Medicines & Healthcare products Regulatory Agency

All Wales Medicines Strategy Group
Grŵp Strategaeth Meddyginiaethau Cymru Gyfan

Making medicines safer

Nicola Wheatley Memorial Lecture

June M Raine

17th November 2022

Nicola Wheatley

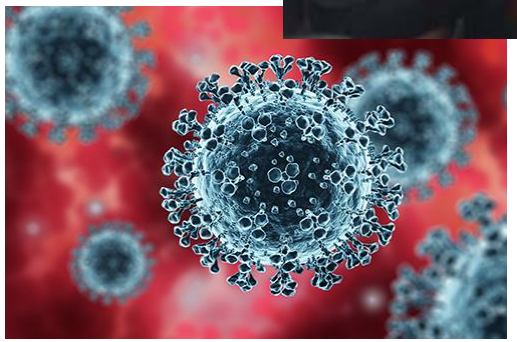
20 September 1981 – 30 October 2021

Making medicines safer

1. **Why** is making medicines safer so important and what is the vital contribution from Wales?

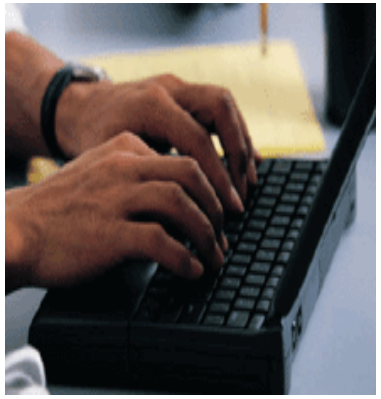
2. **What** were the learnings from safety monitoring for vaccines and therapeutics during pandemic?

3. **Where next**? Better data and new scientific methodologies for safer medicines



MHRA’s mission is to enhance and safeguard the health of the public by ensuring medicines and medical devices work and are acceptably safe

Changing regulatory environment



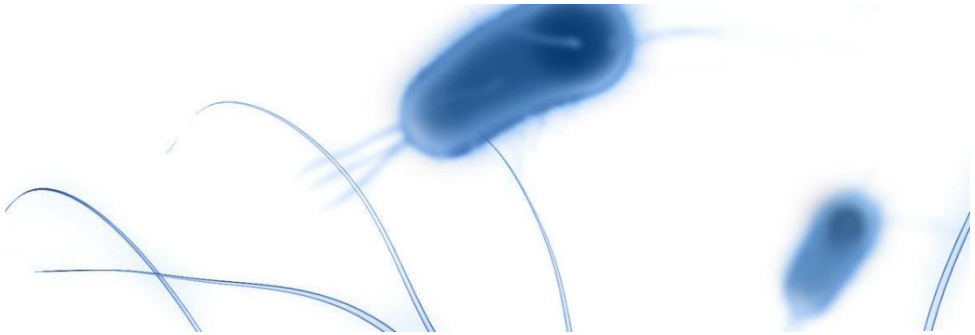
Growing patient expectations for rapid access to breakthroughs

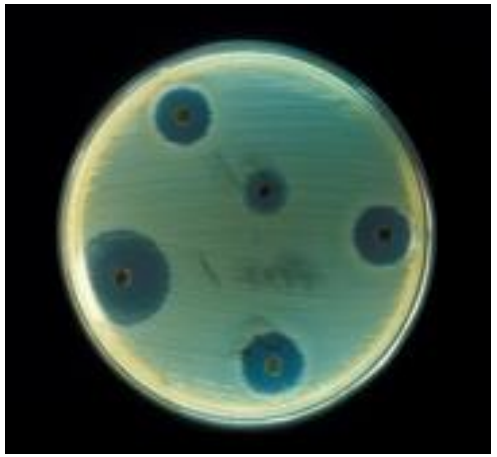
Changing demographics and disease patterns

Digital transformation

Unlocking the potential of transformative medicines

Challenges and opportunities…





MHRA - challenges and opportunities

Following EU Exit, safe transition to new role as independent sovereign regulator

Regulatory reform to support new safer systems and greater patient involvement

Opportunity for new ways of working and safe speedy access to innovation for patients

A new era in regulation

Today's **public and patients** have rightful expectations of safety and involvement in decisions about healthcare products

Today's **health service** deserves safe, speedy access to the most transformative products – medicines and medical devices

Today's **life sciences industry** demands an agile and supportive regulator

- Putting patients first
- World-leading
- Innovative
- Scientific excellence

One Agency delivering for patients

Patient Involvement

Putting patients first, creating a dialogue with patients at every step of regulatory process to maintain public and stakeholder trust

Enable Scientific Innovation

- Clinical trials & clinical investigations
- Global biological standards
- Regulatory science

Accelerate healthcare access

- 17,000 medicines & 2M devices in UK
- Innovative access & reliance procedures
- New medical device regulations in 2022

Strengthen Patient Safety

- 368,000 safety reports on COVID vaccines
- Real world data critical to risk management
- Pro-active surveillance and enforcement

MHRA transformation means four key culture shifts

‘Controller’ to ‘Enabler’

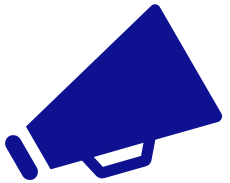
Without losing high standards of safety and efficacy or independence in decision-making, with effective tools to control industry when needed

‘Black box’ to ‘System partner’

Joint working with health technology assessment, leading to ‘end-to-end’ approach with real pull-through to healthcare system and patients

‘Population health’ to ‘Patient Champion’

Influencing clinical practice and helping patient decision-making Moving to life cycle approach, using real world data, responsive to patient views and safety

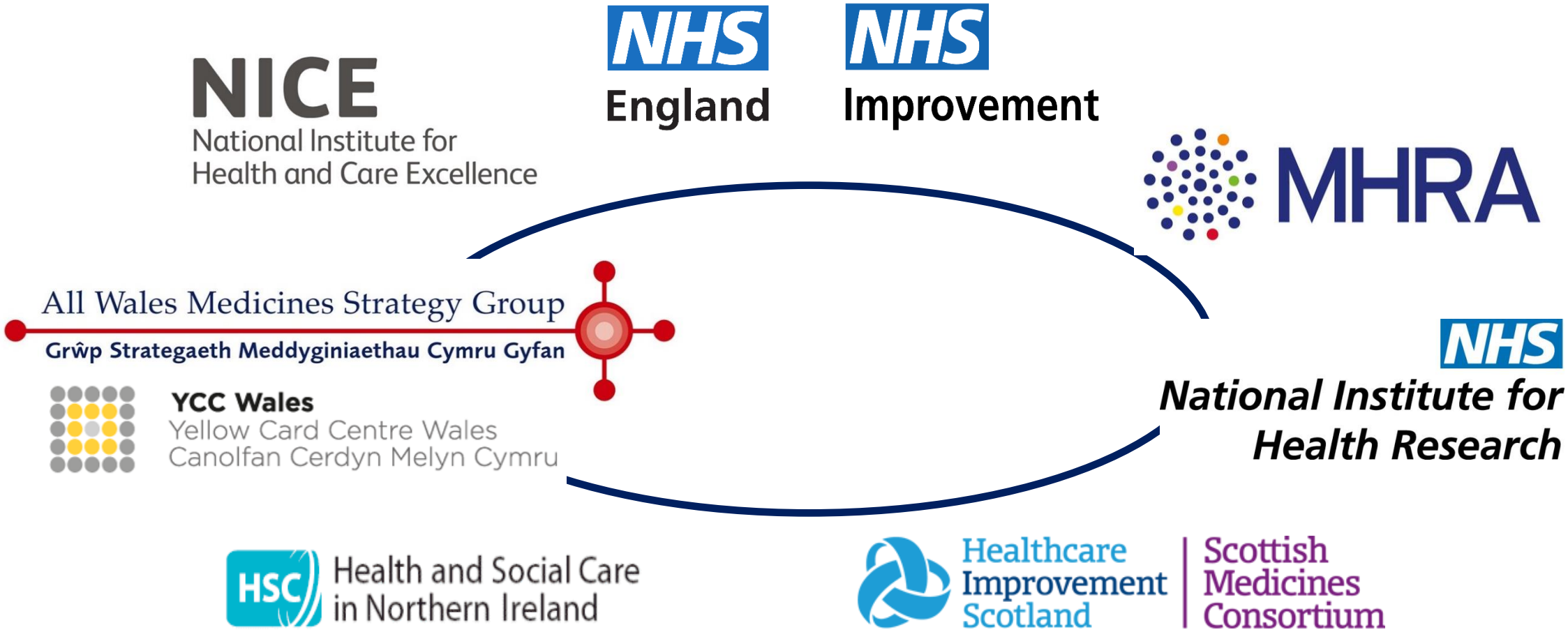


Global voice

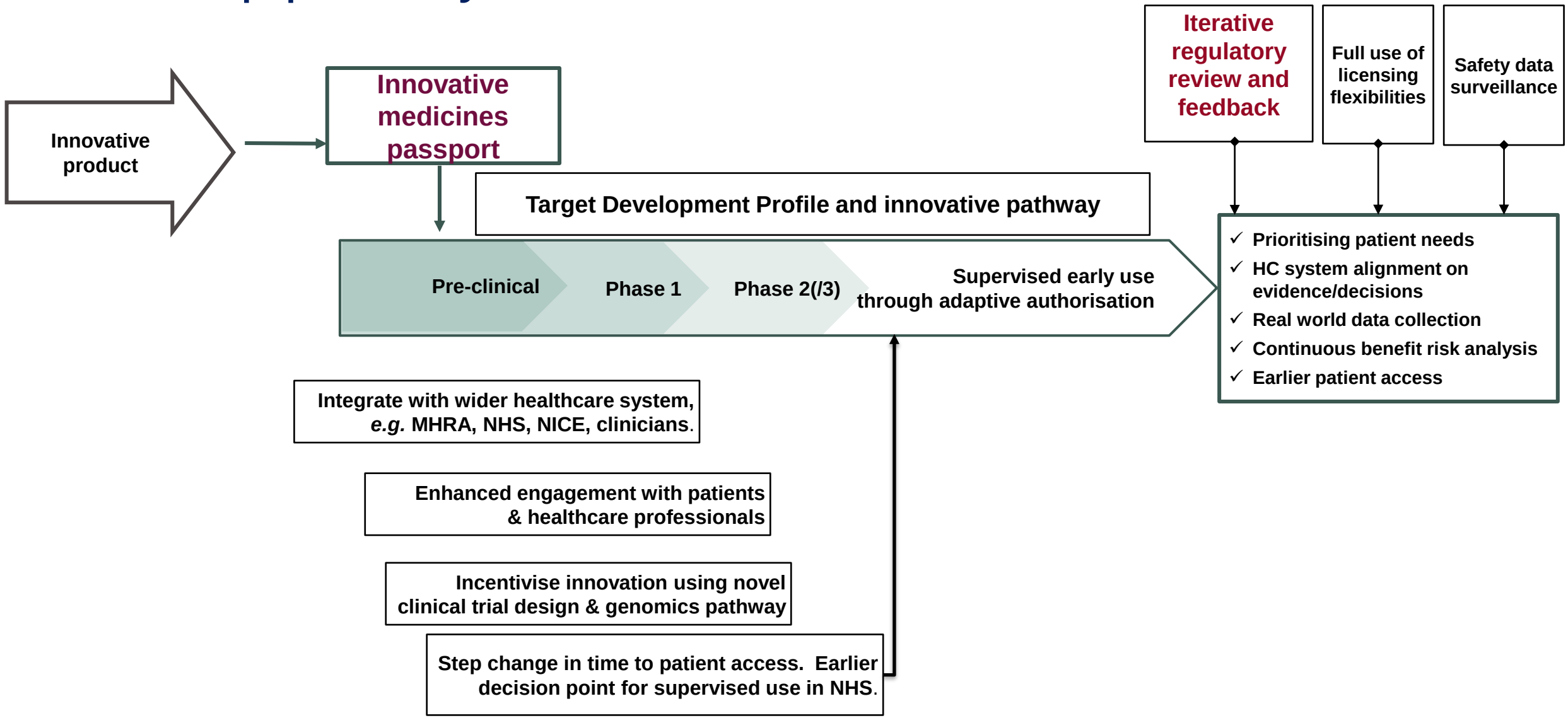
Leading in development of innovative regulatory approaches to new technologies, UK the best environment for clinical trials, global standards followed: ICH and IMDRF

