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SCIENCE MEDICINES HEALTH

Why measure the impact of regulatory action?

Workshop: measuring the impact of pharmacovigilance activities
5-6 December 2016

June M Raine
Chair Pharmacovigilance Risk Assessment Committee

In this introductory talk

- Why current focus on measuring impact of regulatory action?
- What has been learnt from experience of measuring regulatory action impact?
- Where next – what is vision for the future?
- How will regulatory approach to impact measurement be strengthened?

The regulatory role

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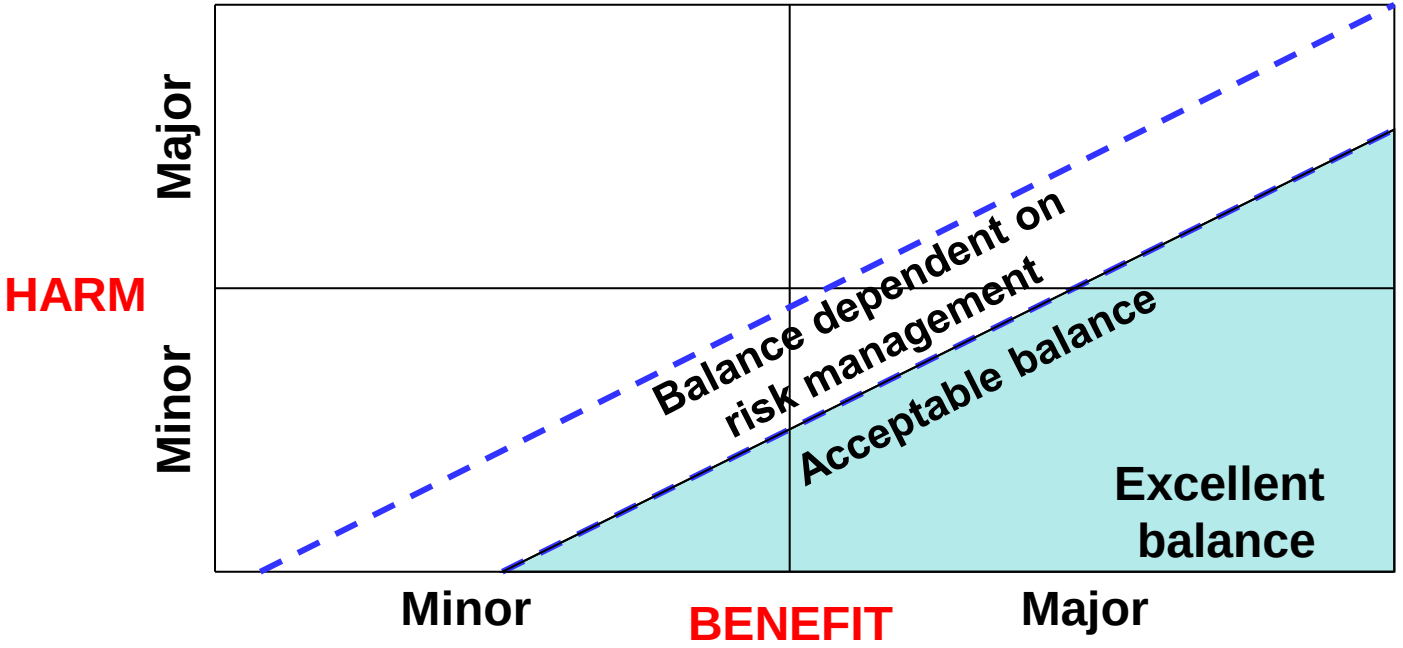
Monitoring benefit risk throughout medicinal product life-cycle

Taking action on safety issues in clinical use to manage and minimise risk

Communicating updated information to healthcare professionals and patients

Benefit harm balance



Regulatory action – an opportunity for debate

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No effective medicine is without risk so how much harm can be prevented?

It's all about benefit risk, so shouldn't patients & public accept a certain amount of risk?

Aren't healthcare professionals responsible for impact of risk management rather than regulators?

Have the major efforts to strengthen EU pharmacovigilance systems had effect?

Do we need to measure impact when regulatory action is agreed to be right?

Isn't regulatory resource better spent improving systems for harm detection?

Whose impact?

Measuring impact of regulatory action – your view?

- Not a routine regulatory responsibility
- Informative for important public health decisions
- All regulatory actions should be subject to systematic impact measurement

Adverse effects of medicines - public health burden

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5% of all hospital admissions due to ADRs

5% of all hospital patients experience an ADR

5th most common cause of hospital death is ADRs

197,000 deaths per year in EU caused by ADRs

Total societal cost €79 billion

5910 lives per year and €237m could be saved

Evidence for EC impact assessment

Studies in EU member states estimated that **20% to 70%** of ADRs preventable

Success of risk minimisation measures needed to be evaluated

If ineffective, alternative strategies need to be evaluated

Pirmohamed et al 2004 BMJ 329; 15-19

Rottenkolber 2011, Pharmacoepi & Drug Safety; 20: 626–634

Drugs leading to hospital admission

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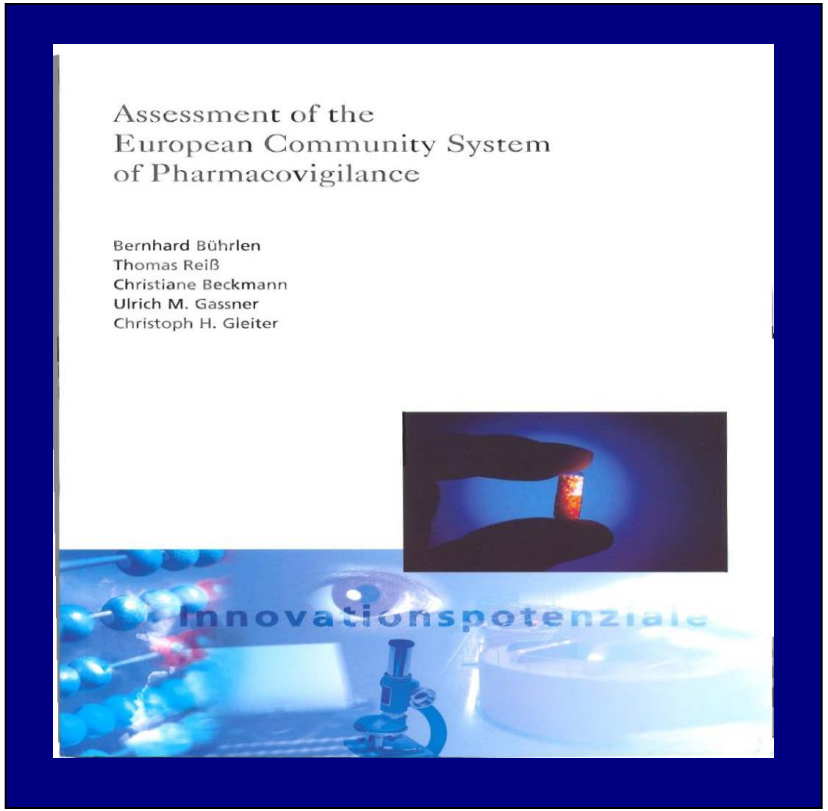
Drug group/drug	No (%) of cases	Individual drugs	Adverse reactions
NSAIDs	363 (29.6)	Aspirin (218), diclofenac (52), ibuprofen (34), rofecoxib (33), celecoxib (8), ketoprofen (6) naproxen (5)	GI bleeding, peptic ulceration, haemorrhagic cerebrovascular accident, renal impairment, wheezing, rash
Diuretics	334 (27.3)	Furosemide (128), bendroflumethiazide (103), bumetanide (43), spironolactone (37), amiloride (19), metolazone (11), indapamide (6)	Renal impairment, hypotension, electrolyte disturbances, gout
Warfarin	129 (10.5)	—	GI bleeding, haematuria, high INR, haematoma
ACE inhibitors/All receptor antagonists	94 (7.7)	Ramipril (28), enalaparil (25), captopril (12), lisinopril (9), irbesartan (6), losartan (5), perindopril (4)	Renal impairment, hypotension, electrolyte disturbance, angioedema
Antidepressants	87 (7.1)	Fluoxetine (17), paroxetine (14), amitriptyline (13), citalopram (9), lithium (8), venlafaxine (8) dosulepin (7),	Confusion, hypotension, constipation, GI bleed, hyponataemia
{beta} blockers	83 (6.8)	Atenolol (69), propranolol (6), sotalol (3), bisoprolol (2), metoprolol (2), carvedilol (1)	Bradycardia, heart block, hypotension, wheezing
Opiates	73 (6.0)	Morphine (20), dihydrocodeine (20), co-codamol (8), tramadol (8), co-dydramol (6), fentanyl (5)	Constipation, vomiting, confusion, urinary retention



European Commission "Fraunhofer" review of pharmacovigilance actions and activities in EU

Independent pan-EU assessment of activities, strengths and weaknesses


OE-0758
OE-0739
"Fix it while you fly"

New EU Pharmacovigilance approaches

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Benefit risk throughout product lifecycle

