Reflections on Research Past, present and future

John Williams
Health and Care Research Wales Conference
5th October 2017

Overview

- Look back at my research career
- Pick out some observations
- Share my vision for the future
- Focus on patients, healthcare and data
- Emphasis on impact, and pragmatism

My career

- Trained at Cambridge University & St Thomas' 1964-70
- Royal Naval Medical Officer 1967-88
  - Trained as a gastroenterologist
  - Professor of Naval Medicine 1984-88
- Established Swansea Postgraduate Medical School in 1988
- Chair in Health Services Research in Swansea University Medical school since 2001
- Director of R&D at WORD 2002-7
- Founding Director of Health Informatics Unit, Royal College of Physicians since 2001

Health Services Research

- may include research from any healthcare discipline including: medical sociology, medical statistics and biostatistics, health psychology, clinical psychology, health economics, modelling, clinical trial methodology and organisation, community-based clinical trials, medical anthropology, medical geography, medical ethics, medical education, healthcare policy evaluation, health service organisation and management, health technology assessment, patient experience, clinical epidemiology and decision analysis, methodologies for complex interventions and health informatics.

http://www.rae.ac.uk/panels/main/b/health

The Navy Days – sea time

- 1972/3 Ships Medical Officer HMS Plymouth

  On hurricane patrol in the Caribbean

Williams JG. Treatment of gonorrhoea and non-gonoccal urethritis with spiramycin. J RNMS 1975;61:44-48.

No Good Clinical Practice
No Ethics infrastructure
No Clinical Trials Units

Back on dry land – RNH Plymouth

– Explored the clinical pharmacology and efficacy of H2-receptor antagonists – metiamide and cimetidine

ds to suppress gastric acid secretion

the management of acid-peptic disorders

THE LANCET

Volume 306, Issue 7944, 29 November 1975, Pages 1069-1072

24-HOUR CONTROL OF INTRAGASTRIC ACIDITY BY CIMETIDINE IN DUODENAL-ULCER PATIENTS

R.E Pounder [a, b], G.J.Milton Thompson [a, b], J.G.Williams [a, b], J.J.Misiewicz [a, b]

Show more

https://doi.org/10.1016/S0140-6736(75

Abstract

The effects of two dose regimen acidity were investigated in six received placebo capsules on t second day. Cimetidine 0·8 g/d

Gut, 1976, **17**, 161-168

Inhibition of food-stimulated gastric acid secretion by cimetidine

R. E. POUNDER[1], J. G. WILLIAMS, R. C. G. RUSSELL[2], G. J. MILTON-THOMPSON, AND J. J. MISIEWICZ

From the Medical Research Council Gastroenterology Unit, Central Middlesex Hospital, London, Royal Naval Hospital, Stonehouse, Plymouth, Devon, and St. Mary's Hospital, London

SUMMARY The effect of cimetidine, a new histamine H_2-receptor antagonist, on gastric acid secretion stimulated by a homogenised meal was studied in six normal volunteers using an *in vivo* intragastric titration technique. The subjects were studied twice, no more than 48 h apart, receiving

BRITISH MEDICAL JOURNAL 10 MAY 1975 307

Relief of Duodenal Ulcer Symptoms by Oral Metiamide

R. E. POUNDER, J. G. WILLIAMS, G. J. MILTON-THOMPSON, J. J. MISIEWICZ

British Medical Journal, 1975, 2, 307-309

Summary

Thirty patients with symptoms of duodenal ulceration were treated for five to eight weeks in a double-blind trial with either metiamide 1 g daily by mouth or a placebo. In the 15 patients receiving metiamide there were significant reductions in nocturnal pain and antacid consumption. Daytime pain was diminished. The results suggest that histamine H_2-receptor antagonists are likely to be useful in the medical management of the symptoms of duodenal ulceration.

The patients were asked at the beginning of the trial to throw away any antiulcer drugs in their possession. Their general practitioners were asked not to prescribe any other treatment during the eight weeks of the trial. No specific advice was offered concerning diet.

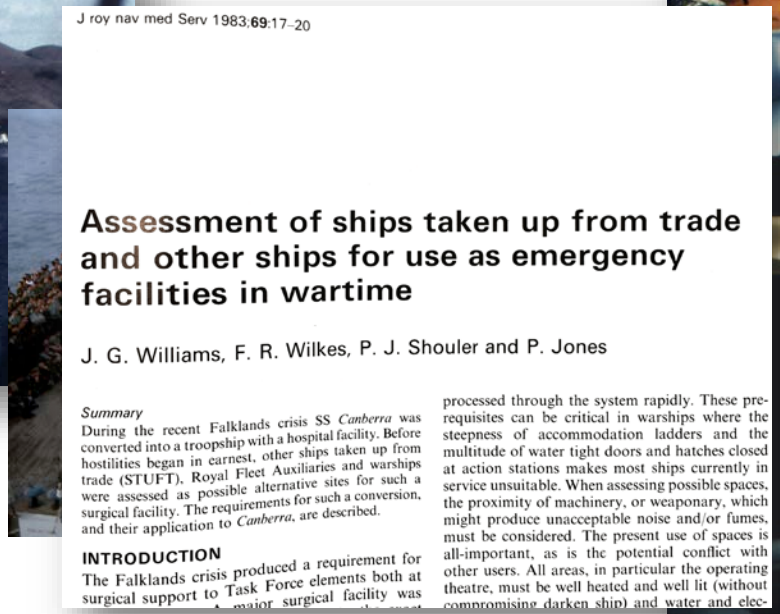
At the start of the trial and at each weekly visit the patients were physically examined and haemoglobin, red cell indices, and total and differential white count were checked. Every four weeks plasma electrolytes, urea, serum creatinine, and liver and thyroid function were checked, urine was analysed, and a chest *x*-ray examination was performed.

