Midwives in 2012: 56,600 (NHS WTE)

ACTIVITY LEVELS

<table>
<thead>
<tr>
<th>Activity</th>
<th>2011/12</th>
<th>5 year Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated GP Patient Contacts</td>
<td>16,539,000</td>
<td>3.3%</td>
</tr>
<tr>
<td>Estimated Practice Nurse Patient Contacts</td>
<td>7,627,000</td>
<td>10.5%</td>
</tr>
<tr>
<td>New A&amp;E Attendances</td>
<td>1,561,529</td>
<td>6.8%</td>
</tr>
<tr>
<td>Total Outpatient Attendances</td>
<td>4,699,868</td>
<td>4.7%</td>
</tr>
<tr>
<td>Total Inpatient/Day Case Discharges</td>
<td>1,582,305</td>
<td>6.8%</td>
</tr>
</tbody>
</table>

Day Case Discharges: 448,782 10.6%
Routine Inpatient Discharges: 441,024 9.5%
Non-Routine (emergency) Inpatient Discharges: 540,890 6.4%

Community Health Number
07 10 64 02 5 0

Date of Birth Sex Check

Linking Data - the key to seamless care
Informatics in Scotland

- **Emergency Care Summary**
- **National PACS**
- **National Chronic Disease Management**

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**Emergency Care Summary**

- Patient Safety is key driver
- Available nationwide
- Clinically Led, Patient Focused
- Twice daily updates from GP systems
- Medications and Adverse Reactions
- **Explicit Consent** to view ECS
- Full audit trail available at any time
- 3.5 Million Accesses per Annum
- Changes management in 20%

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**A nationwide PACS**

- Common user interface across all hospitals
- Managed storage service totalling 1 Petabyte
- 24,000 registered users
- Installation of 350, 3MP monitor diagnostic workstations for use in radiology
- Web-based image viewing in over 2000 wards
- 10% reduction in re-examination
- 100% reduction in film and chemical cost
- Significant reduced time to treatment
- Image database of 17 million studies for care and research

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**A National Diabetes System for Scotland**

- Total Scottish Population 5.2M
- People with diabetes: 268,154 (4.8%)
- People with Type 1 DM: ~27,000 (0.5%)
- All patients nationally are cared for with a single clinical information system SCI-DC
- SCI-DIABETES used in all hospitals
- Nightly secure sharing of data from all 1043 primary care practices across Scotland
Scottish Diabetes Survey 2002-2007
Recording of Key Biomedical Markers

- HbA1c
- Blood pressure
- Cholesterol
- Urinary Microalbumin

Data recorded within the previous 15 months

Source: Scottish Diabetes Survey
Men: an estimated loss in life expectancy with diabetes of 11.1 years (95% CI, 10.1-12.1).
Women: an estimated loss with diabetes of 12.9 years (95% CI, 11.7-14.1).

Livingstone JAMA, 2015

CSO Strategy Refresh 2014

Our Vision

- To build Scotland as a health science nation
- Drive quality improvement and economic growth in NHS Scotland through Research
- Central to Quality Ambitions

Convergence with care and research
Case Studies

Trials
Evaluation of policy
National programmes
International collaboration
Genetics

Computed Tomography
Coronary Angiography

90-95% Specific and Sensitive for Coronary Heart Disease

Male, 55 years, Calcium Agatston Score 1,400

Scottish C0mputed Tomography of the HEART (SCOT-HEART) Trial

Trial Centers

One National Healthcare

12 Centers Across Scotland

Good News – ‘UK First’

NHS TAYSIDE
First global patient
Sanofi

NHS GG&C
Top global recruiter
Eisai

NHS GG&C
First UK patient
Scotland top global recruiter
GSK

NHS HIGHLAND
First global patient
NovoNordisk

Williams et al. Heart 2011:91 1195-1205

CTCA and Clinical Outcome
1.7 Years of Follow-up

CHD Death and Non-Fatal MI

<table>
<thead>
<tr>
<th>Follow-Up (years)</th>
<th>CTCA</th>
<th>Standard Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2073</td>
<td>2073</td>
</tr>
<tr>
<td>1</td>
<td>1957</td>
<td>1957</td>
</tr>
<tr>
<td>2</td>
<td>1869</td>
<td>1869</td>
</tr>
<tr>
<td>3</td>
<td>1851</td>
<td>1851</td>
</tr>
<tr>
<td>4</td>
<td>1835</td>
<td>1835</td>
</tr>
</tbody>
</table>