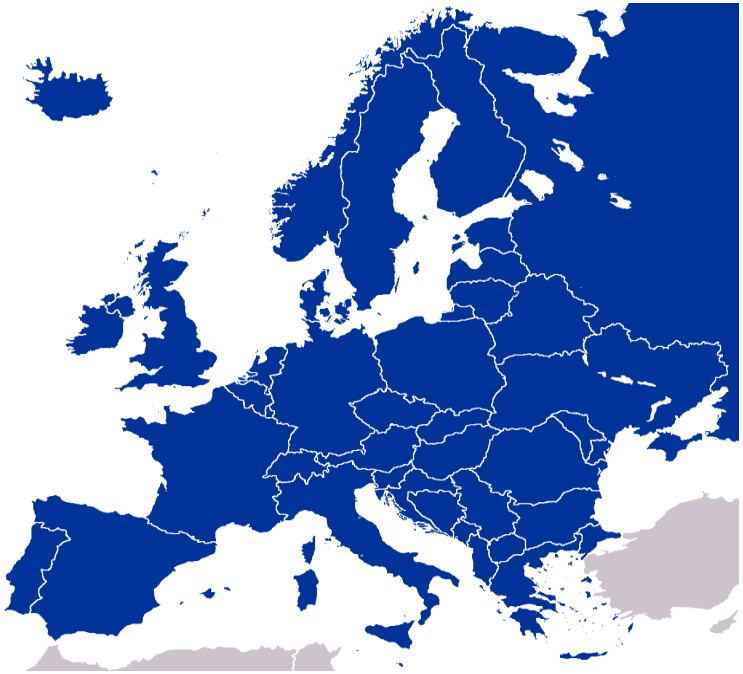
Proactive risk management planning

Effectiveness of risk minimisation

Additional monitoring scheme

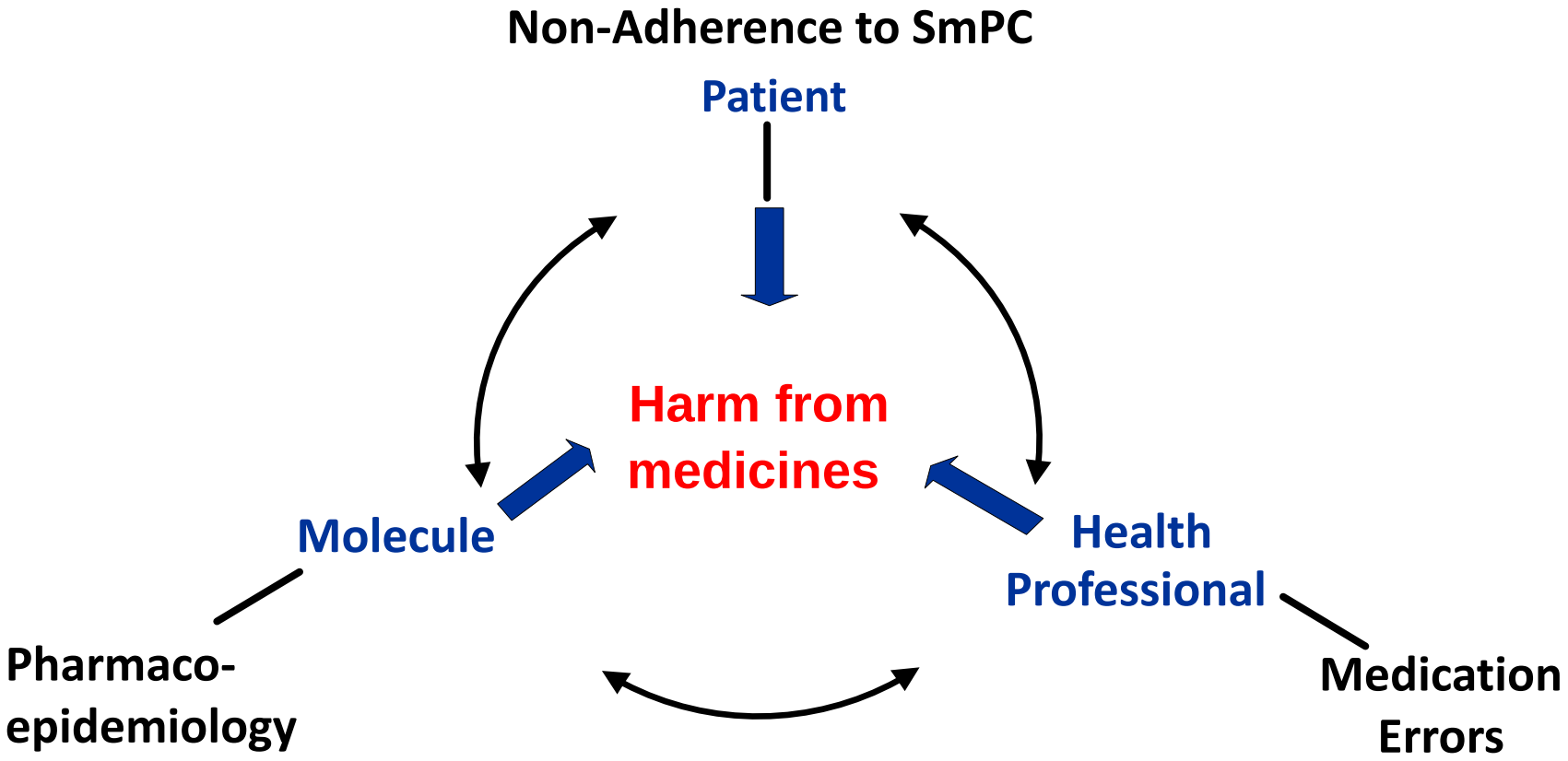
Patient reporting of ADRs

Quality systems & audits



Strengthened pharmacovigilance systems

Wider concept of harms associated with medicines



Supported by extensive EU guidance

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HMA
Heads of Medicines Agencies

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15 April 2014
EMA/204715/2012 Rev 1*

Guideline on good pharmacovigilance practices (GVP)

Module XVI– Risk minimisation measures: selection of tools and effectiveness indicators (Rev 1)

Draft finalised by the Agency in collaboration with Member States and submitted to ERMS FG	21 March 2013
Draft agreed by ERMS FG	27 March 2013
Draft adopted by Executive Director	6 June 2013
Released for consultation	7 June 2013

Good Vigilance Practice XVI

Pharmacovigilance Risk Assessment Committee

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All aspects of the risk management of the use of medicinal products including the detection, assessment, minimisation and communication relating to the risk of adverse reactions, having due regard to the therapeutic effect of the medicinal product, the design and evaluation of post-authorisation safety studies and pharmacovigilance audit

EC Report on 3 years of EU pharmacovigilance

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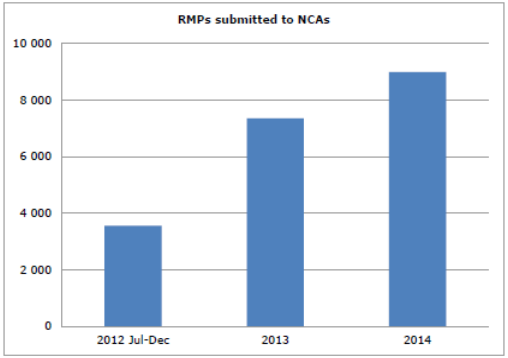
EUROPEAN
COMMISSION