The results were analysed in two ways. The overall comparison of the incidence of pain between the two treatment groups was based on the total number of days (and nights) in each week that severe, mild, or no ulcer pain was recorded. The significance of difference between the treatment groups was determined with the χ^2 test. Comparisons of consumption of antacid and the number of pain-free days (and nights) in individual patients during each week of the trial were made with the Wilcoxon rank sum test.

Think innovative methodologies

1982 Falklands Islands

- Led a Surgical Support Team
- Converted SS Canberra from troop ship to hospital
- Prepared for mass casualties



J roy nav med Serv 1983;**69**:17–20

Assessment of ships taken up from trade and other ships for use as emergency facilities in wartime

J. G. Williams, F. R. Wilkes, P. J. Shouler and P. Jones

Summary
During the recent Falklands crisis SS *Canberra* was converted into a troopship with a hospital facility. Before hostilities began in earnest, other ships taken up from trade (STUFT), Royal Fleet Auxiliaries and warships were assessed as possible alternative sites for such a surgical facility. The requirements for such a conversion, and their application to *Canberra*, are described.

INTRODUCTION

The Falklands crisis produced a requirement for surgical support to Task Force elements both at

processed through the system rapidly. These prerequisites can be critical in warships where the steepness of accommodation ladders and the multitude of water tight doors and hatches closed at action stations makes most ships currently in service unsuitable. When assessing possible spaces, the proximity of machinery, or weaponary, which might produce unacceptable noise and/or fumes, must be considered. The present use of spaces is all-important, as is the potential conflict with other users. All areas, in particular the operating theatre, must be well heated and well lit (without

Preparing for mass casualties

- Devised a very simple resuscitation approach
- Documented the outcome

BRITISH MEDICAL JOURNAL VOLUME 286 5 MARCH 1983 775

MEDICAL PRACTICE

Contemporary Themes

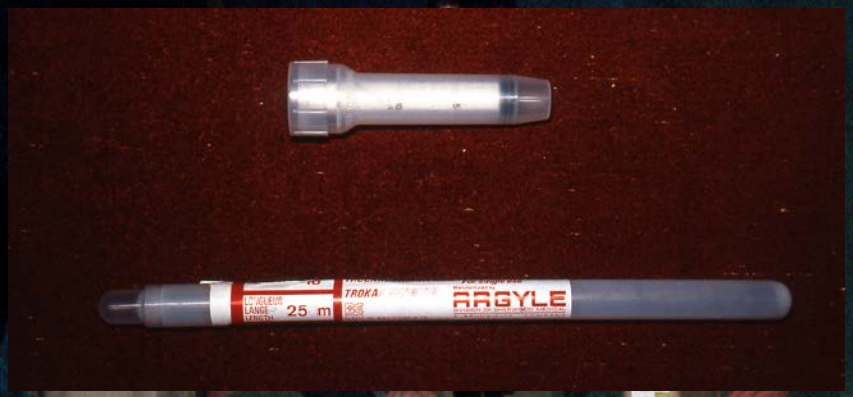
Resuscitation experience in the Falkland Islands campaign

J G WILLIAMS, T R D RILEY, R A MOODY

The recent campaign to retake the Falkland Islands was a novel military exercise from many points of view. This was particularly so for the medical support, which required much improvisation at all levels. Several surgical teams from the Royal Navy and the Royal Army Medical Corps were deployed in support of both the fleet and the troops on land. Two Royal Naval teams embarked in *SS Canberra*, and the journey south on board

in 5 ml of water, and given in small doses (3 mg) often, titrated according to pain. The importance of checking the dose and time of any analgesia given previously was emphasised. For chest injuries it was planned to give buprenorphine hydrochloride 0·3-0·6 mg or, if unavailable, pentazocine 30-60 mg intravenously. Inhalational Entonox (50% nitrous oxide/50% oxygen) would also be available.

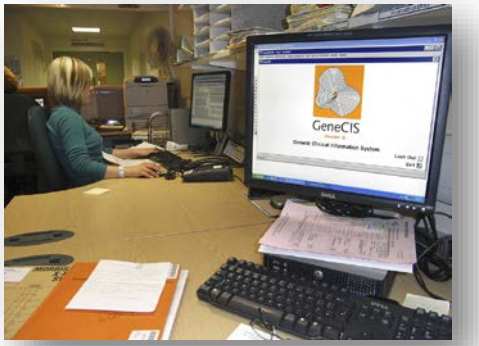
Antibiotics—All patients with open wounds were to be given benzylpenicillin intravenously, one megaunit immediately and repeated