Moving to a product ‘life cycle’ regulatory approach

Working in partnership

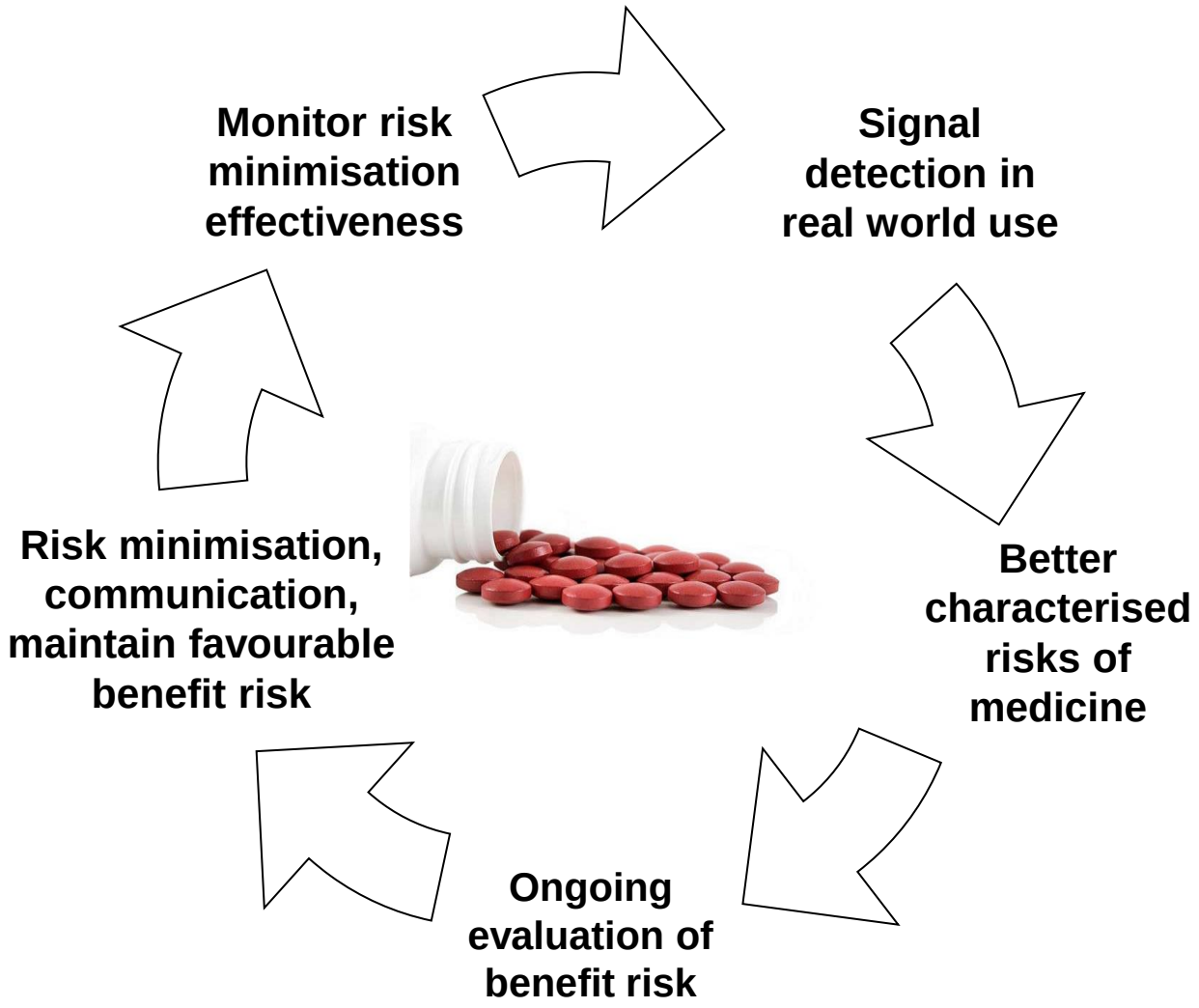


Partnership pathway for innovative medicines



Making medicines safer and the vital contribution from Wales

Medicines safety monitoring cycle



Identifying safety signals

Yellow Card Scheme cornerstone of UK public health protection since 1964

Widely acknowledged as an exemplar among surveillance schemes

Yellow Card continues to evolve to be relevant to work of healthcare professionals and daily lives of patients and public

MHRA and Yellow Card Centres are working together to make medicines safer

Why is making medicines safer so important?

6.5% hospital admissions in UK relate to adverse drug reactions

ADRs were responsible for death in 0.15%

72% were classified as avoidable

Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients

Munir Pirmohamed, Sally James, Shaun Meakin, Chris Green, Andrew K Scott, Thomas J Walley, Keith Farrar, B Kevin Park, Alasdair M Breckenridge

Pirmohamed et al 2004 BMJ 329; 15-19

BMJ Open

An investigation into drug products withdrawn from the EU market between 2002 and 2011 for safety reasons and the evidence used to support the decision-making

derived from EMA reports, PubMed literature search and websites of competent authorities

Drug name	Case reports	Animal studies	Case–control	Cohort	RCTs	Meta-analysis	*Others
Rofecoxib	X		x	x	x	X	
Thioridazine	X	X	x		x	X	
Valdecoxib	X				x	X	
Rosiglitazone	X		x	x	x	X	
Sibutramine	X				x		x
Orciprenaline	X				x		
Benfluorex	X		x	x	x		
Clobutinol	X	X			x		
Buflomedil	X	X					
Veralipride	X						
Rimonabant	X				x	X	
Carisoprodol	X	X		x	x		x
Acepromazine+Acepromazine +Clorazepate	X						x
Dextropropoxyphene	X						x
Nefazodone	X						x
Ximelagatran/melagatran					x		
Lumiracoxib	X				x		
Sitaxentan	X	X					
Bufexamac	X	X					x

*Other studies include non-randomised and/or not controlled clinical trials and incidence studies.
EMA, European Medicines Agency; EU, European Union.

Case reports remain the most significant method of medicines safety monitoring

McNaughton et al 2015 BMJ Open Jan 15

Sir William Asscher

Chair Committee on Safety of Medicines
1987-1992

Professor Philip Routledge

Chair Herbal Medicines advisory Committee

ATROPINE AS POSSIBLE CONTAMINANT OF COMFREY TEA

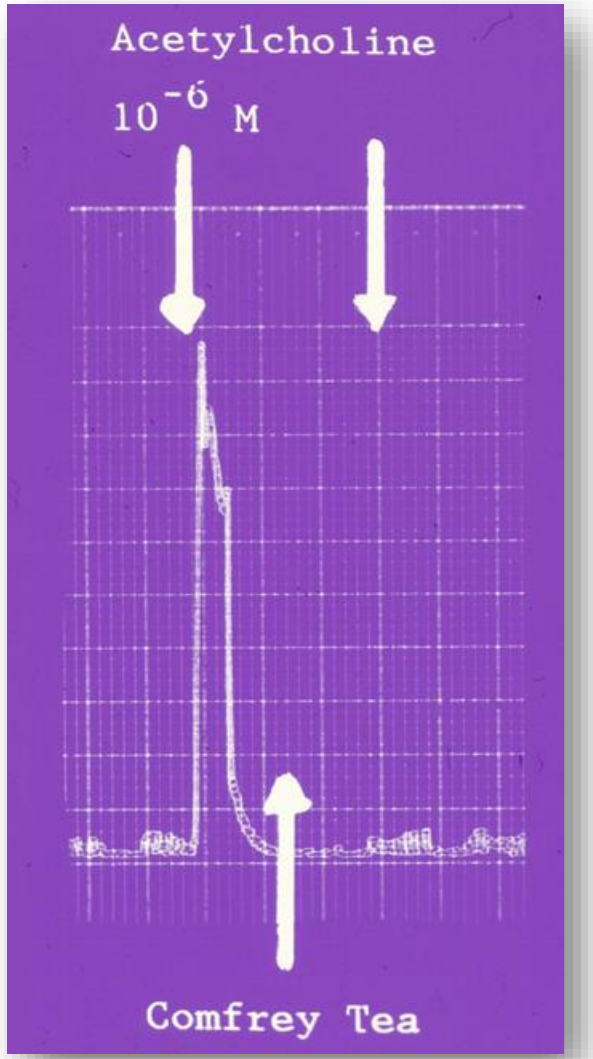
SIR,—A 30-year-old man visited a health-food store complaining of flatulence. Comfrey tea was recommended. He put 28 g into boiling water. He had several cups of the infusion, after which he felt light-headed, agitated, and confused, and had difficulty in micturition. He also complained of dry mouth and he had sinus tachycardia of 120/min, dilated pupils, and a warm dry skin. He was admitted and his symptoms resolved over the next 24 h

An infusate of the comfrey tea competitively blocked the contractile response of guineapig ileum to acetylcholine and the tea contained a minimum of 4 mg atropine per 28 g of leaf. This is likely to have been due to contamination with *Atropa belladona* (deadly nightshade), which was noted in a previous batch of comfrey tea from a different supplier.[1]

Use of comfrey tea has been associated with veno-occlusive disease of the liver, as Dr Ridker and Professor McDermott discuss (March 25, p 657), probably due to the presence of pyrrozilidine alkaloids.[2,3] These alkaloids, however, do not seem to have anticholinergic properties, and belladona toxicity should be considered in patients with atropine-like symptoms after ingestion of comfrey tea.

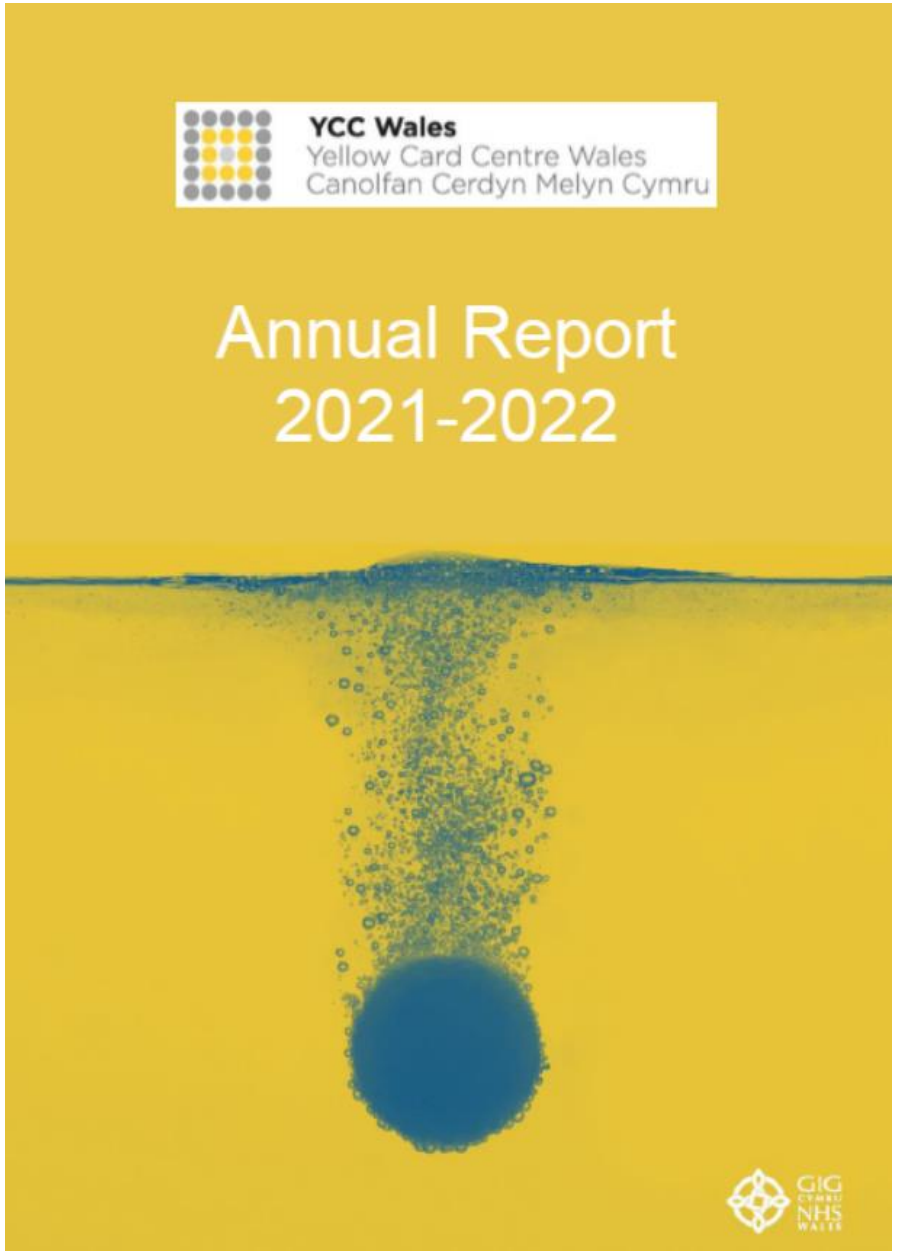
Welsh National Poisons Unit,
Department of Pharmacology and Therapeutics,
University of Wales College of Medicine,
Heath Park, Cardiff CF4 4XN