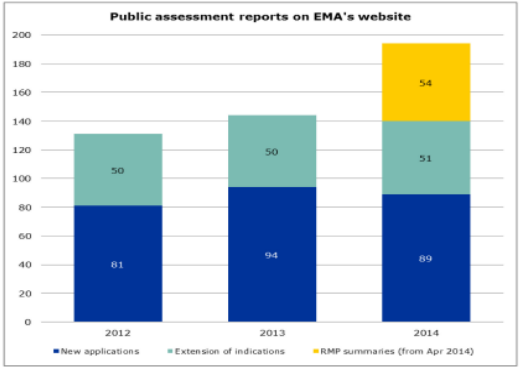
Brussels, 8.8.2016
SWD(2016) 284 final

COMMISSION STAFF WORKING DOCUMENT
Accompanying the document

Commission Report

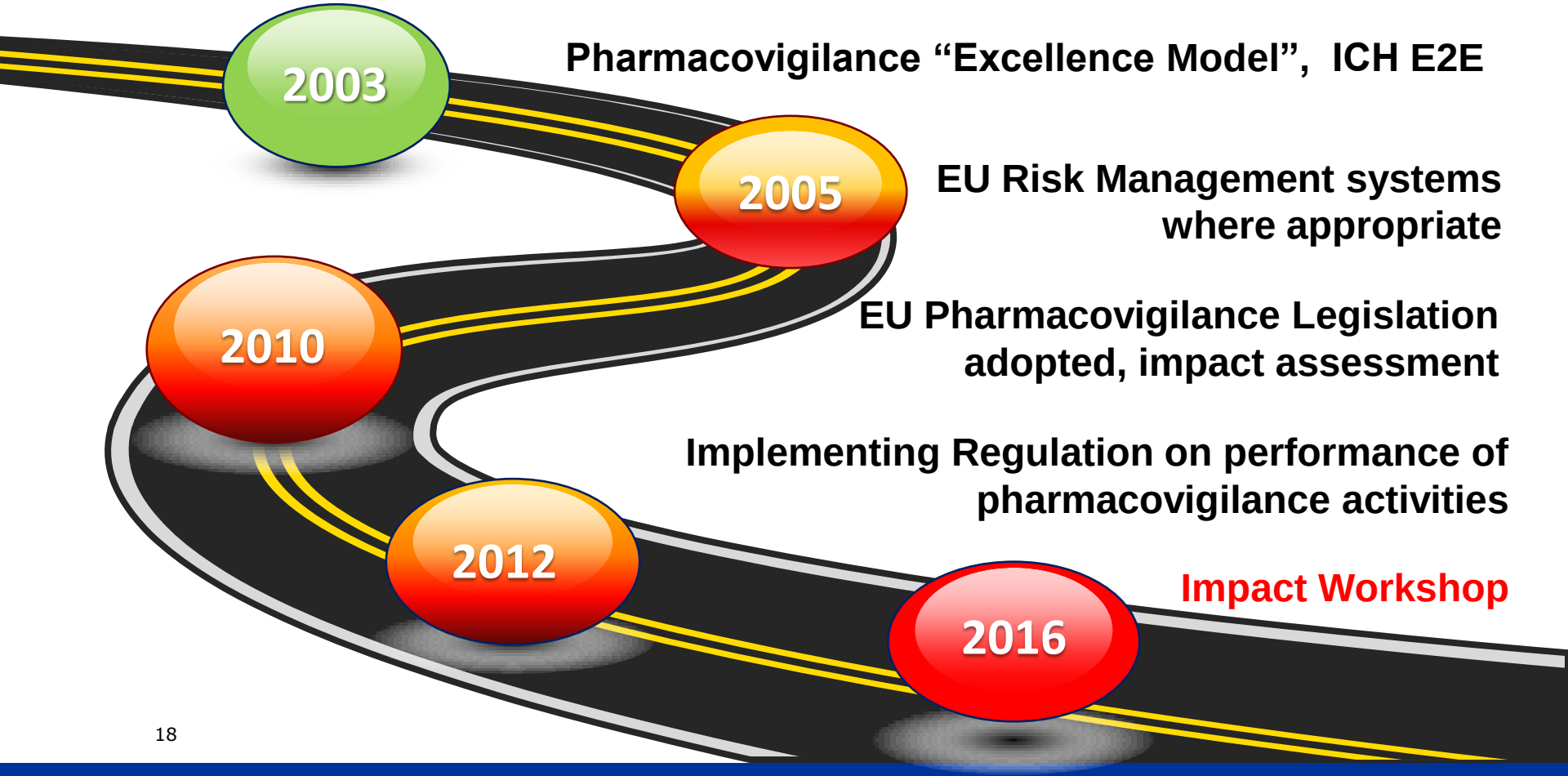
Pharmacovigilance related activities of Member States and the European Medicines Agency concerning medicinal products for human use (2012 – 2014)



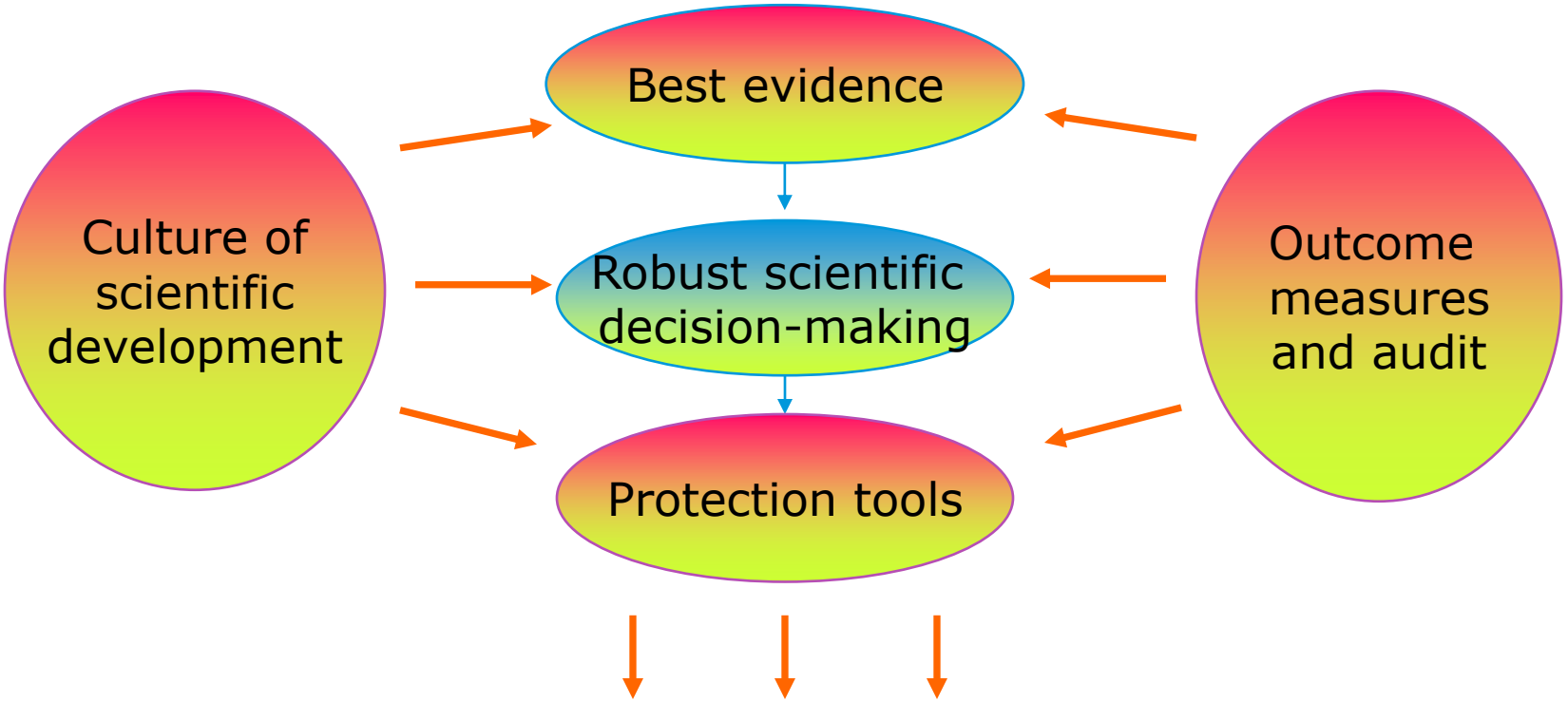


Impact of strengthened pharmacovigilance?

Impact –regulatory evolution

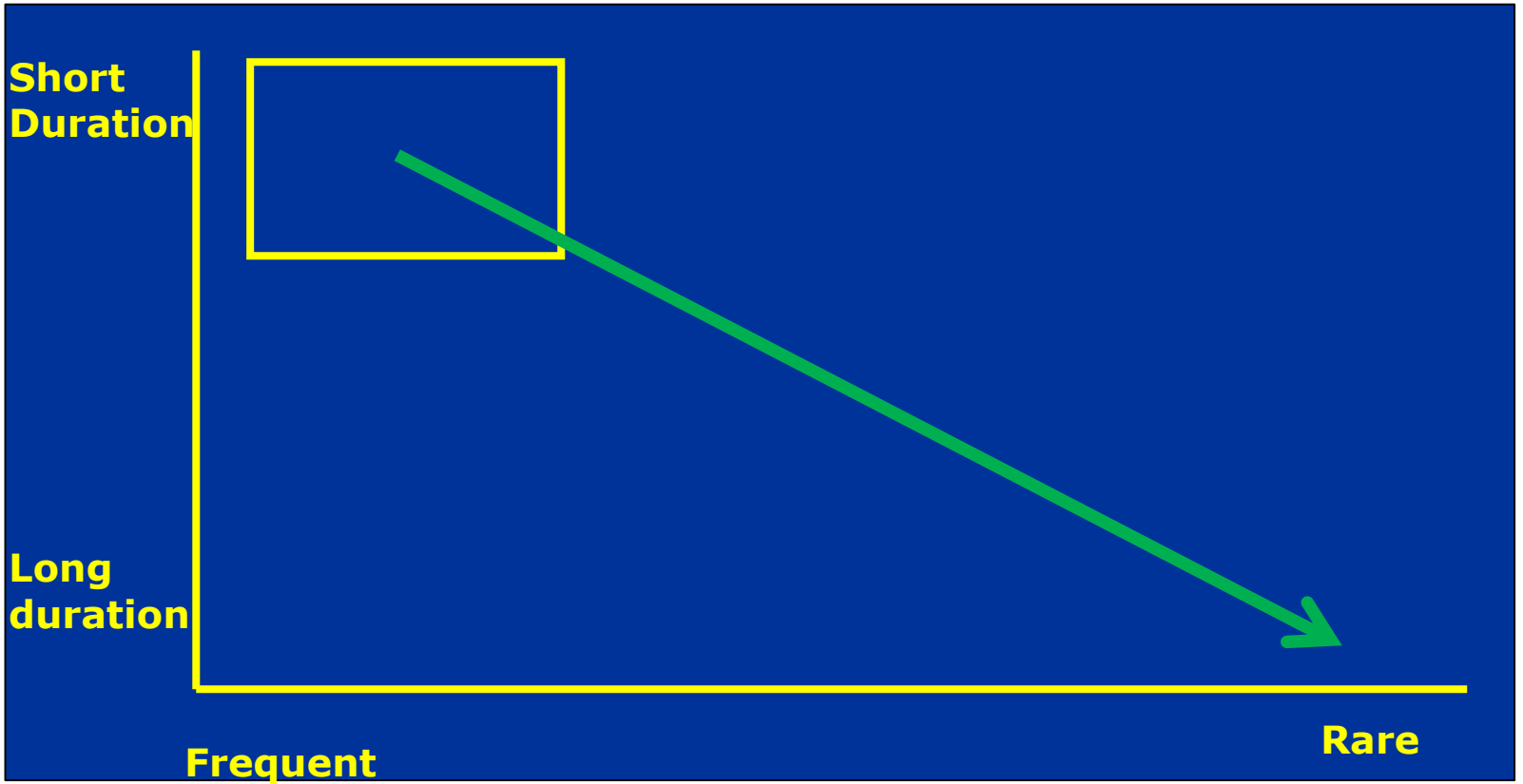


Excellence in pharmacovigilance model



Measurable excellence in terms of public health benefit

Demonstrating a greater degree of safety



Measuring impact – regulatory history

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Ad hoc regulatory risk minimisation measures & effectiveness monitoring