Williams JG A disposable proctoscope Lancet 1982;ii:1228

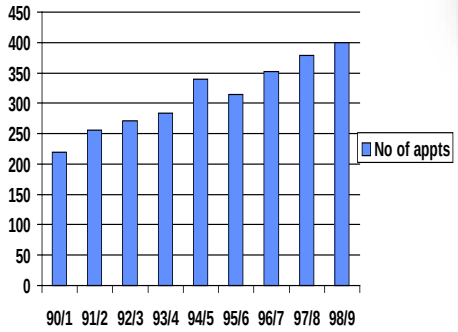
Swansea Postgraduate Medical School (1988-2001)

- Established the Postgraduate School
- Consultant at Neath General Hospital
  - Built up a clinical service in gastroenterology
  - Supported by in-house EPR



International Journal of Medical Informatics
ELSEVIER Volume 56, Issues 1–3, December 1999, Pages 151-159

The use of clinical information to help develop new services in a district general hospital



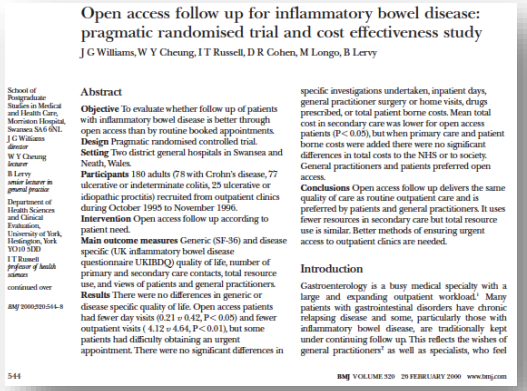
Impact:
Informed both policy and practice. Basis for a 4* impact case study in REF 2012

  - Pragmatic trials in service delivery

BMJ RESEARCH

Effectiveness of nurse delivered endoscopy: findings from randomised multi-institution nurse endoscopy trial (MINuET)

John Williams, professor,[1] Ian Russell, professor and director,[2] Dharmaraj Durai, consultant gastroenterologist,[3] Wai Yee Cheung, senior lecturer,[1] Amanda Farrin, director and principal statistician (health sciences division),[4] Karen Bloor, senior research fellow,[5] Simon Coulton, reader in health services research,[6] Gerry Richardson, senior research fellow[7]



Open access follow up for inflammatory bowel disease: pragmatic randomised trial and cost effectiveness study

J G Williams, W Y Cheung, I T Russell, D R Cohen, M Longo, B Lervy

Abstract

Objective To evaluate whether follow up of patients with inflammatory bowel disease is better through open access than by routine booked appointments.
Design Pragmatic randomised controlled trial.
Setting Two district general hospitals in Swansea and Neath, Wales.
Participants 180 adults (78 with Crohn's disease, 77 ulcerative or indeterminate colitis, 25 ulcerative or idiopathic proctitis) recruited from outpatient clinics during October 1995 to November 1996.
Intervention Open access follow up according to patient need.
Main outcome measures Generic (SF-36) and disease specific (UK inflammatory bowel disease questionnaire UKIBDQ) quality of life, number of primary and secondary care contacts, total resource use, and views of patients and general practitioners.
Results There were no differences in generic or disease specific quality of life. Open access patients had fewer day visits (0.21 *v* 0.42, P< 0.05) and fewer outpatient visits (4.12 *v* 4.64, P< 0.01), but some patients had difficulty obtaining an urgent appointment. There were no significant differences in specific investigations undertaken, inpatient days, general practitioner surgery or home visits, drugs prescribed, or total patient borne costs. Mean total cost in secondary care was lower for open access patients (P< 0.05), but when primary care and patient borne costs were added there were no significant differences in total costs to the NHS or to society. General practitioners and patients preferred open access.
Conclusions Open access follow up delivers the same quality of care as routine outpatient care and is preferred by patients and general practitioners. It uses fewer resources in secondary care but total resource use is similar. Better methods of ensuring urgent access to outpatient clinics are needed.

Introduction

Gastroenterology is a busy medical specialty with a large and expanding outpatient workload.[1] Many patients with gastrointestinal disorders have chronic relapsing disease and some, particularly those with inflammatory bowel disease, are traditionally kept under continuing follow up. This reflects the wishes of general practitioners[2] as well as specialists, who feel

Swansea University Medical School (2001 – now)

- Pragmatic trials - health records & gastroenterology
- Validation of PROMS:
  - UK Inflammatory Bowel Disease Questionnaire
  - Gastrointestinal Endoscopy Satisfaction Questionnaire
  - Gastrointestinal Symptom Rating Questionnaire
  - Crohns and Ulcerative Colitis Questionnaire
- Use of operational data for RCTs
- Health records and data provenance

Use of HES and PEDW data for research

- WORD (2002-7) – forerunner of NISCHR and HCRW
  - Clinical Research Collaboration Cymru (CRCCymru)
  - Health Information Research Unit
    - Explore the use of routinely collected data for research
    - Established the SAIL database – research using data linkage

BMJ

RESEARCH

Mortality in patients with and without colectomy admitted to hospital for ulcerative colitis and Crohn's disease: record linkage studies