P. A. ROUTLEDGE
T. L. B. SPRIGGS



THE LANCET
Volume 333, Issue 8644, 29 April 1989, Pages 963–964

YCC Wales
Yellow Card Centre Wales
Canolfan Cerdyn Melyn Cymru



YCC Wales / CCM Cymru @YCCWales · Nov 7

Dewch i'n weld ni i siarad am diogelwch meddyginiaethau a pwysigrwydd adrodd am sgil-effeithiau.

Come and see us to talk about medicines safety and the importance of reporting side effects.

Concourse, UHW @CV_UHB #MedSafetyWeek

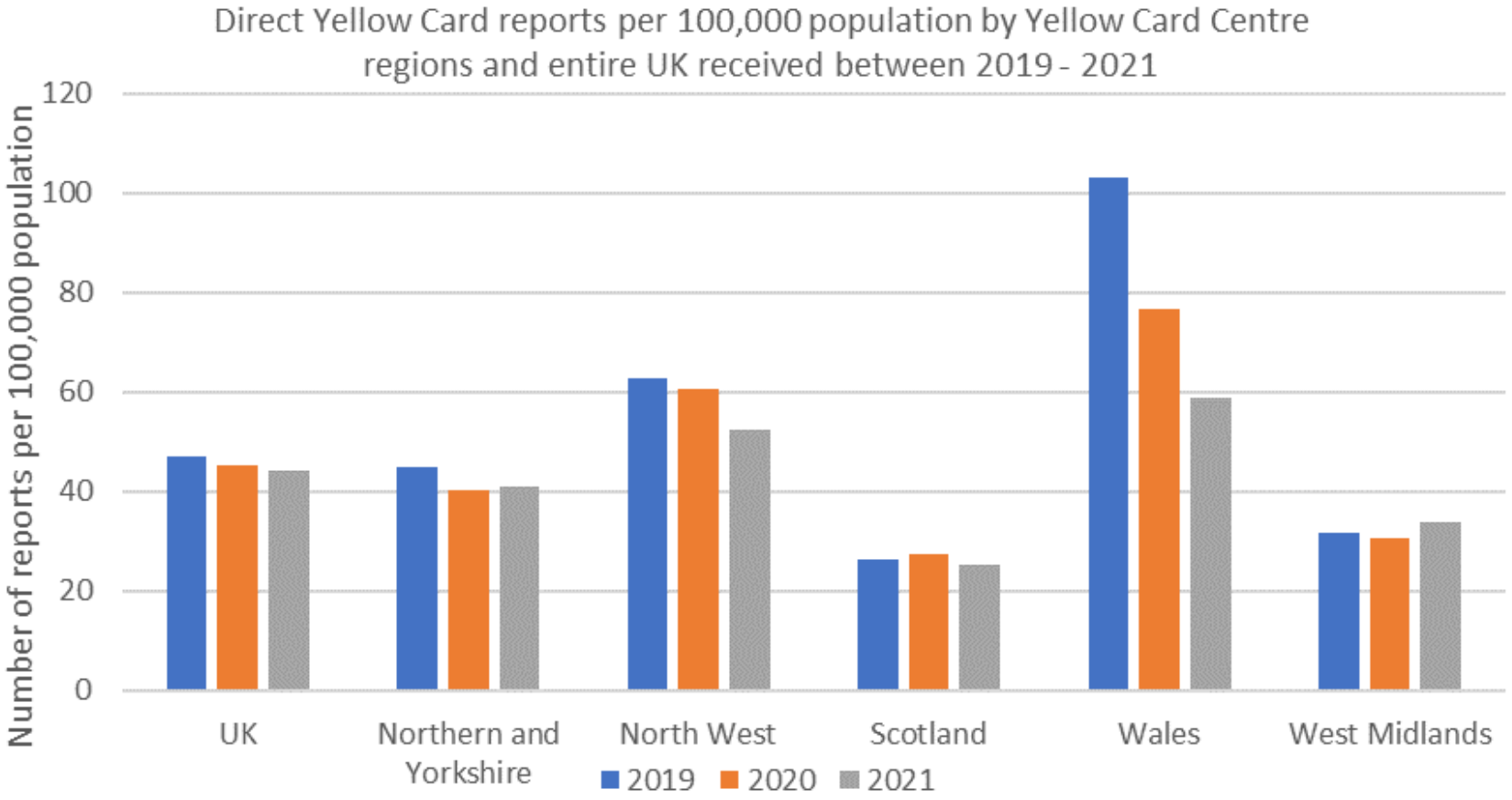
1 12 19

Yellow Card Centre Wales initiatives

- Yellow Card Champions initiative
- E-learning modules for pharmacy in Wales
- Inviting public & healthcare professionals to make pledge to report adverse reactions
- Publishing papers
- Herbal campaigns

Cerdyn Melyn

Helpu i wneud meddyginiaethau yn ddiogelach



Received: 19 October 2021 | Revised: 9 February 2022 | Accepted: 14 March 2022
DOI: 10.1111/bcp.15326

ORIGINAL ARTICLE

Changes in suspected adverse drug reaction reporting via the yellow card scheme in Wales following the introduction of a National Reporting Indicator

Paul N. Deslandes[1,2] | Robert Bracchi[1] | Karen Jones[1] | Kath E. Haines[1] | Emma Carey[3] | Alana Adams[3] | Jenna Walker[3] | Alison Thomas[3,4] | Philip A. Routledge[4]

[1]All Wales Therapeutics and Toxicology Centre, University Hospital Llandough, United Kingdom
[2]University of South Wales, Lower Glyntaf Campus, Treforest, UK
[3]Yellow Card Centre Wales, UK
[4]School of Medicine, Cardiff University, UK

Correspondence
Paul N Deslandes, All Wales Therapeutics and Toxicology Centre, University Hospital Llandough.
Email: paul.deslandes@wales.nhs.uk

Aims: This study aimed to assess the impact of a National Reporting Indicator (NRI) on rates of reporting of suspected adverse drug reactions using the Yellow Card scheme following the introduction of the NRI in Wales (UK) in April 2014.

Methods: Yellow Card reporting data for general practitioners and other reporting groups in Wales and England for the financial years 2014–15 (study period 1) and 2015–16 (study period 2) were obtained from the Medicines and Healthcare Products Regulatory Agency and compared with those for 2013–14 (pre-NRI control period).

Results: The numbers of Yellow Cards submitted by general practitioners in Wales were 271, 665 and 870 in the control period, study period 1 and study period 2, respectively. This is equivalent to an increase of 145% in study period 1 and 221% in study period 2 compared with the 12-month control period (2013–14). Corresponding increases in England were 17% and 37%, respectively ($P < .001$ chi-squared test). The numbers of Yellow Cards submitted by other groups in Wales were 906, 795 and 947 in each of the study periods.

Conclusions: Introduction of the NRI corresponded with a significant increase in the number of Yellow Cards submitted by general practitioners in Wales. General practitioner reporting rates continued to increase year on year through to 2018–19 with the NRI still in place. No concomitant change was found in reporting rates by other groups in the health boards in Wales.

KEYWORDS
adverse drug reaction reports, incentives, National Reporting Indicator

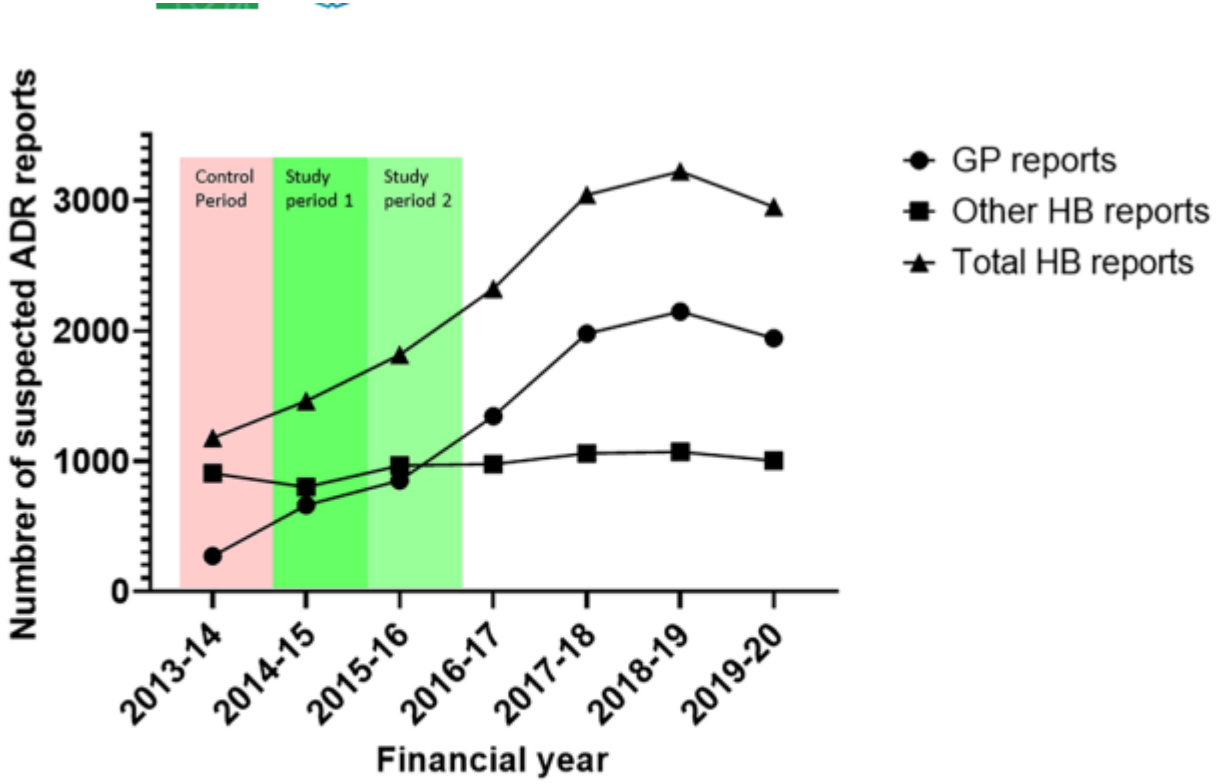


FIGURE 2 Number of Yellow Cards submitted by general practitioners and other reporters in Wales (2013–14 to 2019–20)

#MedSafetyWeek 7-13 November 2022

YCC Wales / CCM Cymru @YCCWales · Nov 9

Ydych chi erioed wedi profi sgil-effaith o feddyginiaeth?
Rhowch wybod am unrhyw sgil-effeithiau a amheuir 👉
cttcg.gig.cymru/optimeiddio-a-...
Helpwch ni i wneud meddyginiaethau'n fwy diogel i bawb.
#WythnosDiogelwchMeddyginiaethau #DiogelwchCleifion
#CynllunCerdynMelyn