Clozapine and agranulocytosis 1989

Population studies on impact of key regulatory warnings and restrictions

Aspirin & Reye's Syndrome in children 1990s
HRT and breast cancer 2001
Paracetamol in overdose 2004

Monitoring impact of regulatory action has been undertaken followed significant EU decisions

Withdrawal of rosiglitazone 2007
Withdrawal of co-proxamol 2010

Clozapine Patient Monitoring Service

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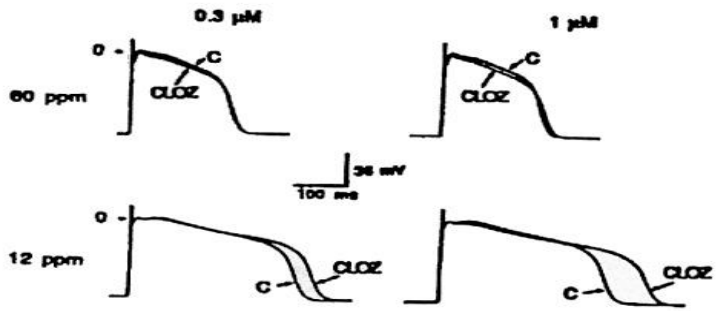
No blood no drug database

Data from over 12,000 subjects

Neutropenia cumulative incidence 2.7% with peak risk at 6-18 weeks

Risk factors - age, ethnicity, baseline WBC, dose (inverse)

No haematological fatalities



Impact of regulatory action – what learnt from experience?

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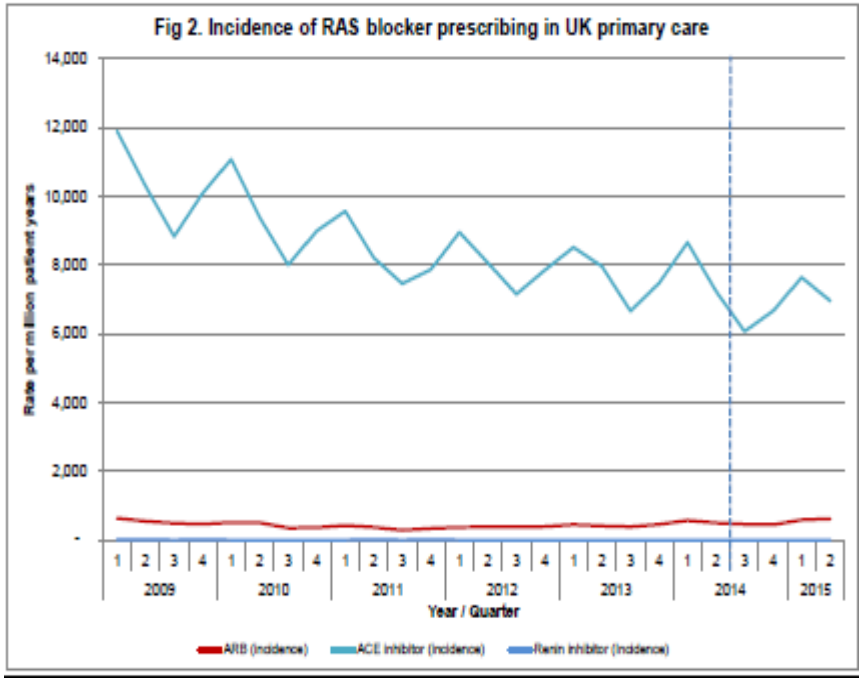
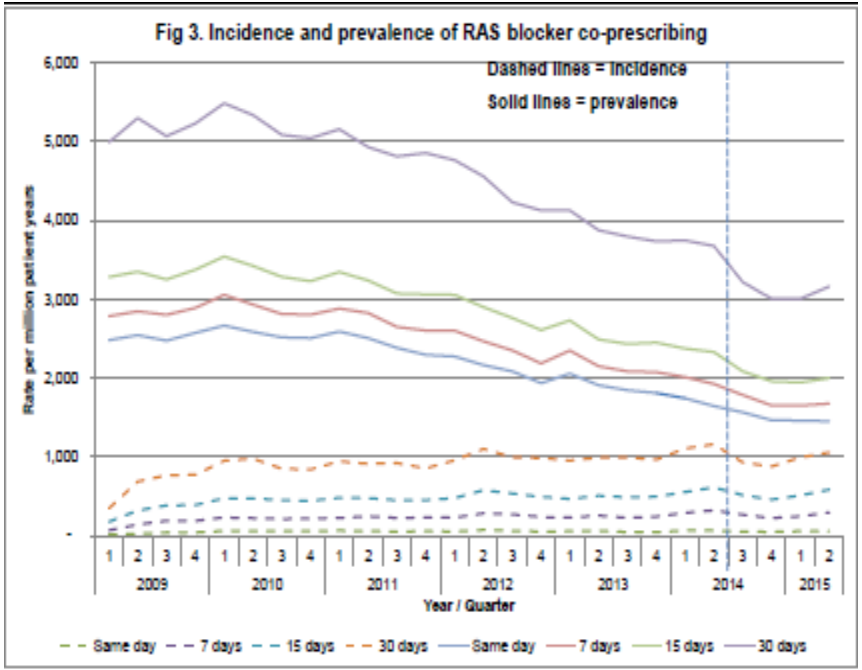
Uptake and effect of measures?	*Concomitant RAS agents* *Benzodiazepines Rx duration*
Measurable public health impact?	*HRT and breast cancer*
Therapeutic consequences?	*Thioridazine and CVS risk* *SSRIs in children*

Concomitant use of RAS blocking agents in UK





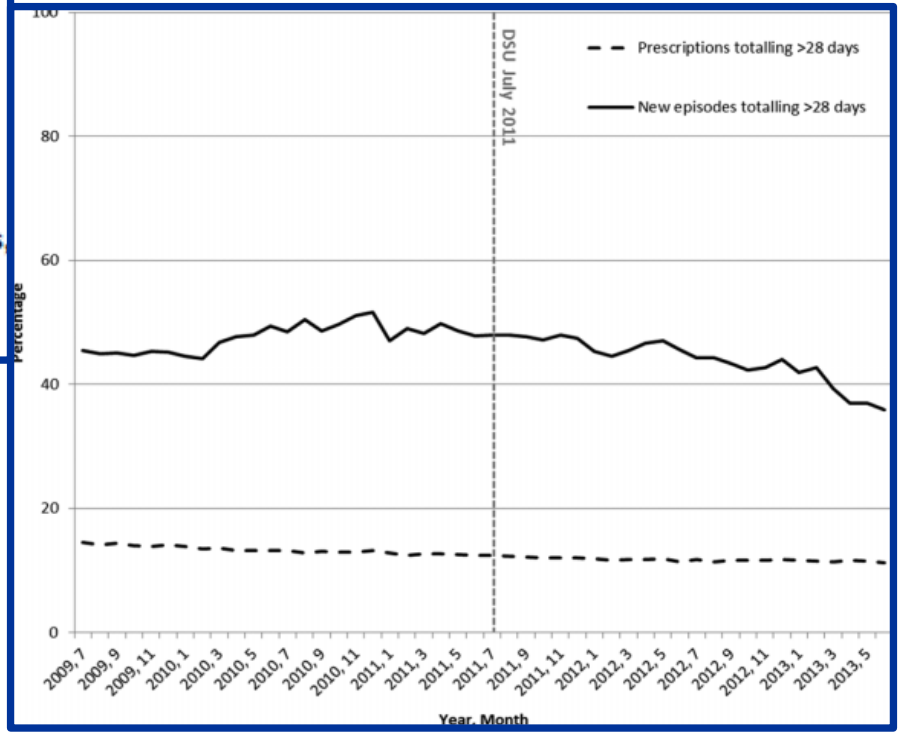
Allen C and Donegan K, 2016

Analytical Report

Monitoring and Evaluating the Effect of Regulatory Action: Some Recent Case Studies

Andrew Thomson, MA, MSc, PhD[1,2], Wilhelmine Hadler Meeraus, Jenny Wong, BSc[1], and Rafe Suvarna, MBBS, BSc, FFPM[1]

Trends in proportion of benzodiazepine prescription longer than 28days in UK primary care