HR 0.62 [0.38-1.01]  
P=0.053

HR 0.64 [0.41-1.01]  
P=0.056

CHD Death, Non-Fatal MI and Non-fatal Stroke

Changes Diagnosis 1 in 4
Changes Management 1 in 4

Non-experimental evaluation (policy)
Effect of smoking legislation in Scotland

Admissions fell by 17% - 67% of reduction was in non-smokers
Fall in England 4% (no legislation);
long term trend 3%

Before ban 5.2% increase per annum
After ban 18.2% decrease per annum

Acute Coronary syndrome

Childhood asthma

Diabetic Retinopathy Screening

Launched 2005
Annual screening interval
85% of population screened (n=174,152 in 2011)
Single field 45 degree mydriasis (if required)

Can we stratify to increase screening interval?

- 11,275 cases of referable retinopathy
- No retinopathy 0.6% vs. 5.1% background for type 2 diabetes
- Transition lowest among people with two consecutive exams showing no visible retinopathy.
- If people with T2DM and two examinations showing no visible retinopathy were offered two-yearly screening
- 44% fewer people in 2009.

Looker et al 56; 1716-25; 2013

Case Studies

Trials
Evaluation of policy
National programmes
International collaboration
Genetics

The Research and Innovation Landscape
the need for collaboration
Case Studies

Trials
Evaluation of policy
National programmes
International collaboration
Genetics

Case Studies

Trials
Evaluation of policy
National programmes
International collaboration
Genetics & "Personalised Medicine"

Internationalisation
Kuwait Scotland eHealth Innovation Network

“A Health Science and Quality Package”
• Scientific Research
• Education
• Clinical Skills
• Informatics

POPULATION PHARMACOGENETICS

• METFORMIN
  • In use for over 50 years
  • We still don't understand how it works
    • 25% of patients get GI intolerance;
    • 5% cannot continue it
  • Can we use genetics to help us?
  • Ability to link genetics with drug exposure and therapeutic response

GWAS Metformin Response
Q-Q plot
Common variants near ATM are associated with glycemic response to metformin in type 2 diabetes

The gene links cancer pathways, metformin pathways and type 2 diabetes

100,000 genomes in 5 years

THE MODEL

Exemplar Programme 3: RhA & respiratory
Exemplar Programme 2: Heart disease & diabetes
Exemplar Programme 1: Oncology

Tissue/Bio-repositories/ Datasets
Imaging
Genomic/’omic’ medicine
Biomedical Informatics/e Health

Innovation Centre Business Platform

STRATIFIED MEDICINE SCOTLAND – INNOVATION CENTRE
THE RIGHT TREATMENT, TO THE RIGHT PATIENT, AT THE RIGHT COST........
NEW APPROACHES TO DATA MANAGEMENT

- Full genome sequence ~£700; ~3GB
- New approaches needed for accessing, manipulating, visualizing
- Requires entirely new perspective
- Capacity building key
- Let’s align computer science and mathematics with medicine
- Opportunity for economies of scale – private cloud infrastructure – subscription models
- Software as a service; platform as a service

APPLE’S NEW RESEARCH KIT: ETHICAL QUAGMIRE OR MEDICAL RESEARCH AID?

"THE SOFTWARE PLATFORM COULD BE GREAT FOR MEDICINE, BUT IT HAS SOME GROWING UP TO DO"

Launched March 2015
Apps in asthma, Parkinson’s, Heart disease monitoring
**Core Principles**

- Clinically led
- Be agnostic as to the type, scale, platform, and storage location of the data
- Use public APIs and open standards, interfaces, and protocols
- Encrypt data at rest and in transit
- Separate key management from data management
- Include with the data the corresponding metadata, context, and provenance information
- Represent the data as atomic data with associated metadata
OUR VISION

“To harness health data for patient and public benefit by setting the international standard in trustworthy reuse of electronic patient records and related linkable data for large-scale research.”