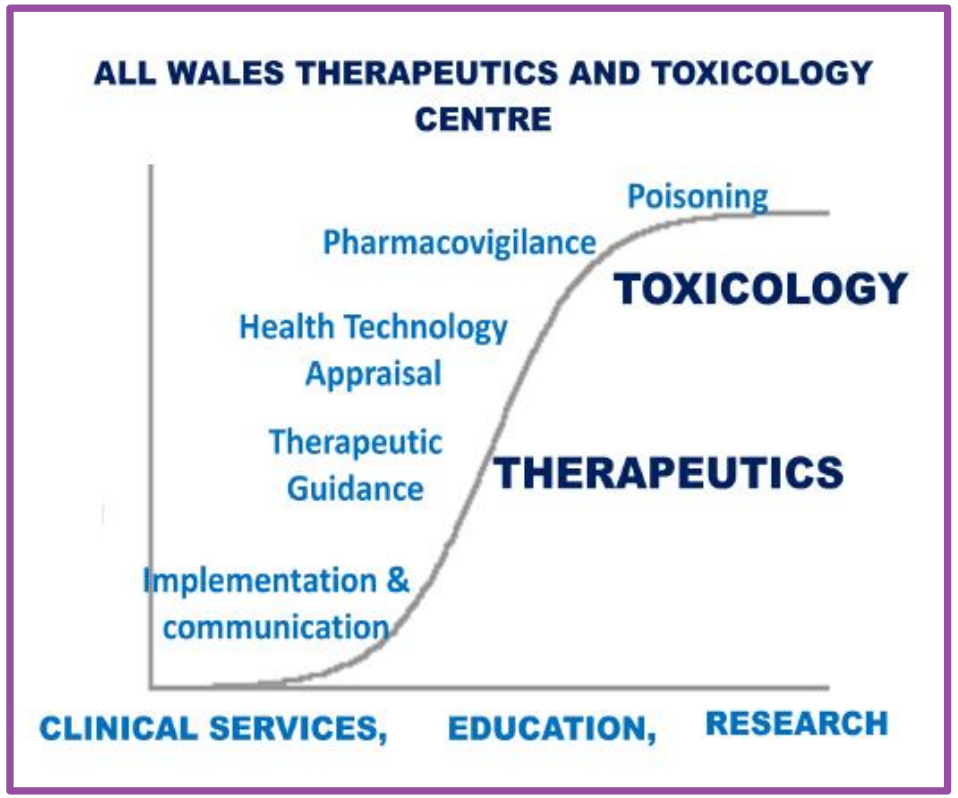
YCC Wales / CCM Cymru Retweeted

Jessica Jenkins @jessjenkins01 · Nov 11

Swansea Bay University Health Board trainee pharmacists have been busy engaging with staff and public to promote Medication Safety Week
#MedSafetyWeek #yellowcard #patientsafety @UhbBay @Jat_man

6 15

Bringing together poisons data and adverse reaction data



ALL WALES THERAPEUTICS AND TOXICOLOGY CENTRE

Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

promoting the safe, clinically- and cost-effective use of medicines in Wales

NPIS
National Poisons Information Service

NHS WALES GIG CYMRU

All Wales Therapeutics and Toxicology Centre
Academic Building, University Hospital Llandough
Penlan Road, Penarth CF64 2XX

Email: awttc@wales.nhs.uk

Making medicines safer – asking the important questions

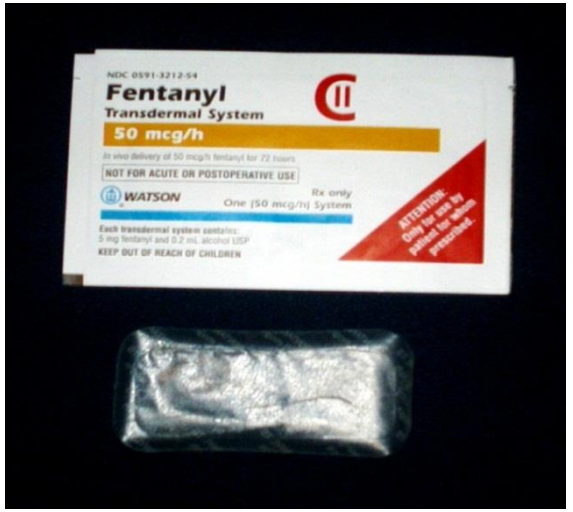
90. Trends in enquiries to the UK National Poisons Information Service (NPIS) involving "preschool" (0–4 years) children in 2015. Might knowledge of circumstances help plan prevention strategies?

Nicola Wheatley[a], Gillian A. Cooper[a], John P. Thompson[a], Sally M. Bradberry[b], Euan A. Sandilands[c] and Simon H. L. Thomas[d]

[a]UK National Poisons Information Service, Cardiff, UK; [b]UK National Poisons Information Service, Birmingham, UK; [c]UK National Poisons Information Service, Edinburgh, UK; [d]UK National Poisons Information Service, Newcastle, UK

Objective: To investigate trends in the ingestions of the "preschool" population to see if knowledge of circumstances of exposures might help in planning prevention strategies to prevent suspected poisonings. The UK National Poisons Information

NPIS



Making medicines safer – asking the important questions

282. A poisoning prevention program aimed at adolescents in Wales: Is it needed?

Nicola Wheatley[1], Gillian Cooper[1], Gloria A Alldridge[1], John P Thompson[1], Michael Eddleston[2], J Allister Vale[3], Simon HL Thomas[4]

[1]National Poisons Information Service (Cardiff Unit), Cardiff and Vale University Health Board, Cardiff, UK; [2]National Poisons Information Service (Edinburgh Unit), Royal Infirmary of Edinburgh, Edinburgh, UK; [3]National Poisons Information Service (Birmingham Unit), City Hospital, Birmingham, UK; [4]National Poisons Information Service (Newcastle Unit), Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK

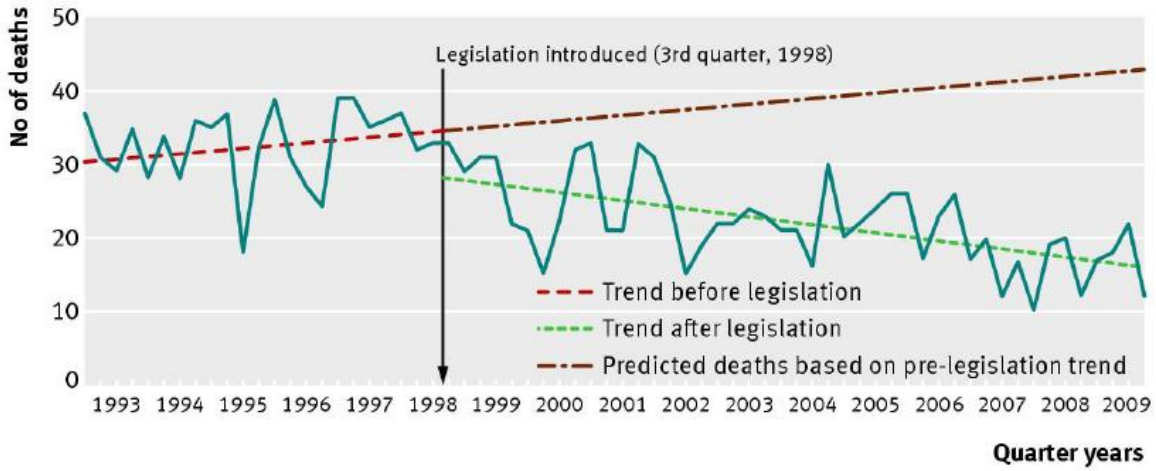
PUBLISHED
8 FEB 2013

SHARE THIS

Smaller packs of paracetamol have reduced overdose deaths by 43%

HEALTH

UK legislation to limit paracetamol pack sizes has seen a 43% reduction in the number of deaths due to paracetamol overdoses, a study led by Oxford University researchers has found.



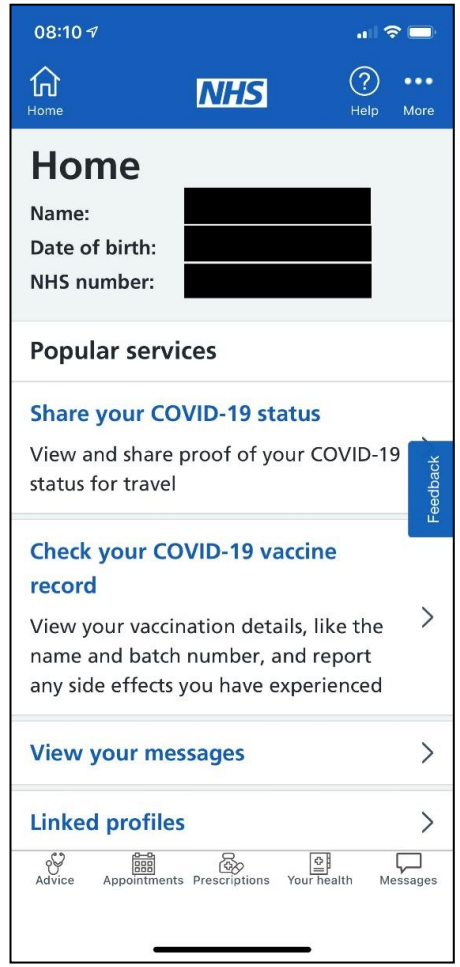
What were learnings of pandemic for safety monitoring?

Pandemic challenges and opportunities

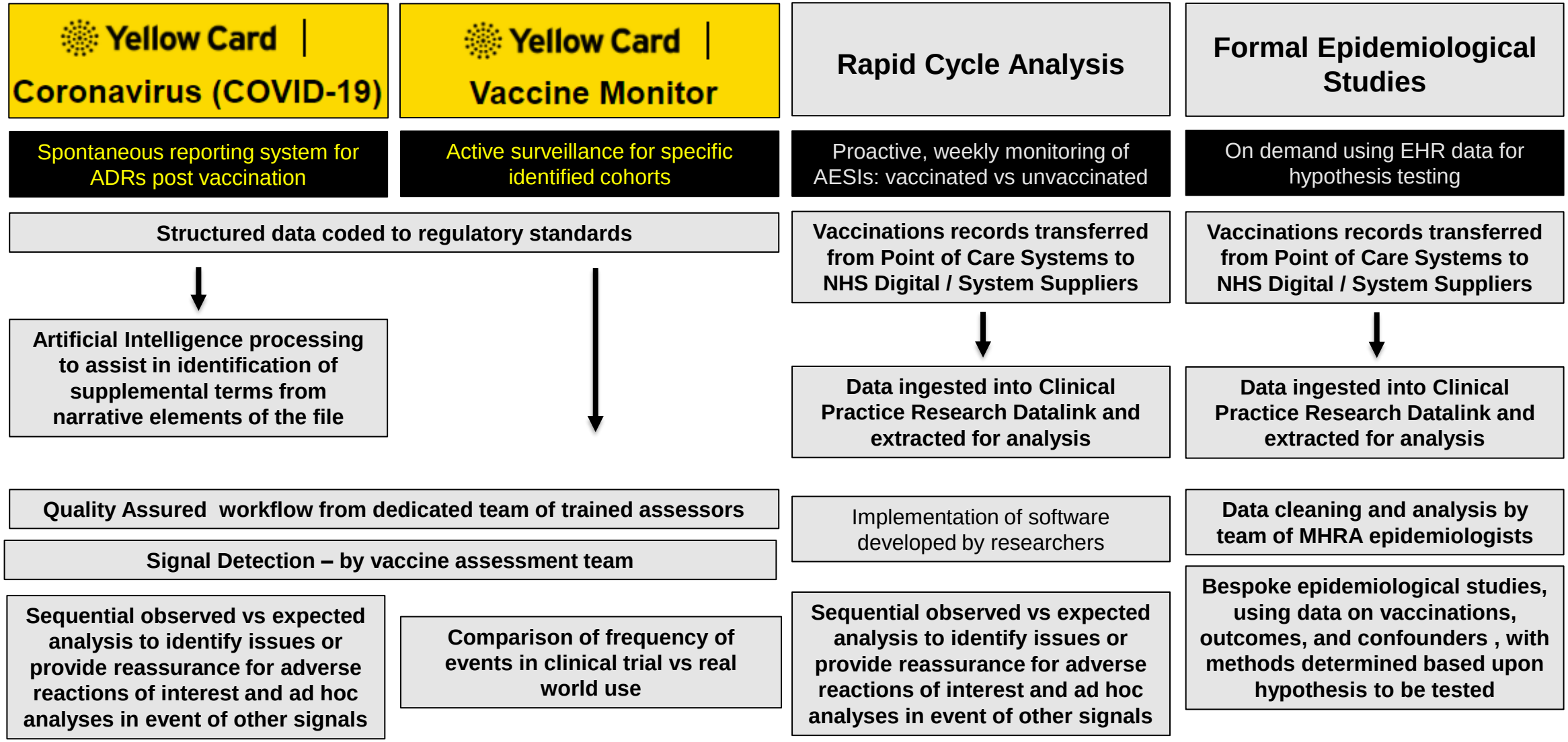
Guidance

MHRA regulatory flexibilities resulting from coronavirus (COVID-19)

Guidance for industry on flexible approaches to regulation we are taking during the COVID-19 outbreak.