Thomson et al. Therapeutic Innovation and Regulatory Science 2015, 49 (4) 473-482

Public health impact of action on HRT

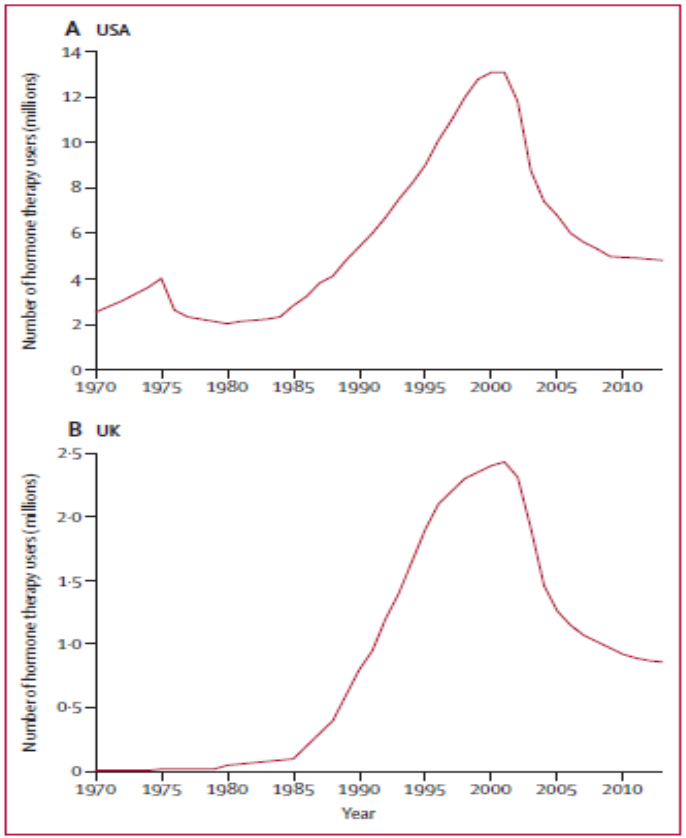


Figure 1: **Trends in hormone therapy use in the USA and the UK since 1970**
For source of data, see appendix p 4.

Impact of removal of first-line HRT indication in osteoporosis in 2001 after WHI study showed evidence of harms

Trends in use of hormone therapy for menopause since 1970, USA and UK

Ref- Harrison-Woolrych 2015

HRT and risk of breast cancer

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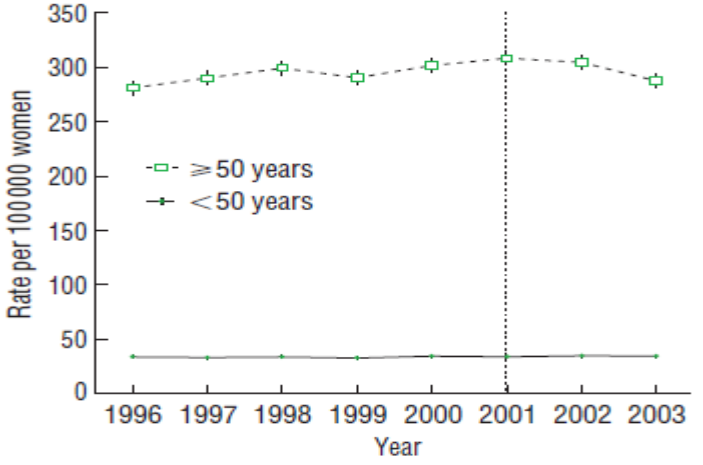
1 Hormone replacement therapy (HRT) prescriptions among concession cardholders in Australia, 1996–2003

Vertical dotted line indicates commencement of the period over which HRT prescriptions were expected to decline. ◆

2 Age-standardised incidence of invasive breast cancer in women in Australia, 1996–2003



Vertical bars represent 95% CIs (confidence intervals are very small for women aged <50 years). Vertical dotted line indicates commencement of the period over which there was a hypothesised decrease in breast cancer incidence in women aged ≥ 50 years but not in women aged <50 years. ◆

MJA • Volume 188 Number 11 • 2 June 2008

Prescribing of antipsychotics after thioridazine action

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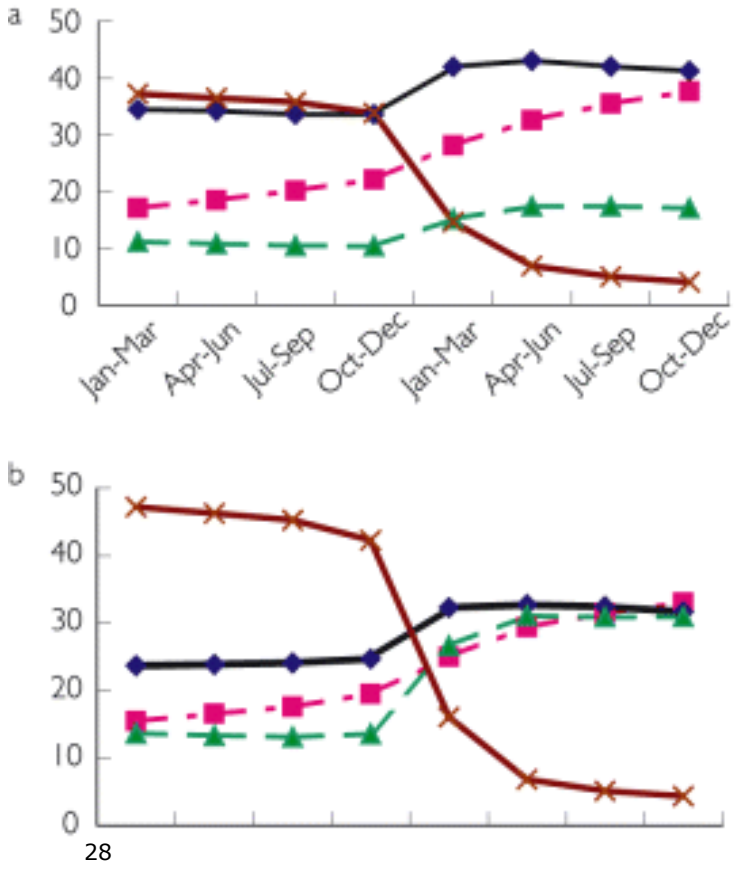

Prescribing of antipsychotic drugs per QTR 2000–2001 expressed as % of total antipsychotics

a, **Percentage England** Others ■risperidone, olanzapine ▲chlorpromazine × thioridazine

b, **Percentage Scotland** ■risperidone, olanzapine; ▲chlorpromazine; × thioridazine

BJCP British Journal of Clinical Pharmacology

Explore this journal >

Effects of licence change on prescribing and poisons enquiries for antipsychotic agents in England and Scotland

D. N. Bateman, A. M. Good, R. Afshari, C. A. Kelly

Regulatory action restricting SSRIs in children

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Article

Early Evidence on the Effects of Regulators' Suicidality Warnings on SSRI Prescriptions and Suicide in Children and Adolescents

Robert D. Gibbons, Ph.D.

Objective: In 2003 and 2004, U.S. and European regulators issued public health

Results: SSRI prescriptions for youths decreased by approximately 22% in both

Gibbons et al 2007 Am J Psych 164:1356-1363

FIGURE 5. Suicide Rate in Children and Adolescents (Up to Age 19) in the Netherlands, 1998–2005

Regulatory action restricting SSRIs in children

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Research

The population impact on incidence of suicide and non-fatal self harm of regulatory action against the use of selective serotonin reuptake inhibitors in under 18s in the United Kingdom: ecological study

BMJ 2008 ; 336 doi: http://dx.doi.org/10.1136/bmj.39462.375613.BE (Published 06 March 2008)
Cite this as: *BMJ* 2008;336:542

Wheeler, B. W et al. BMJ 2008;336:542-545

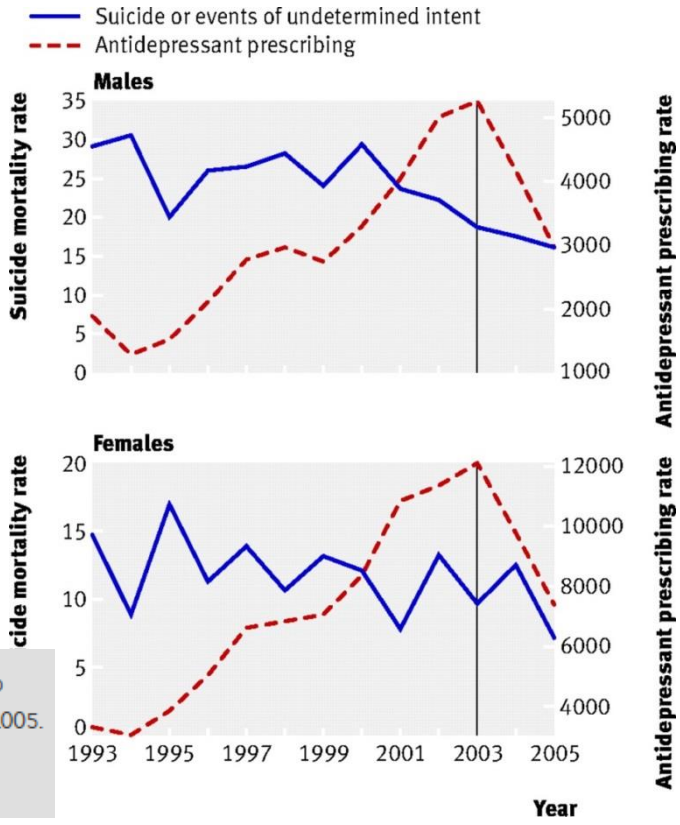
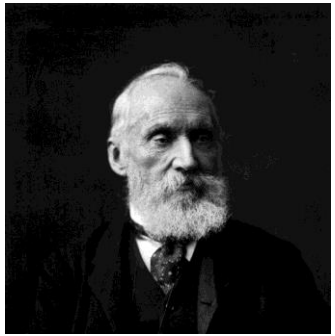


Fig 1 Trends in rates of antidepressant prescribing in 12-19 year olds per 100 000 population in UK[9] and mortality due to suicide or events of undetermined intent in 12-17 year olds per one million population in England and Wales,[10] 1993 to 2005. Vertical lines indicate year in which regulatory action was taken against prescriptions for selective serotonin reuptake inhibitors in under 18s

What is Vision for regulatory action impact evaluation?