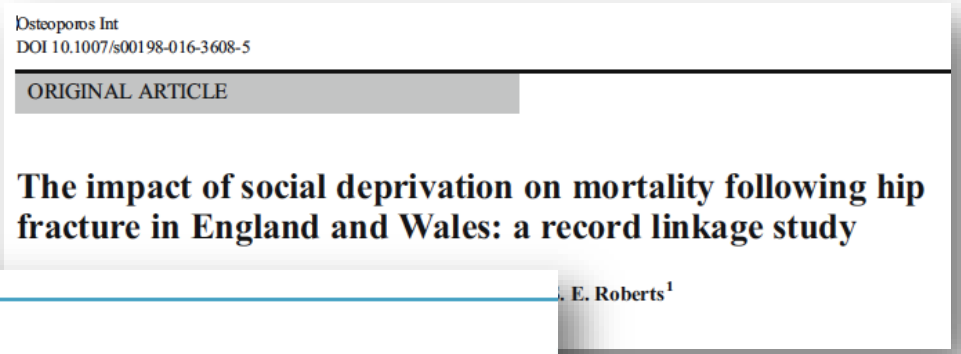
Stephen E Roberts, senior lecturer in epidemiology,[1] John G Williams, professor of health services research,[1] David Yeates, computer scientist,[2] Michael J Goldacre, professor of public health[2]

[1]School of Medicine, Swansea University, Swansea SA2 8PP
[2]Department of Public Health, University of Oxford
Correspondence to: S E Roberts
stephen.e.roberts@swansea.ac.uk

ABSTRACT

Objective To compare mortality outcomes in the three years after elective colectom... emergency colectomy amon... for inflammatory bowel dise... threshold for elective colect... appropriate.

The incidence of ulcerative colitis in the United Kingdom and Europe has been more stable than that for

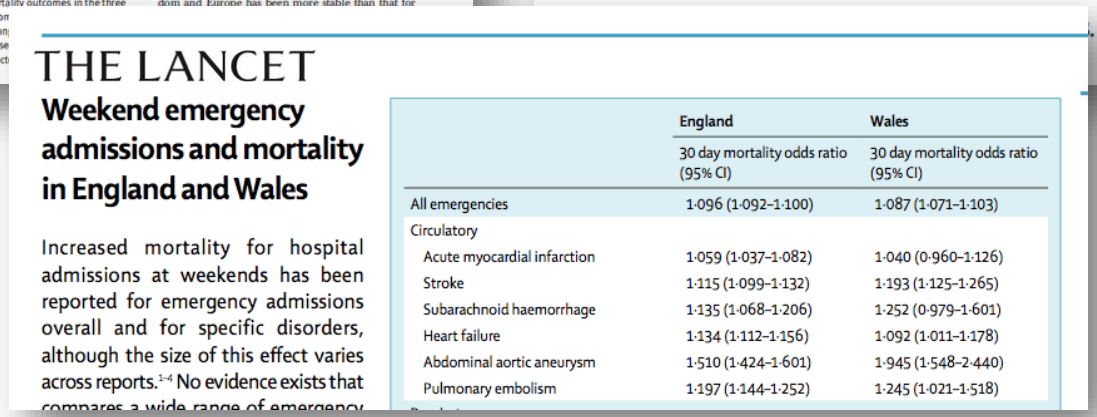


Osteoporos Int
DOI 10.1007/s00198-016-3608-5

ORIGINAL ARTICLE

The impact of social deprivation on mortality following hip fracture in England and Wales: a record linkage study

... E. Roberts[1]



THE LANCET

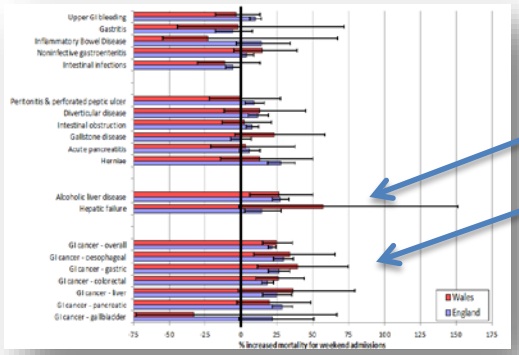
Weekend emergency admissions and mortality in England and Wales

Increased mortality for hospital admissions at weekends has been reported for emergency admissions overall and for specific disorders, although the size of this effect varies across reports.[3-4] No evidence exists that compares a wide range of emergency

	England	Wales
	30 day mortality odds ratio (95% CI)	30 day mortality odds ratio (95% CI)
All emergencies	1·096 (1·092–1·100)	1·087 (1·071–1·103)
Circulatory		
Acute myocardial infarction	1·059 (1·037–1·082)	1·040 (0·960–1·126)
Stroke	1·115 (1·099–1·132)	1·193 (1·125–1·265)
Subarachnoid haemorrhage	1·135 (1·068–1·206)	1·252 (0·979–1·601)
Heart failure	1·134 (1·112–1·156)	1·092 (1·011–1·178)
Abdominal aortic aneurysm	1·510 (1·424–1·601)	1·945 (1·548–2·440)
Pulmonary embolism	1·197 (1·144–1·252)	1·245 (1·021–1·518)

What causes the ‘weekend effect’?