COVID-19 vaccine safety strategy



PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2001; **10**: 483–486
DOI: 10.1002/pds.677

ORIGINAL REPORT

Use of proportional reporting ratios (PRRs) for signal generation from spontaneous adverse drug reaction reports

S. J. W. Evans, P. C. Waller* and S. Davis

Post-Licensing Division, Medicines Control Agency, Market Towers, 1, Nine Elms Lane, London SW8 5NQ

SUMMARY

Background The process of generating 'signals' of possible unrecognized hazards from spontaneous adverse drug reaction reporting data has been likened to looking for a needle in a haystack. However, statistical approaches to the data have been underutilised.

Professor Stephen Evans

Table 1. Calculation of PRRs

	Drug of interest	All other drugs in database
Reaction(s) of interest	a	b
All other reactions	c	d

Table 2. Example of a PRR calculation-rifabutin and uveitis

	Rifabutin	All other drugs
Uveitis	41	754
All other ADRs	14	591 958
TOTAL	55	592 712

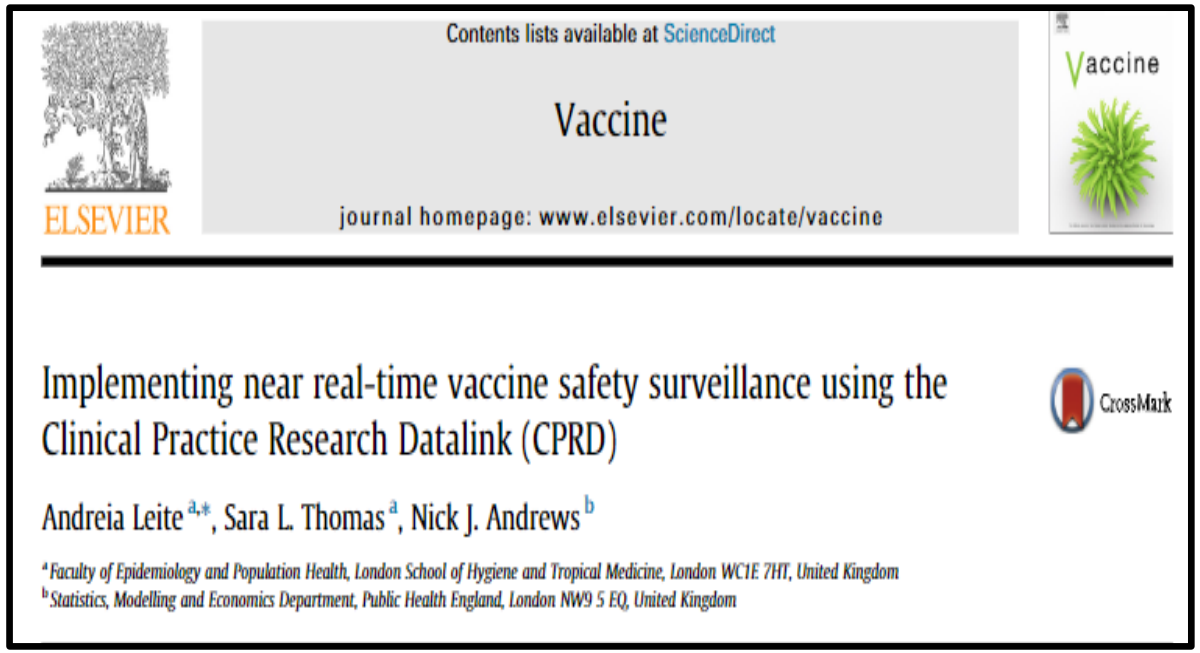
PRR = 41/55 divided by 754/592, 712 = 586.
Chi-squared (1 df) = 22 740.

Signal strengthening through rapid cycle analysis

Proactive use of large healthcare record databases to monitor Adverse Events of Special Interest

Implemented from start of vaccine deployment with expertise from London School of Hygiene and Tropical Medicine and UKHSA

Supported initial decision making on risk of Bell's Palsy and Guillain Barre Syndrome and provided reassuring data on safety from 2.4 million doses in 2 months



Signal – reports of thrombosis with thrombocytopenia

Very rare events of thromboembolic events with concurrent thrombocytopenia associated with COVID-19 vaccines

Initially identified as safety concern with AZ vaccine Feb / March 2021

Several EU countries halted use of AZ vaccine in March while the issue was investigated by regulators

FINANCIAL TIMES

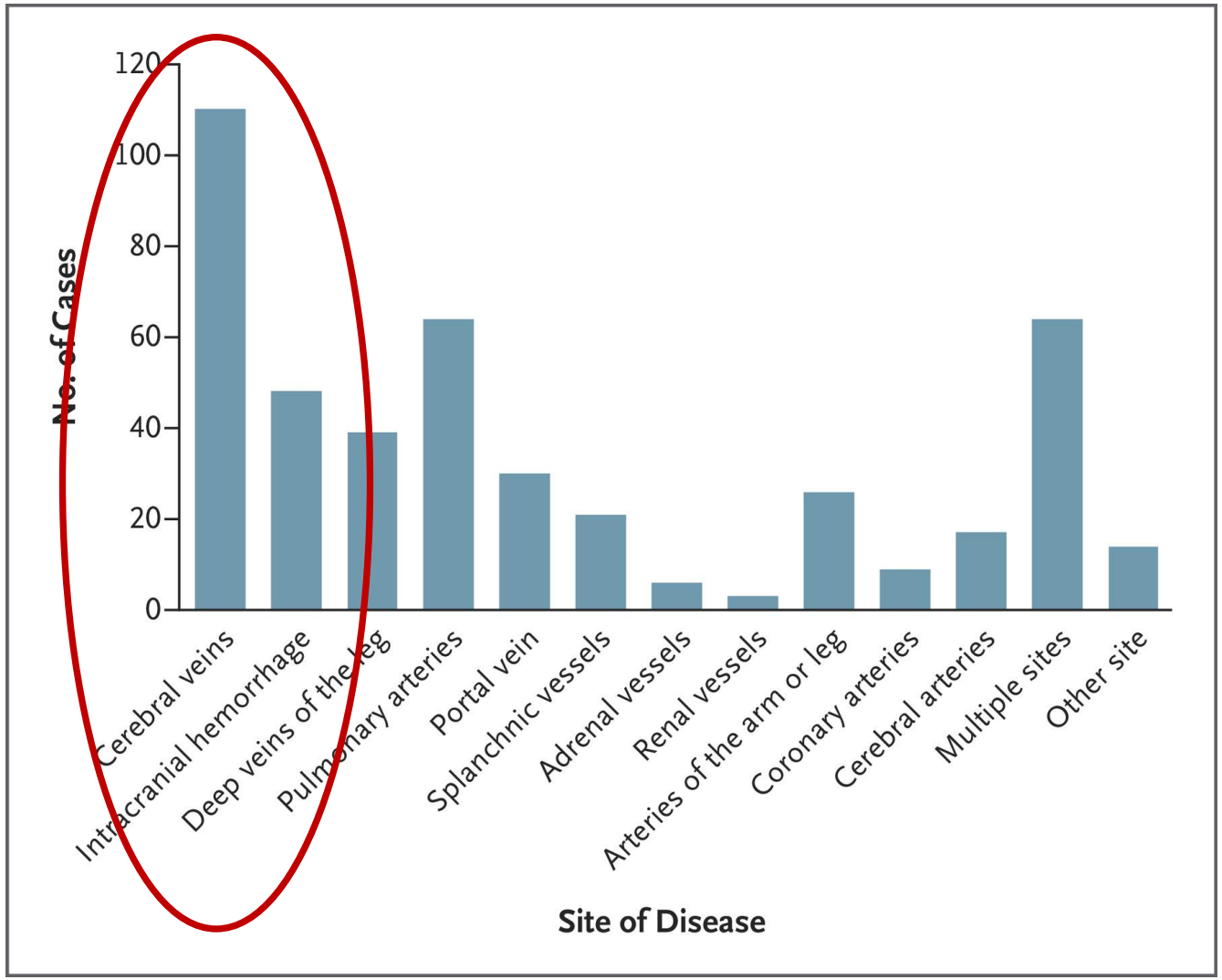
Blood clots and the AstraZeneca Covid vaccine: is there a link?

Regulators say shot is safe but UK records new clotting cases and growing number of countries restrict its use

Oxford university and AstraZeneca say their trials show that the vaccine is safe and effective © Andreas Solaro/AFP via Getty

Donato Paolo Mancini in Rome and **Anna Gross** in London APRIL 2 2021 589

https://www.gov.uk/government/publications/covid-19-vaccination-blood-clotting-information-for-healthcare-professionals/information-for-healthcare-professionals-on-blood-clotting-following-covid-19-vaccination

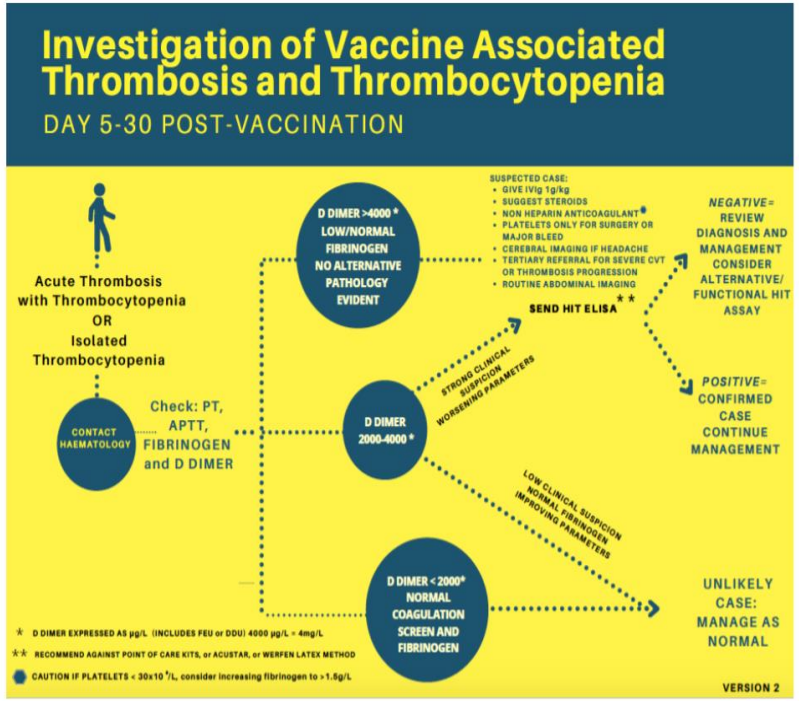


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Clinical Features of Vaccine-Induced Immune Thrombocytopenia and Thrombosis

Sue Pavord, F.R.C.Path., Marie Scully, M.D., Beverley J. Hunt, M.D., William Lester, M.D., Catherine Bagot, M.D., Brian Craven, M.B., B.Ch., Alex Rampotas, M.R.C.P., Gareth Ambler, Ph.D., and Mike Makris, M.D.