If you cannot measure it,
you cannot improve it



William Thomson
Lord Kelvin
1824-1907

$$\text{Effectiveness} = \frac{\text{Achieved}}{\text{Desired}}$$

Vision for regulatory action impact evaluation

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Robust scientific methodology	*Paracetamol toxicity in overdose*
Decision-relevant data	*Valproate and pregnancy harms*
Timely results – even real time	*Pertussis vaccine in pregnancy*
Clarity of roles	*Bisphosphonates and ONJ*

Paracetamol toxicity in overdose

Regulatory action in UK aimed to balance access by normal users with toxicity in overdose

Combination of pack limits and explicit warnings to patients and public

Inclusion of all OTC analgesics (paracetamol, aspirin and ibuprofen) equally in the measures

British Journal of Psychiatry (1996), **168**, 43–48

Paracetamol Self-Poisoning

Characteristics, Prevention and Harm Reduction

KEITH HAWTON, CHRISTOPHER WARE, HAMANT MISTRY, JONATHAN HEWITT, STEPHEN KINGSBURY, DAVE ROBERTS and HEATHER WEITZEL

Background. Paracetamol is now the most common drug used for self-poisoning in the UK and is associated with potentially fatal liver dam
of paracetamol overdoses were studied in order t
which might have deterred them from taking p
overdose.
Method. Eighty patients were studied in hospi
measures of depression and suicidal intent, inform
System for Attempted Suicide, and the results
Results. Acute liver dysfunction (25 patients) wa
25 tablets (odds ratio 4.46, 95% CI 1.31 to 17.41
from blister packs (60%) and loose preparations
their general availability. More of those who took
25 or more tablets (69%) than those who us
ratio = 3.0, 95% CI 1.12 to 9.95, P=0.028). Only
label would have deterred them from taking a p
Conclusions. Establishing a maximum number
individual preparations is likely to reduce the d
potential effects of other measures are uncerta

Paracetamol toxicity in overdose

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BMJ

BMJ 2013;346:f403 doi: 10.1136/bmj.f403 Page 1 of 9

RESEARCH

Long term effect of reduced pack sizes of paracetamol on poisoning deaths and liver transplant activity in England and Wales: interrupted time series analyses

OPEN ACCESS

Keith Hawton *professor of psychiatry and director centre for suicide research*[1], Helen Bergen *researcher*[1], Sue Simkin *researcher*[1], Sue Dodd *scientific assessor*[2], Phil Pocock *principal statistician*[3], William Bernal *reader in hepatology*[4], David Gunnell *professor of epidemiology*[5], Navneet Kapur *professor of psychiatry and population health*[6]

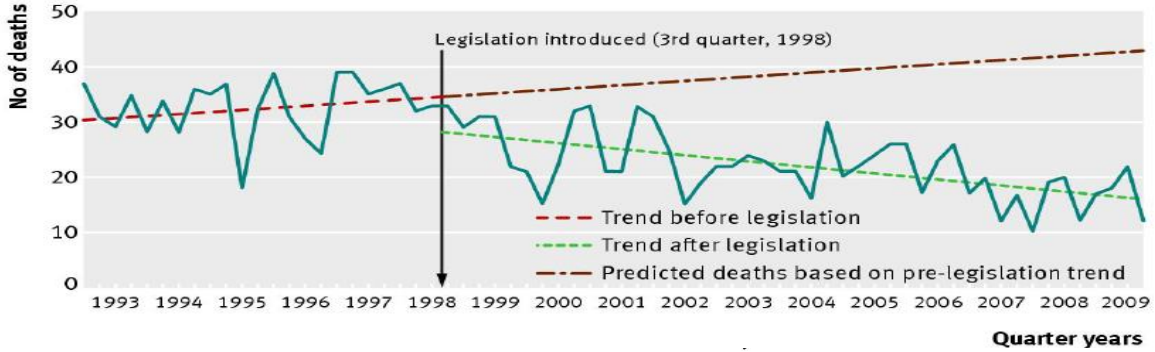

Fig 1 Suicide and open verdict deaths involving paracetamol only, in people aged 10 years and over in England and Wales 1993-2009, and best fit regression lines related to 1998 legislation

Valproate in pregnancy & neurodevelopmental delay

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 16, 2009 VOL. 360 NO. 16

Cognitive Function at 3 Years of Age after Fetal Exposure to Antiepileptic Drugs

Kimford J. Meador, M.D., Gus A. Baker, Ph.D., Nancy Browning, Ph.D., Jill Clayton-
Deborah T. Combs-Cantrell, M.D., Morris Cohen, Ed.D., Laura A. Kalayjian, M.D., And
Joyce D. Liporace, M.D., Page B. Pennell, M.D., Michael Privitera, M.D., and David W
for the NEAD Study Group*

ABSTRACT

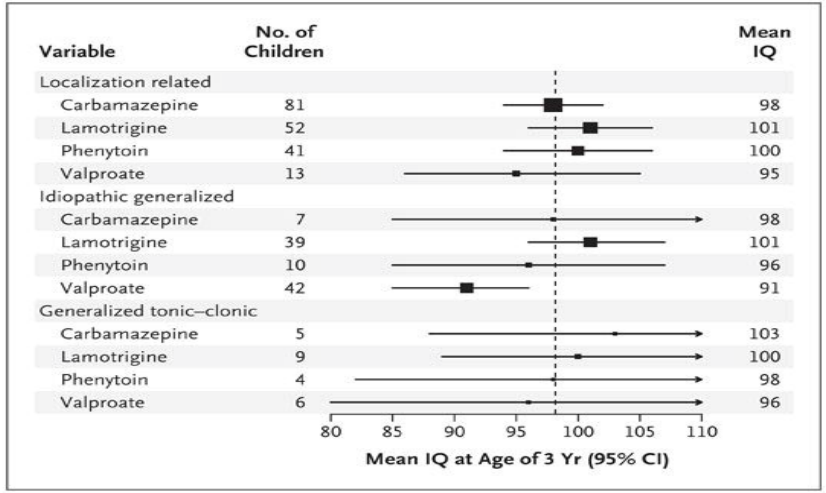

Figure 2. IQ Scores of Children Who Were Exposed to Antiepileptic Drugs In Utero, According to Drug and Type of Maternal Epilepsy.

Meador et al NEJM 2009

Sodum Valproate patient exposure in EU

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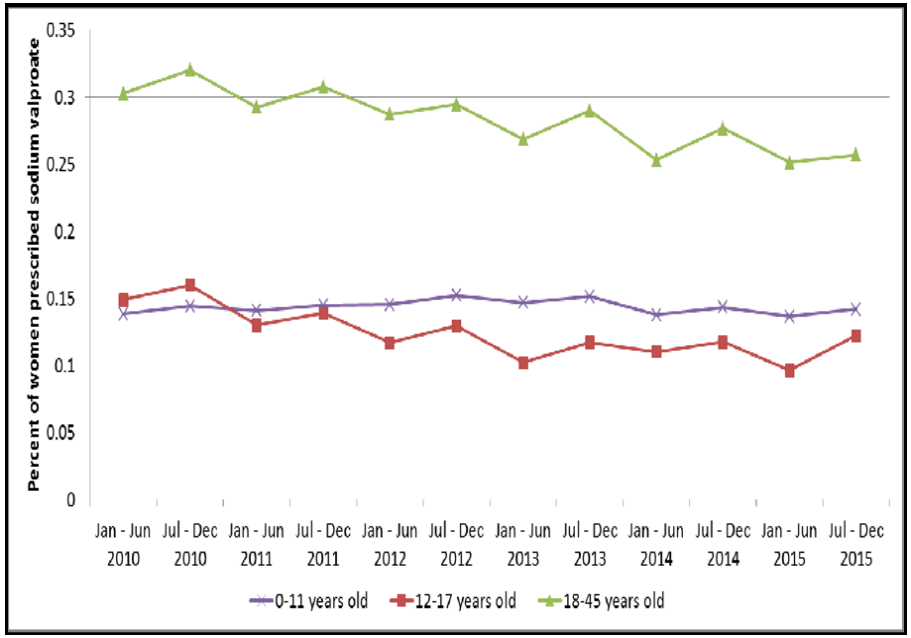
	From 2010 to 2012				
MSs	**Epilepsy**	**Bipolar disorder**	**Migraine**	**Other**	**Total**
UK	42 409 (**43.7%**)	17 232 (**17.7%**)	740 (0.8%)	36 745 (37.8%)	97 125
France	7 432 (**4.8%**)	98 286 (**63.1%**)	402 (0.3%)	49 650 (31.9%)	155 770
Germany	19 410 (**70.7%**)	120 (**0.4%**)	348 (1.3%)	7 566 (27.6%)	27 444
Italy	46 222 (**46.4%**)	17 481 (**17.5%**)	204 (0.2%)	35 716 (35.9%)	99 623
Spain	21 545 (**42.9%**)	15 877 (**31.6%**)	352 (0.7%)	12 455 (24.8%)	50 229
Total	137 018 (**31.9%**)	148 995 (**34.6%**)	2 046 (0.5%)	142 132 (33.0%)	430 191