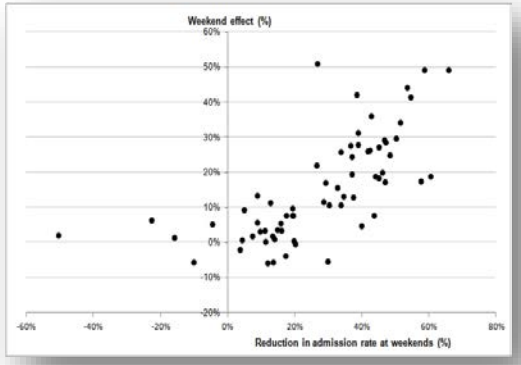
- The weekend effect by GI diagnosis:

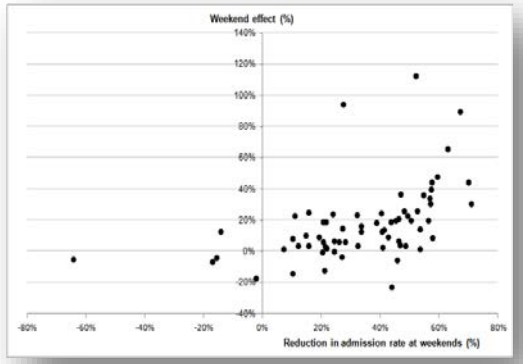


Severe liver disease

GI malignancy

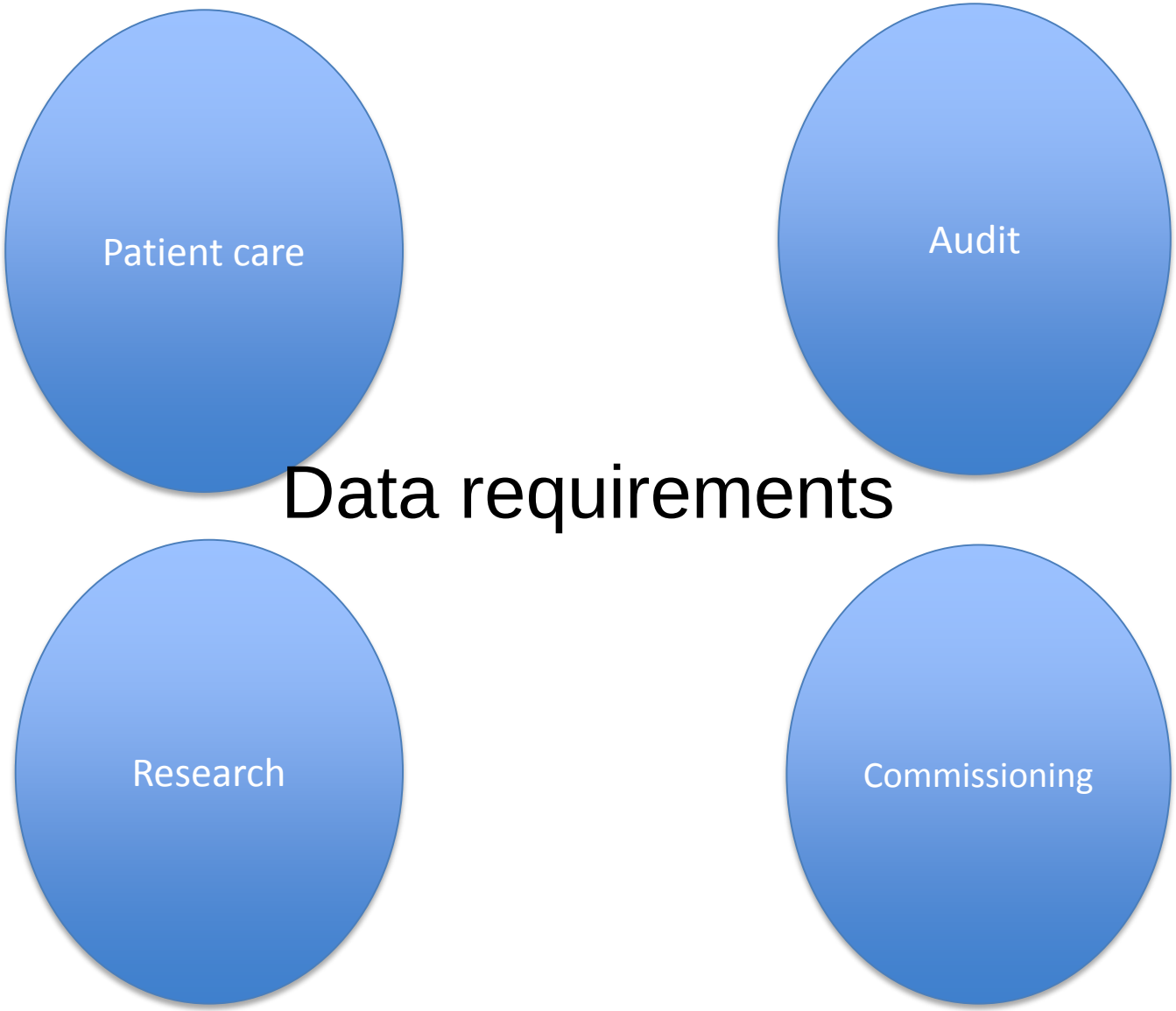
- The weekend effect in relation to % reduction in admissions at weekends:





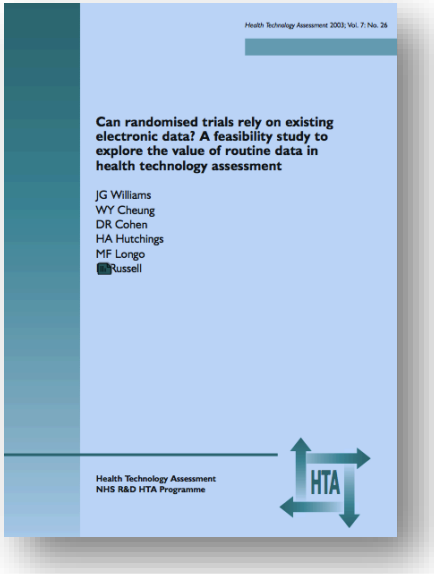
Analysable patient data

- Operational data captured and coded at the point of care
- Routine data – collected as a by-product of care, using a secondary extraction and coding process from paper or electronic records – eg PEDW or HES
- Designed data – bespoke for audit or research and other specific purposes


Patient care
Audit
Data requirements
Research
Commissioning

Can operational electronic data support randomised controlled trials?