OUR TEN KEY ACTIVITIES

1. Collaborative Leadership
2. Cutting edge Research
3. Public engagement
4. Governance (safe havens)
5. Methods development
6. Cohort enablement
7. Harmonised eInfrastructure
8. Partnerships
9. Training/Capacity Building
10. Communications

To deliver impact nationally and internationally
### National level data resources

<table>
<thead>
<tr>
<th>Birth</th>
<th>Education</th>
<th>Looked after children</th>
<th>Marriage</th>
<th>Community care</th>
<th>Care homes</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HMRC</td>
<td>DWP</td>
<td>Census</td>
<td>(Scotland &amp; UK)</td>
<td></td>
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</tbody>
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<table>
<thead>
<tr>
<th>Birth</th>
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<th>Marriage</th>
<th>Community care</th>
<th>Care homes</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP consultations</td>
<td>Mental Health</td>
<td>Hospital Admissions</td>
<td>Substance misuse</td>
<td>Community care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neonatal Record</td>
<td>Out patients</td>
<td>A&amp;E</td>
<td>Screening</td>
<td>Suicide</td>
<td>Cancer registrations</td>
<td></td>
</tr>
<tr>
<td>Maternity</td>
<td>Prescription</td>
<td>Immunisation</td>
<td>Imaging</td>
<td>Laboratory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child health surveillance</td>
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</tr>
</tbody>
</table>

### Adding Value to UK Cohort Studies

- 34 cohorts
- 2.5m people have taken part and currently around 2.2m people – 3.5% of the population – are cohort members.
- We owe them a debt of gratitude
- 500,000 people are part of UK Biobank and soon the entire cohort will be genotyped.
- Participants from the UK cohort studies have given consent for their personal data to be linked to NHS records and other data sources such as education and the census.
The purpose of the Institute is to build on the legacy of Alan Turing by developing new algorithms to unlock the power of large-scale digital data and change the shape of the future.

Our mission is to make the UK world leading in data science research by harnessing the collective knowledge and expertise of our founding members.

The Alan Turing Institute

Our vision is to enable knowledge and predictions to be extracted from big data to make scientific discoveries.

www.ref.ac.uk

Technologies

<table>
<thead>
<tr>
<th>Past</th>
<th>Future</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensors</td>
<td>Ubiquitous networked</td>
</tr>
<tr>
<td>Robotics</td>
<td>Full humanoid</td>
</tr>
<tr>
<td>Natural language</td>
<td>Across media</td>
</tr>
<tr>
<td>Speech recognition</td>
<td>Real-time natural</td>
</tr>
<tr>
<td>Machine learning</td>
<td>Commodity tools</td>
</tr>
<tr>
<td>Data linkage</td>
<td>Semantic Web</td>
</tr>
<tr>
<td>Data architectures</td>
<td>Cloud + havens</td>
</tr>
<tr>
<td>Social computation</td>
<td>Social intelligence</td>
</tr>
<tr>
<td>Security</td>
<td>Personalised security</td>
</tr>
</tbody>
</table>

The University of Edinburgh

Physical data

Medical Informatics

Organisational data

Populations

People

Agents

Systems

Personal data

Confluence
BIG ISSUE 5 (THE BIGGEST OF ALL)

Designing for Transparency and Trust

"With Big Data Goes Big Responsibilities"

The whistleblower
I can't allow the US government to destroy privacy and basic liberties

The guardian
DATA LINKAGE FRAMEWORK – SUPPORTED BY POLICY

A Data Vision for Scotland - supports trustworthy uses of data for public benefit, continuing our reputation for the safe, secure and transparent use of data.

The Data Linkage Strategy – ‘Joined Up Data for Better Decisions’ sets out our ambitions for making better use of data that already exists in Scotland through linkage.

http://www.gov.scot/Topics/Statistics/datalinkageframework

Federated Network of Safe havens

Safe Havens:

- One in each of the four NHS Research Scotland (NRS) nodes
- National Safe Haven
- These providing services and support to other units

- Working to common security and data sharing principles and standard
- Work collaboratively – allows data sharing, inter-operability
- External accreditation to provide assurance to data controllers, patients and the public

PROPORTIONATE GOVERNANCE

Category 0: Public domain
No further conditions

Single National Privacy Advisory Committee
April 2015
MEDICINE IN THE INFORMATION AGE
EIGHT “C’S” FOR SUCCESS

- Commitment to public engagement in everything we do
- Clinical focus – the patient as the focus
- Convergence of care with innovation and research
- Collaboration of health care providers/ academia
- Commercial engagement - encouraged but with transparent governance and benefit sharing
- Computer Science key ingredients for change
- Chief Information Officers for Quality, Safety and Research at Board Level
- Clarity about GOVERNANCE and data sharing

An Opportunity for the UK to Lead the Way?
Defragmentation and Alignment is key