Treatment-years by country & indication females 15-49 years

UK Prevalence of Prescribing Sodium valproate-CPRD



Rate of prescribing in younger females relatively consistent

Suggestion of flattening of expected increase in prescribing in women 18-45yrs Jul-Dec 2015

Valproate

Patient Guide

Valproate action Healthcare Professional awareness

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Strengthening Collaborations for Operating Pharmacovigilance in Europe

	GPs	Cardiologists	Pharmacists	Others	Total	p-value (Chi2)
1. No	445 (25%)	145 (65%)	283 (22%)	122 (36%)	995 (27%)	<0.001
2. Yes, via DHPC	759 (43%)	40 (18%)	465 (36%)	102 (30%)	1366 (38%)	<0.001
3. Yes, via website or newsletter	470 (27%)	21 (9%)	415 (32%)	81 (24%)	987 (27%)	<0.001
4. Yes, via educational materials	272 (15%)	7 (3%)	140 (11%)	30 (9%)	449 (12%)	<0.001
5. Yes, via professional body	191 (11%)	11 (5%)	216 (17%)	29 (9%)	447 (12%)	<0.001
6. Yes, via a colleague	104 (6%)	5 (2%)	87 (7%)	15 (4%)	211 (6%)	0.043
7. Yes, via medical journal	170 (10%)	11 (5%)	129 (10%)	22 (7%)	332 (9%)	0.031
8. Yes, via lay media (newspaper/television)	20 (1%)	1 (0%)	16 (1%)	5 (1%)	42 (1%)	0.717
9. Other, please specify	29 (2%)	4 (2%)	41 (3%)	8 (2%)	82 (2%)	0.046

Analysis of HCP survey responses by member state

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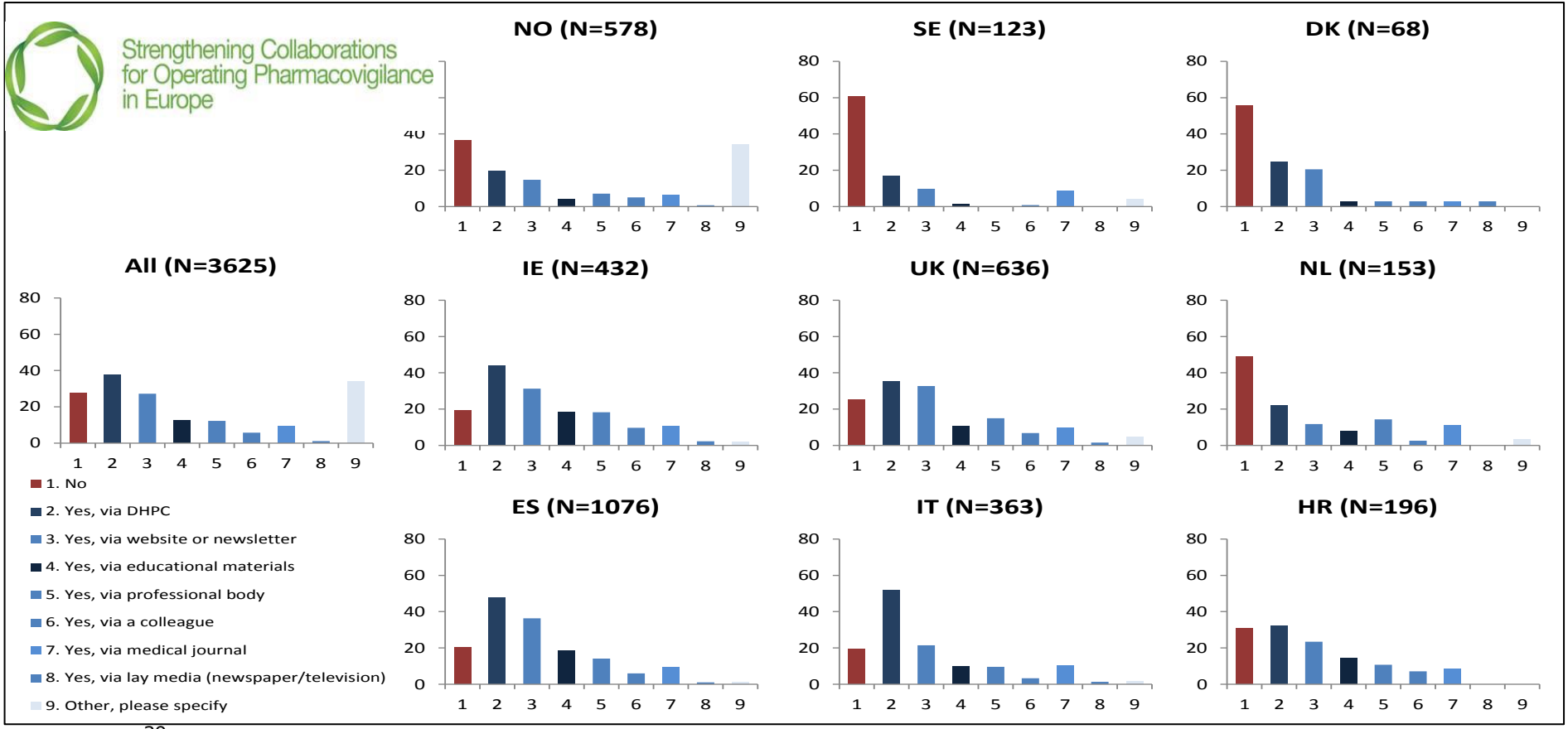
Strengthening Collaborations for Operating Pharmacovigilance in Europe



Valproate Dashboard to monitor impact in UK

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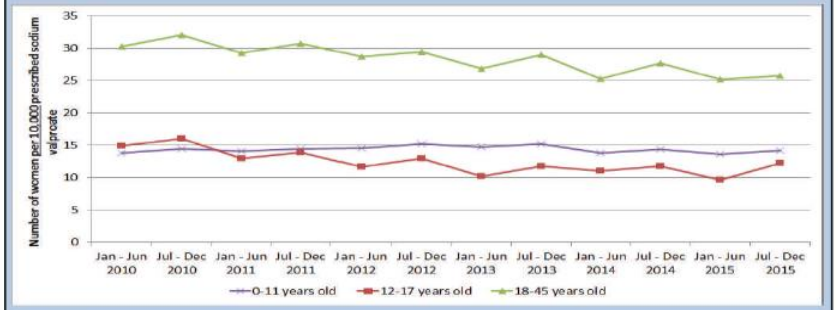
Supporting the safe use of sodium valproate

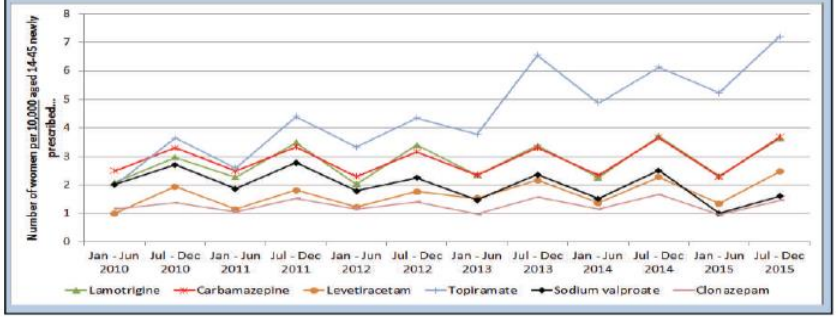
Aims/objectives:

- That sodium valproate is only provided to women who may become pregnant when there is no safe and effective alternative
- That all women who need valproate fully understand the risks associated with pregnancy

Prescribing by GPs *

Target - To reduce use in women aged 14-45 by ~80%





In July—December 2015 for every **10,000** women aged 14-45*at least...

- **15** were prescribed sodium valproate and had epilepsy
- **4** were prescribed valproate and had bipolar disorder
- **4** were prescribed valproate and had migraines

5/10,000 pregnancies

Rate of exposure to sodium valproate in pregnancy in 2015 *

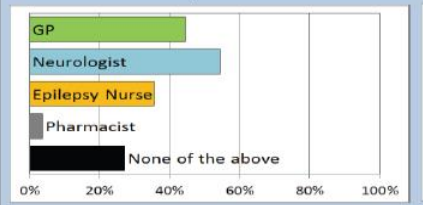
Patient awareness †

Target - 100% awareness & communication

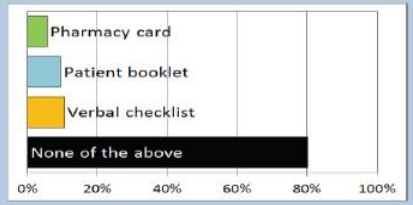
Of 620 epileptic women aged 16-50 currently taking valproate...