- In 2000, we repeated the analysis of four completed RCT's using data extracted from local PAS, Pathology, Radiology and Clinical systems, and PEDW
- Studies were small multi-centre trials addressing four different technologies:
  - open access to outpatients
  - investigation of sleep apnoea
  - autologous blood transfusion
  - surgery for incontinence
- Funded by the HTA Programme



We concluded:

- Routinely collected data can support RCT's
- If clinically rich enough, and held in electronic form (ie in patient focused electronic records, as well as patient administration systems)
- Costs would be less, and larger trials could be run
- The quality of electronic data needs to improve

- *Williams JG et al The value of routine data in health technology assessment: can randomised trials rely on existing electronic data? Health Technology Assessment 2003;vol 7:no 6*
- *Cohen et al Estimating the marginal value of 'better' research output: 'Designed' vs 'routine' data in randomised controlled trials. Health Economics 2003;12:959-74*
- *Hutchings HA et al Can electronic routine data act as a surrogate for patient-assessed outcome measures? International Journal of Technology Assessment in Health Care 2005;21:138-143*

Why does data quality matter?

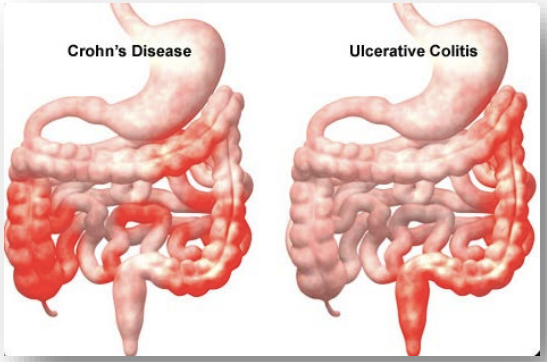
- Quality of patient care
- Patient safety
- Integrated records
- Rigour of data linkage studies
- Detailed phenotyping for precision medicine

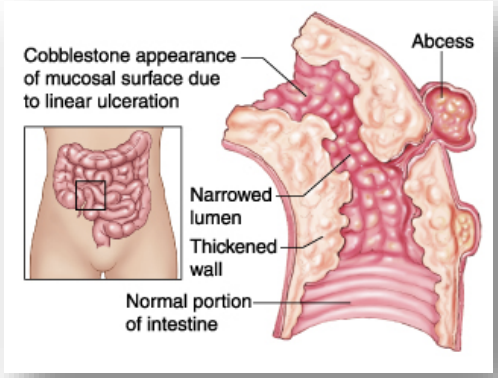
Weaknesses of HES & PEDW data

- **Timeliness**:
  - Delay in availability
- **Content**
  - **Quality**: Diagnosis and procedures are inaccurate in up to 20% of cases
  - **Breadth**: no data on presenting complaint or medication; poor data on co-morbidities
  - **Depth**: Diagnosis terms and codes lack attributes such as disease extent; behaviour; severity; evidence

For example: Inflammatory Bowel Disease

- Diagnosis: Crohn's, Ulcerative Colitis or Indeterminate?
- Diagnosis attributes
  - Anatomical distribution
  - Severity
  - Behaviour – inflammation/fistulisation/stenosis
  - Evidence (?history, imaging, histology)
- Lifestyle (smoking; diet)
- Family history
- Treatment
- Response to treatment
- Patient recorded outcomes





Weaknesses of source data

- **Timeliness**: Delay in availability of data
- **Content** of clinical :ral returns from hospitals (HES in)W in Wales)
  - **Quality**: Diagnosi es are inaccurate in up to 20% of cases
  - **Breadth**: no data :omplaint or medication; poor data on co-m
  - **Depth**: Diagnosis es lack attributes such as disease extent; be ty; evidence

- **Operational clinical systems** do not meet Good Clinical Practice requirements applicable to research systems

construct

- Multicentre, pragmatic RCT, using mixed methods in 62 s
- Compared the c
effectiveness of
steroid resistan
- Primary outcome HRQoL @ two years
- S nes: colectomy; readmissions; a ortality
- I al clinical system to reco a ata (GeneCIS)
- S nspection by the MHRA

Infliximab versus ciclosporin for steroid-resistant acute severe ulcerative colitis (CONSTRUCT): a mixed methods, open-label, pragmatic randomised trial

John G Williams, M Fasih Alam, Laith Alrubaiy, Ian Arnott, Clare Clement, David Cohen, John N Gordon, A Barney Hawthorne, Mike Hilton, Hayley A Hutchings, Aida U Jawhari, Mirella Longo, John Mansfield, Jayne M Morgan, Frances Rapport, Anne C Seagrove, Shaji Sebastian, Ian Shaw, Simon P L Travis, Alan Watkins, for the CONSTRUCT investigators

Summary

Background Infliximab and ciclosporin are of similar efficacy in treating acute severe ulcerative colitis, but there has been no comparative evaluation of their relative clinical effectiveness and cost-effectiveness.