DOI: 10.1056/NEJMoa2109908.
https://www.nejm.org/doi/full/10.1056/NEJMoa2109908

Further research into VITT mechanism

Cross-disciplinary research consortium

- ✓ Epidemiological evidence supporting COVID-19 benefit risk assessment
- ✓ Genetic risk factors for TTS
- ✓ Biomarker for platelet activation
- ✓ A diagnostic test for TTS
- ✓ Development of modified vaccine without the propensity to cause TTS

The aetiopathogenesis of vaccine-induced immune thrombotic thrombocytopenia

Authors: Cheng-Hock Toh,[A] Guozheng Wang[B] and Alan L Parker[C]

Clinical Medicine March 20, 2022

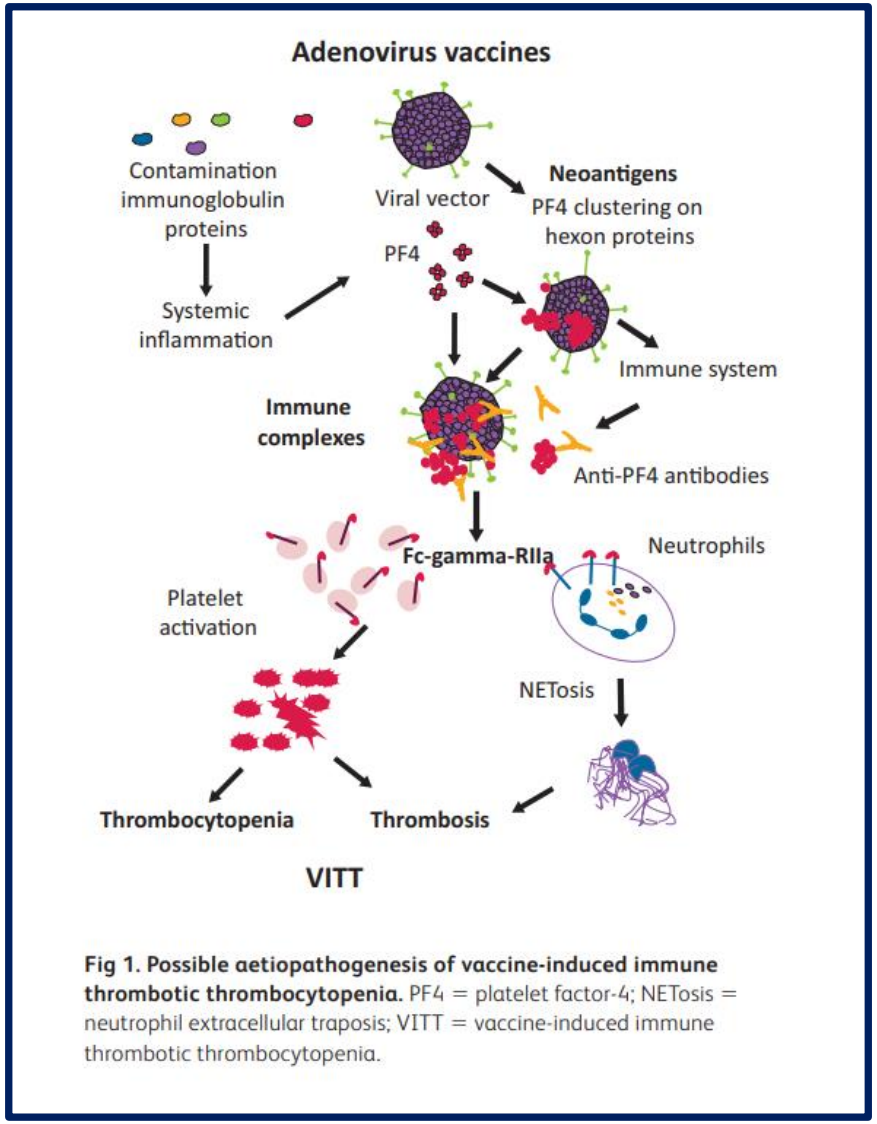
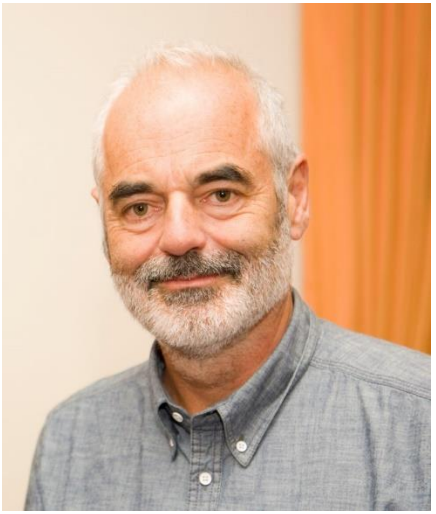


Fig 1. Possible aetiopathogenesis of vaccine-induced immune thrombotic thrombocytopenia. PF4 = platelet factor-4; NETosis = neutrophil extracellular traposis; VITT = vaccine-induced immune thrombotic thrombocytopenia.

Weighing up the potential benefits and harms of the Astra-Zeneca COVID-19 vaccine

For 100,000 people with medium exposure risk*

Potential benefits: ICU admissions due to COVID-19 prevented every 16 weeks:	Age group	Potential harms: Serious harms due to the vaccine:
2.2	20-29yr	1.1
8.0	30-39yr	0.8
16.7	40-49yr	0.5
31.0	50-59yr	0.4
41.3	60-69yr	0.2



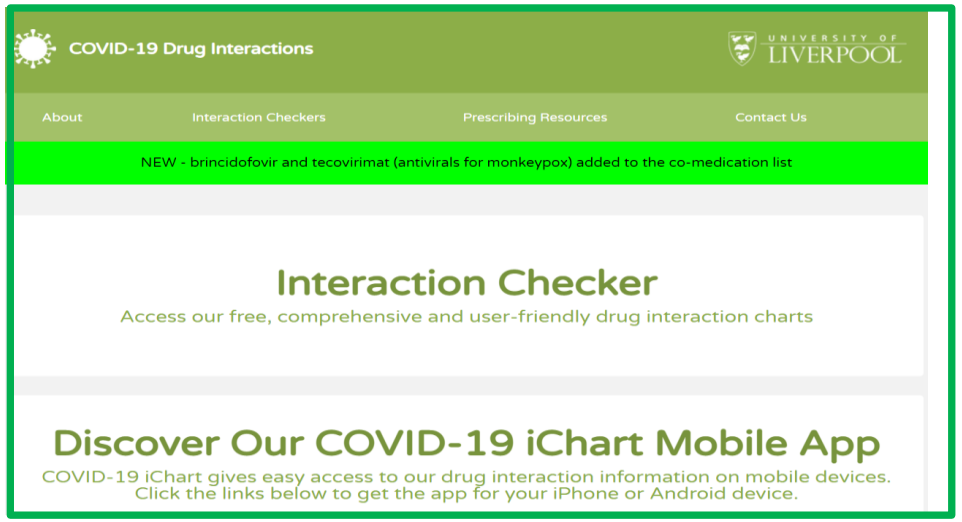
David Spieglhalter, Keble1971

* Based on coronavirus incidence of 6 per 10,000: roughly UK in February

New approach to transparency about regulatory decisions

Chair Commission on Human Medicines


NHS
Search
Health A-Z
Live Well
Mental health
Care and suppor
Home
Medicines A to Z
Paxlovid
Taking Paxlovid with other medicines and herbal supplements
If you are taking ritonavir as part of your treatment for HIV or hepatitis C infection, you can continue taking your treatment as usual
Cautions with other medicines
Some medicines do not mix well with Paxlovid. Tell your doctor if you're taking:


COVID-19 Drug Interactions
UNIVERSITY OF LIVERPOOL
About
Interaction Checkers
Prescribing Resources
Contact Us
NEW - brincidofovir and tecovirimat (antivirals for monkeypox) added to the co-medication list
Interaction Checker
Access our free, comprehensive and user-friendly drug interaction charts
Discover Our COVID-19 iChart Mobile App
COVID-19 iChart gives easy access to our drug interaction information on mobile devices.
Click the links below to get the app for your iPhone or Android device.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Therapies
Antiviral Therapy
Summary Recommendations
Remdesivir
Ritonavir-Boosted Nirmatrelvir
Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir (Paxlovid) and Concomitant Medications
Drug Info
Drug-Drug Interactions
Last Updated: May 13, 2022

Where next? New data, tools and scientific methodologies to strengthen safety surveillance

The SafetyConnect programme

Engaging & transparent

Fully integrated into the healthcare system

With latest tools and innovation

Using multiple data sources to generate better evidence for safety

Use of Real World Data to support safety and innovation

CPRD

Clinical Practice Research Datalink

Over 3 billion consultations coded from primary care records and linked to other data sources

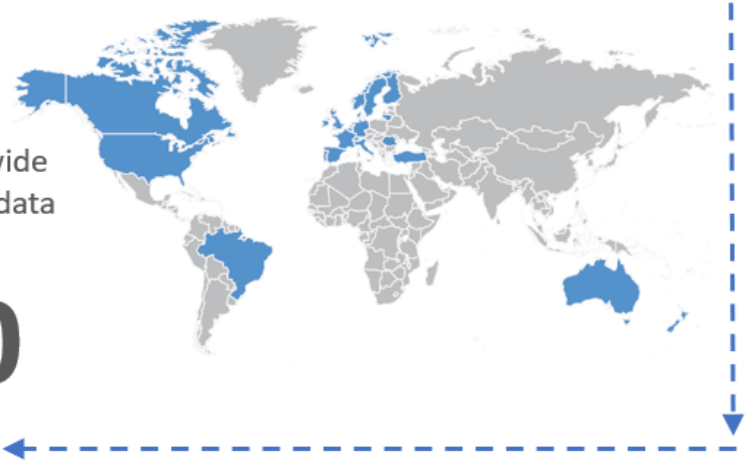
30 years of electronic health record data collection