Lancet Gastroenterol Hepatol 2016

Clinical Gastroenterology and Hepatology

Volume 12, Issue 8, August 2014, Pages 1246-1256.e6

Perspectives in clinical gastroenterology and hepatology

Patient-Reported Outcomes as Primary End Points in Clinical Trials of Inflammatory Bowel Disease

Nicolas Williet *, William J. Sandborn ‡, Laurent Peyrin–Biroulet *

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https://doi.org/10.1016/j.cgh.2014.02.016 Get rights and content

Referred to by Stephen B. Hanauer

Issue Highlights

Clinical Gastroenterology and Hepatology, Volume 12, Issue 8, August 2014, Pages 1205-1207

PDF (730KB)

The Food and Drug Administration (FDA) is moving from the Crohn's Disease Activity Index to patient-reported outcomes (PROs) and objective measures of disease, such as findings from endoscopy. PROs will become an important aspect of assessing activity of inflammatory bowel disease (IBD) and for labeling specific drugs for this disease. PROs

Standards for electronic records

- **GCP -** for data
- **Technical** – operating systems, networkin
  interfaces
- **Information** – terminology (SNOMED-CT)
  communication (HL7; FIHR), NHS & profe
- **Professional** – structure and content
  - National standards for structure and content of electronic patient records - endorsed by the Academy of Medical Royal Colleges, Professional Record Standards Body and NHS Digital
  - Information models have been developed to facilitate their incorporation in clinical systems

    https://www.rcplondon.ac.uk/projects/outputs/standards-clinical-structure-and-content-patient-records

Making it happen….

- Promote professional culture change

Royal College of Physicians | Clinical Medicine

Hospital episode statistics: time for clinicians to get involved?

J G Williams, FRCP, Professor of Health Services Research and R Y Mann,

Author Affiliations

Address for correspondence: Professor JG Williams, Professor of Health Serv of Postgraduate Studies, University of Wales Swansea, Singleton Park, Swans

PROFESSIONAL ISSUES

Standards in medical record keeping

Robin Mann and John Williams

Abstract – Medical records serve many functions but their primary purpose is to support patient care. The RCP Health Informatics Unit (HIU) has found variability in the quality of records and discharge summaries in England and Wales. There is currently a major drive to computerise medical records across the NHS, but without improvement in the quality of paper records the full benefits of computerisation are unlikely to be realised.

The onus for improving records lies with individual health professionals. Structuring the record can bring direct benefits to patients by improving patient outcomes and doctors' performance.

cians at the Mayo Clinic in Minnesota kept all their patients' records in a personal leather-bound ledger. This was replaced in 1907 with patient-based records, and this method of record-keeping is still used today by some domiciliary health visitors.

The first major attempt to standardise medical records in the UK came in 1965 with the publication of the Tunbridge report.[1] This produced some of the standard hospital medical records forms we use today (Box 1).

In his report, Tunbridge also described the problems of extracting information from records for secondary purposes. He proposed that medical

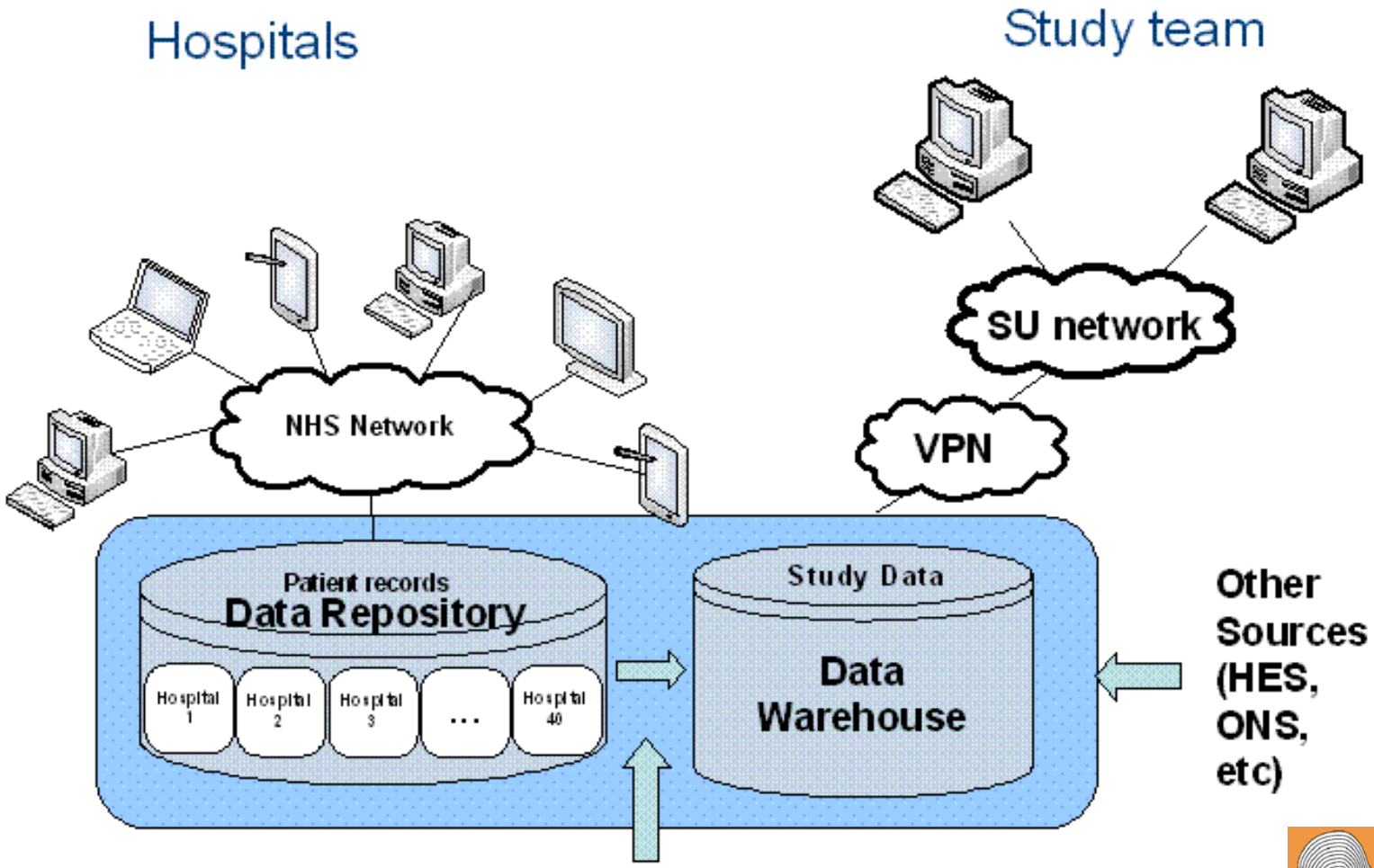
Robin Mann MBBch, Health Informatics Unit, Royal College of Physicians