90% of UK healthcare consultations are in primary care

60M patient lives

Over **16M** currently registered patients

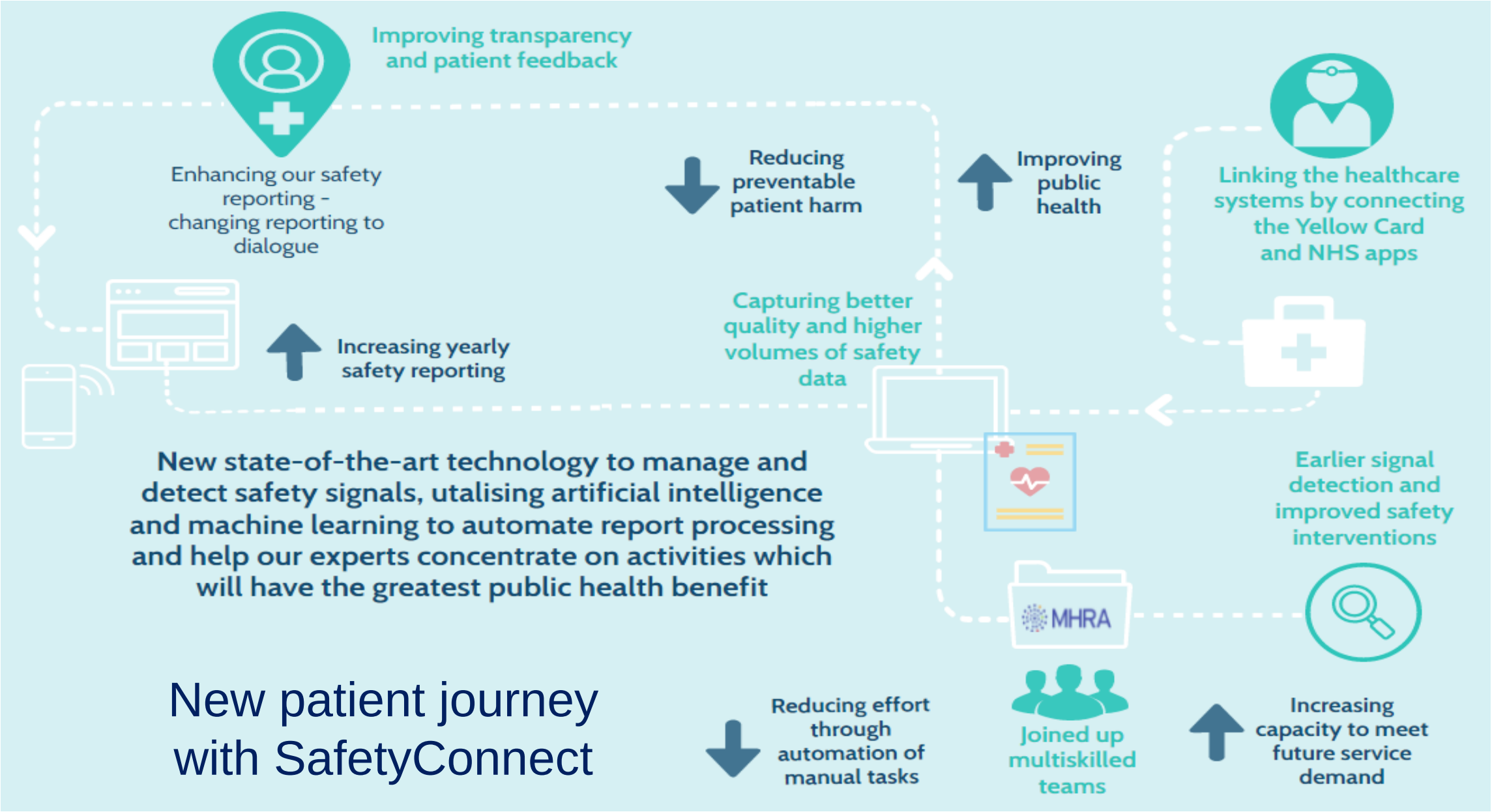
More than **20** countries worldwide have used CPRD data producing over **2800** peer-reviewed publications



Longitudinal
cradle to grave

Representative
age, sex and ethnicity

Data linkage



New patient journey with SafetyConnect

Impact of pharmacogenomics on drug safety

Why is Pgx research needed?

£530M cost of ADRs on NHS due to hospital admissions

An estimated **20-30%** of ADRs could be prevented by pharmacogenetic testing

Virtually everyone has at least one genetic variation (pharmacogene) which affects their response to drugs

89% of people over 70 will have been prescribed at least one drug linked with a pharmacogene[3]

What are the benefits?

- ✓ Improved understanding of safety profile of medicinal products
- ✓ Discovery of genomic markers to identify patients most at risk of ADRs
- ✓ Generating evidence to support development of screening tests
- ✓ Maintaining access of life saving medicine to those at least risk of harm
- ✓ Supporting implementation of pharmacogenomics in the clinical care: pre-emptive PGX approach
- ✓ Reducing clinical burden of ADRs
- ✓ Supporting future drug development

Using genomic data to prevent adverse drug reactions

Yellow Card data is unique data pool for research into adverse drug reactions

Opportunity to link with phenotypic data via Clinical Practice Research Datalink

Pharmacogenetics: an opportunity for a safer and more efficient pharmacotherapy

M. INGELMAN-SUNDBERG

From the Division of Molecular Toxicology, IMM, Karolinska Institutet, Stockholm, Sweden

the PHARMACEUTICAL JOURNAL

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Adverse drug reactions

25 May 2018

By **Julia Robinson**

Medication-related harm in older adults costs the NHS £400m each year, study finds

In the first UK study to investigate medication harm in older adults following hospital discharge, the authors concluded that there was "considerable scope for improving patient safety".

Yellow Card Biobank

The Biobank would collect and sequence **DNA samples** for a ‘watchlist’ of research topics to establish if specific **genetic variants** can **predispose** individuals to a certain side effect to a drug or vaccine

Participants’ **Electronic Health Records** and other **relevant phenotypic data** would be collected to support the research

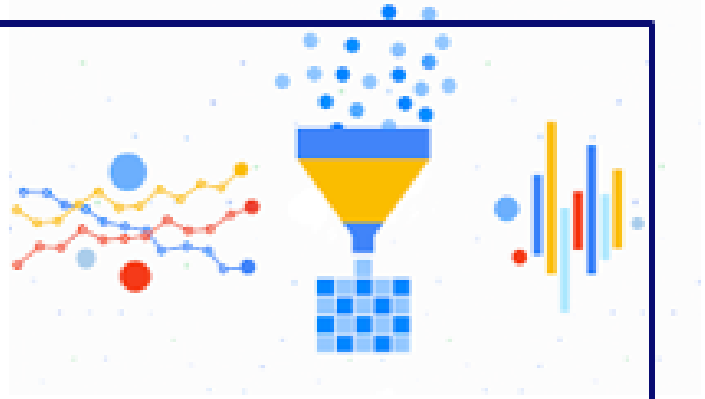
External researchers could apply to **access anonymised data** or **add their own topic** to the watchlist

Ultimate aim is to support development of **genetic screening tests** to be used prior to prescription and reduce burden of ADRs

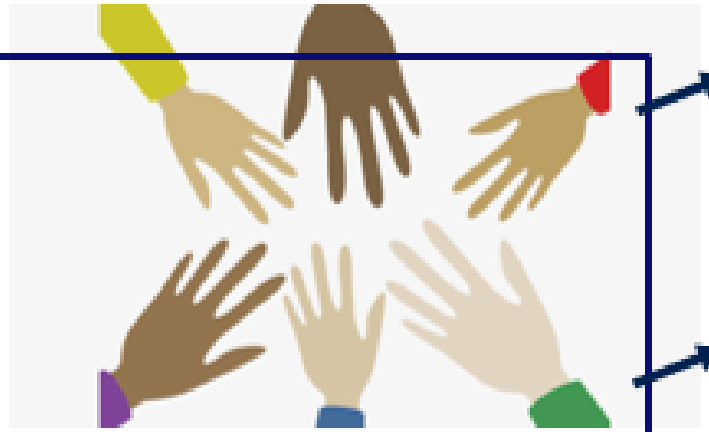
Improving representativeness of our clinical practice data

Ethnicity Algorithm

Updated SES Measures



Updating and Value-Adding



Answering Key Questions

Ethnicity Completeness and Distribution

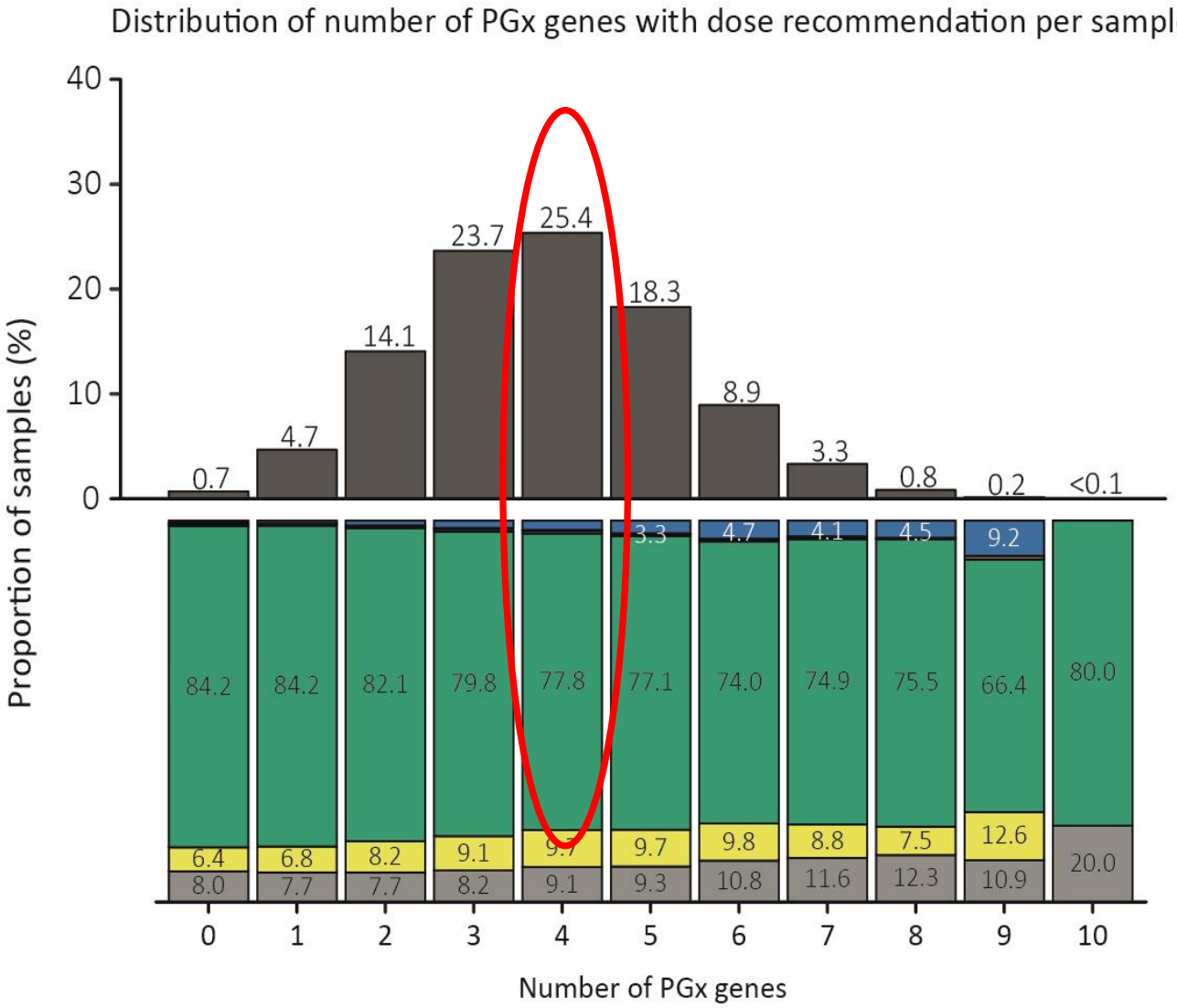
SES Completeness and Distribution

Are we representative of the general population?

Where are our data gaps?