John Williams FRCP, Professor of Health Services Research, University of Wales, Swansea

Clin Med 2003;3:329–32

- Demonstrate the feasiblity of using operational data for research….

IT infrastructure to support patient care and research



construct

GeneCIS

Data linkage studies
Stratified Medicine

Symptoms
Diagnoses
Tests/results
Treatment/procedures

Performance monitoring
Audit
Registries
Appraisal
Pharmaco-vigilance

Research data

Guidelines
Technology appraisals
Quality standards

HEALTH TECHNOLOGY ASSESSMENT

VOLUME 18 ISSUE 43 JULY 2014
ISSN 1366-5278

The opportunities and challenges of pragmatic point-of-care randomised trials using routinely collected electronic records: evaluations of two exemplar trials

Tjeerd-Pieter van Staa, Lisa Dyson, Gerard McCann, Shivani Padmanabhan, Rabah Belatri, Ben Goldacre, Jackie Cassell, Munir Pirmohamed, David Torgerson, Sarah Ronaldson, Joy Adamson, Adel Taweel, Brendan Delaney, Samhar Mahmood, Simona Baracaia, Thomas Round, Robin Fox, Tommy Hunter, Martin Gulliford and Liam Smeeth

DOI 10.3310/hta18430

The NEW ENGLAND JOURNAL of MEDICINE

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REVIEW ARTICLE

THE CHANGING FACE OF CLINICAL TRIALS

Jeffrey M. Drazen, M.D., David P. Harrington, Ph.D., John J.V. McMurray, M.D., James H. Ware, Ph.D., Janet Woodcock, M.D., Editors

Randomized, Controlled Trials in Health Insurance Systems

Niteesh K. Choudhry, M.D., Ph.D.
N Engl J Med 2017; 377:957-964 | Septemb

SUSTAINING UNIVERSAL HEALTHCARE IN THE UK:
MAKING BETTER USE OF INFORMATION

A Report by Volterra Partners for EMC
SEPTEMBER 2014

Volterra

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Perspective

Lost in Thought — The Limits of the Human Mind and the Future of Medicine

Ziad Obermeyer, M.D., and Thomas H. Lee, M.D.
N Engl J Med 2017; 377:1209-1211 | September 28, 2017 | DOI: 10.1056/NEJMp1705348

Policy

- **Academy of Medical Royal Colleges** *Standards for the clinical structure and content of patient records* 2013 https://www.rcplondon.ac.uk/sites/default/files/standards-for-the-clinical-structure-and-content-of-patient-records.pdf
- **DH** *Personalised health and care 2020: Using data and technology to transform outcomes for patients and citizens. A framework for action.* https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/384650/NIB_Report.pdf
- **NHS England** *NHS Contract 2017* http://www.england.nhs.uk/nhs-standard-contract/17-18/
- **National Information Board Roadmaps** *Setting technical and data standards* https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/433174/NIB_WS_2_1.pdf
- **NHS Digital** *Transfer of care initiative* http://systems.hscic.gov.uk/interop/tci
- **SNOMED CT** *http://systems.hscic.gov.uk/data/uktc/snomed*

- Practice is now up to the practitioners!

Impact:
Basis for a 4* impact case study in REF 2012

In summary…..

- Practitioners – explore and evaluate everything you do
- Observational studies have impact
- Data is the new currency
- Clinical trial methodology is changing
- Operational data will feed multiple purposes in the future
- But the depth and quality of routinely recorded digital clinical data must improve

Thank you

for listening…

…and to all those with whom I have worked over the last 45 years.

Too many to list, but you know who you are. I am very grateful.