Describing our Data

Frequency of PGX gene variants in whole genome sequences



Genomics England Cohort

Participants n = 76,805

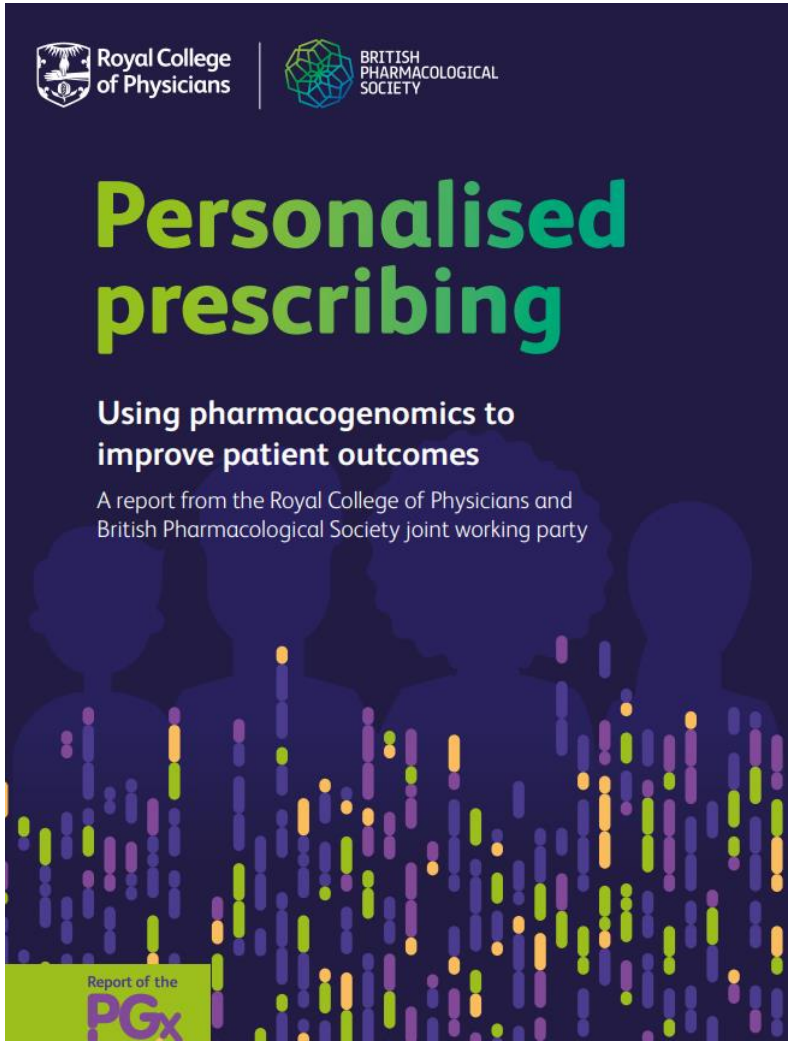
Ethnicity breakdown:

- African = 1,916
- American = 173
- East Asian = 450
- European = 60,388
- South Asian = 7,019
- Mixed ancestry = 6,859

~99.5% of participants have haplotypes in at least 1 PGX gene

25.4% participants have haplotypes in 4 PGX genes

Ancestry African American East Asian European South Asian Mixed ancestry



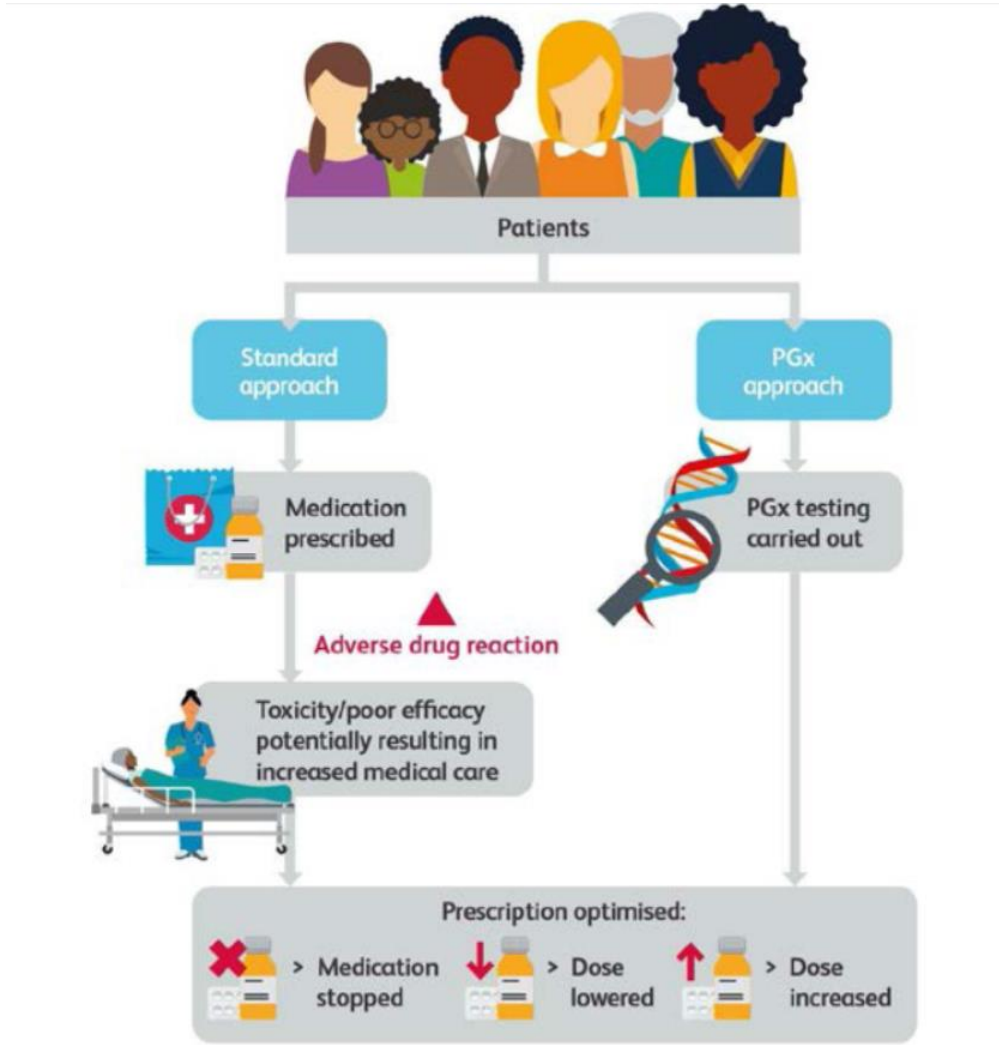
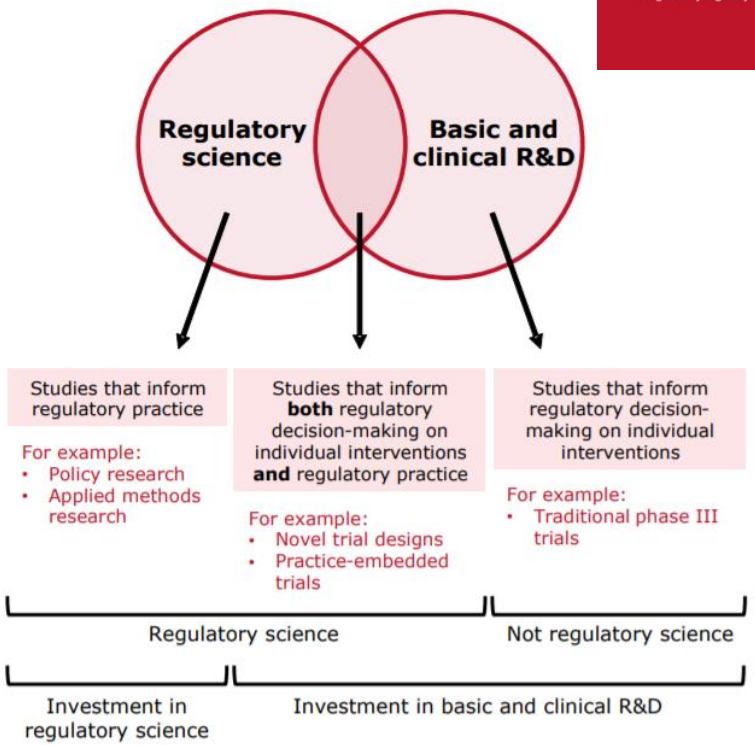


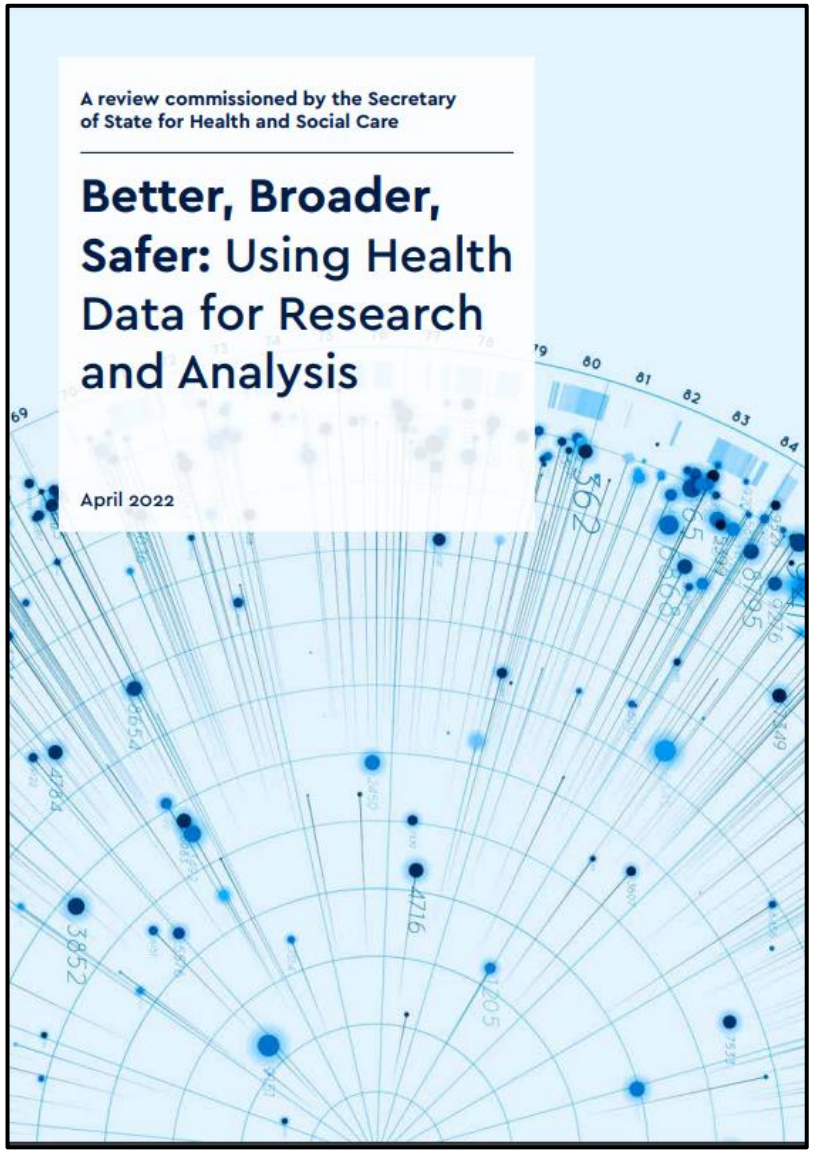
Fig 8. Comparing pharmacogenomic and standard approaches to prescribing

Regulatory Science

MHRA priority research areas

1. **Regulatory science in key licensing areas**
   The role of the patient in decision-making; women's health; drug repurposing; orphan medicines; biosimilars, among others
2. **Genomics and diagnostics**
   Precision medicine; companion diagnostics; infectious disease diagnostics; exploring a Yellow Card Biobank
3. **Data science**
   Synthetic data for artificial intelligence algorithms; data-enabled clinical trials; real-world evidence in clinical trials; near real-time pharmacovigilance
4. **Advanced therapies**
   Stem cell supply (UK Stem Cell Bank); 'What's in the tube'; innovative regulation; point of care manufacture
5. **A prioritised laboratory science portfolio for biological standardisation and control**
   Biological standardisation; smart control testing of biologicals
6. **Supporting emergency response to disease**
   Pandemic preparedness (current and next); emerging pathogens




A review commissioned by the Secretary of State for Health and Social Care
Better, Broader, Safer: Using Health Data for Research and Analysis
April 2022


UK Digital Strategy
Department for Digital, Culture, Media & Sport


The power of data
Data Saves Lives
#DataSavesLives


NHSX
Data saves lives
Our strategy to reshape health and care with data

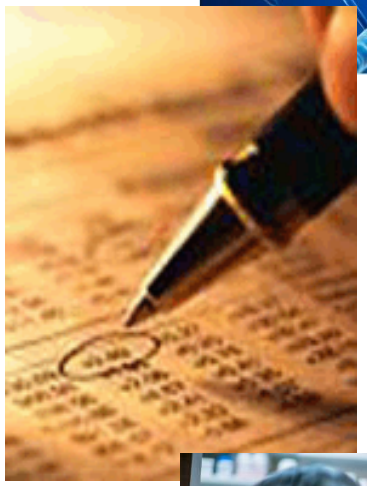
Making medicines safer – in summary

Opportunities from EU Exit and learnings from pandemic have catalysed the new proactive collaborative regulatory approach

Aim is to enable innovation and bring new medicines to patients and the healthcare service safely based on best science

Safety systems bringing together all relevant data more important than ever with accelerated access to innovative products

Together we can maximise the opportunities of new tools, data and methodologies for strengthened surveillance



Nicola Wheatley

A gifted and dedicated scientist,
who made significant contributions to the field of toxicology

Together with NPIS we celebrate the life and lasting legacy of Nicola Wheatley