80% are aware of any effects on development and/or physical health of a child born to a woman taking sodium valproate

Have ever discussed pregnancy and sodium valproate with a....



Have received the following information...



† Data from a survey conducted by Epilepsy Society, Epilepsy Action, and Young Epilepsy

* Data from the UK Clinical Practice Research Datalink (www.cprd.com)

Pertussis vaccine in 3rd trimester of pregnancy

EUROPEAN MEDICINES AGENCY

thebmj

BMJ 2014;349:g4219 doi: 10.1136/bmj.g4219 (Published 11 July 2014)

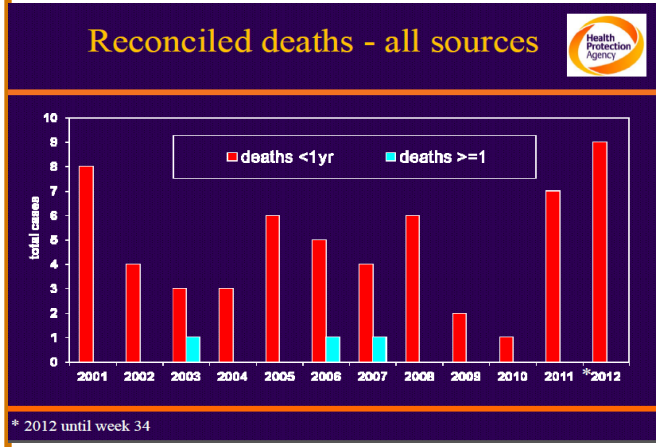
RESEARCH

Safety of pertussis vaccination in pregnant women in UK: observational study

OPEN ACCESS

Katherine Donegan *pharmacoepidemiologist*, Bridget King *scientific assessor*, Phil Bryan *scientific assessor*

Vigilance and Risk Management of Medicines, Medicines and Healthcare products Regulatory Agency, London SW1W 9SZ, UK



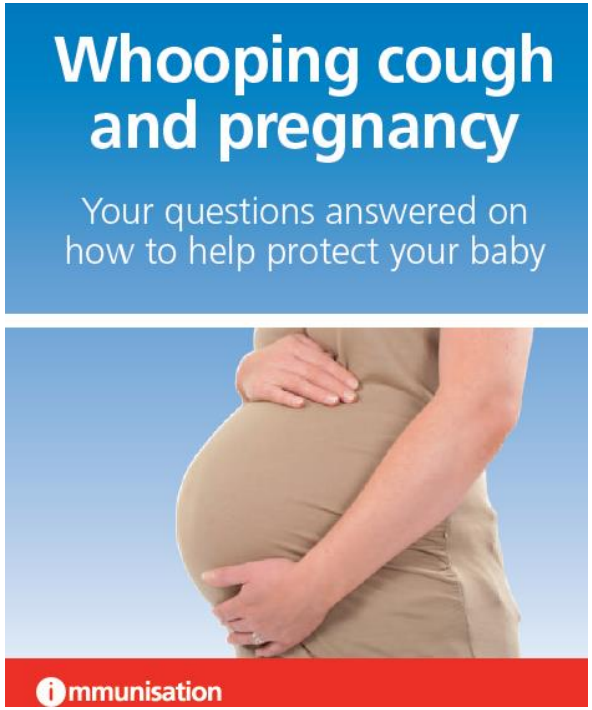
Observational cohort study using CPRD data in 20,074 pregnant women median age 30 who received pertussis vaccine and matched historical unvaccinated controls

No evidence of increased risk of stillbirth in 14 days post-vaccine (incidence rate ratio 0.69 95% CI 0.23-1.62) or later in pregnancy (0.85, 0.44-1.61)

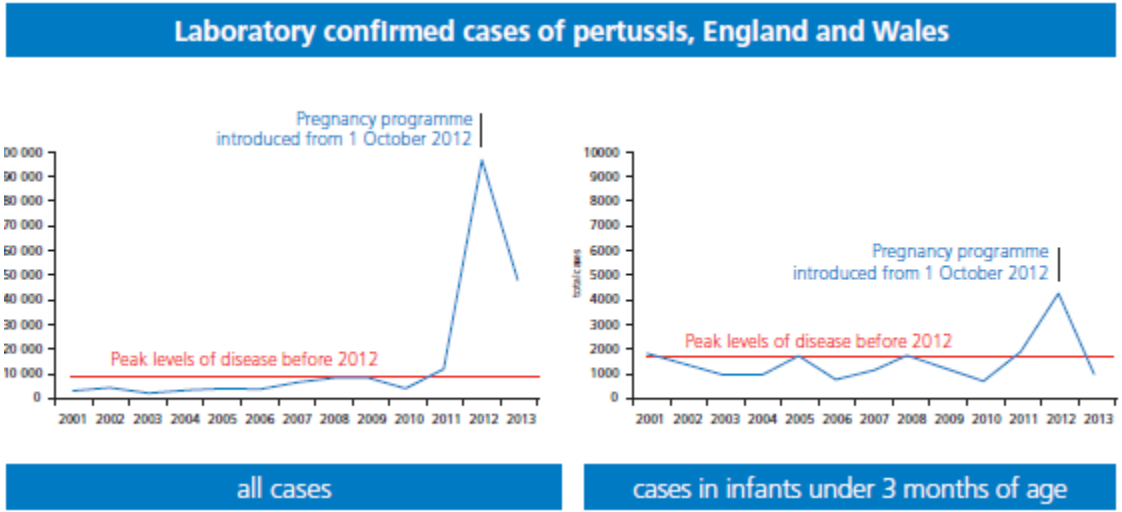
No evidence of an increased risk of range of other adverse effects

Donegan K et al BMJ 2014

Regulatory action based on observational data



EU Marketing Authorisation for Repevax updated to remove recommendation against use in pregnancy



Real-time risk management

3.26pm take-off

3.27pm engine trouble

9 min

3.36pm first picture onTwitPic

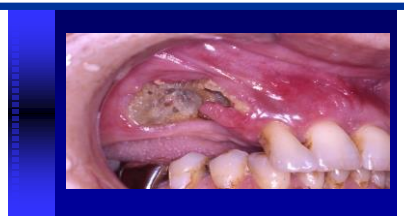
"There's a plane in the Hudson. I'm on the ferry going to pick up the people. Crazy."

12 min

3.48pm: NY Times 'breaking'

Minimising ONJ risk - bisphosphonates, denosumab

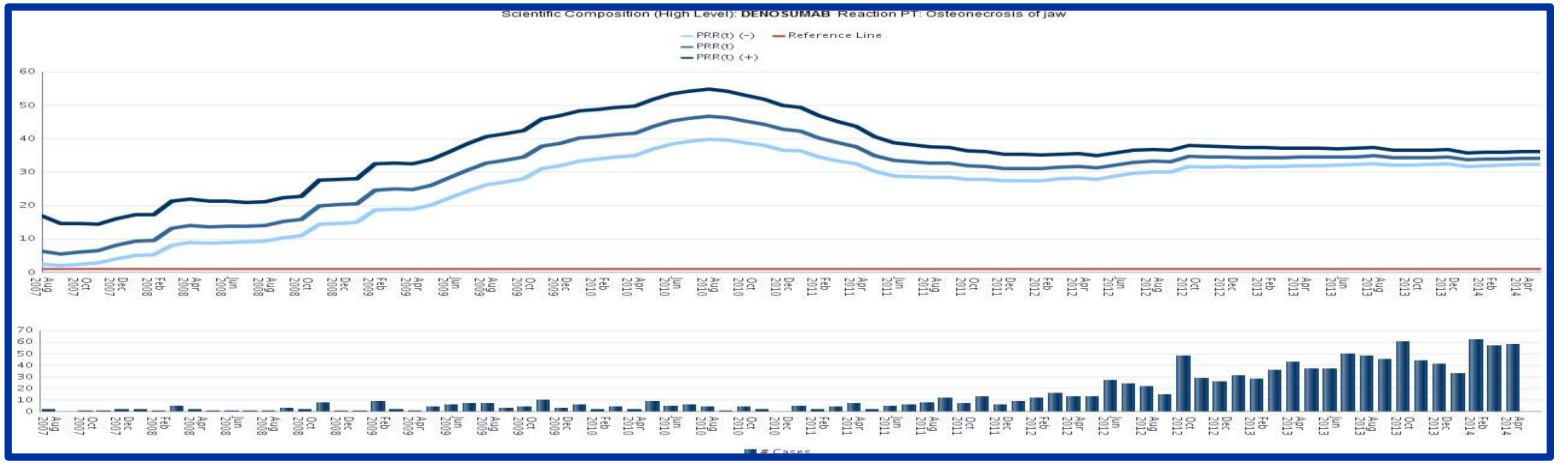
Denosumab (Xgeva▼, Prolia); intravenous bisphosphonates: osteonecrosis of the jaw—further measures to minimise risk



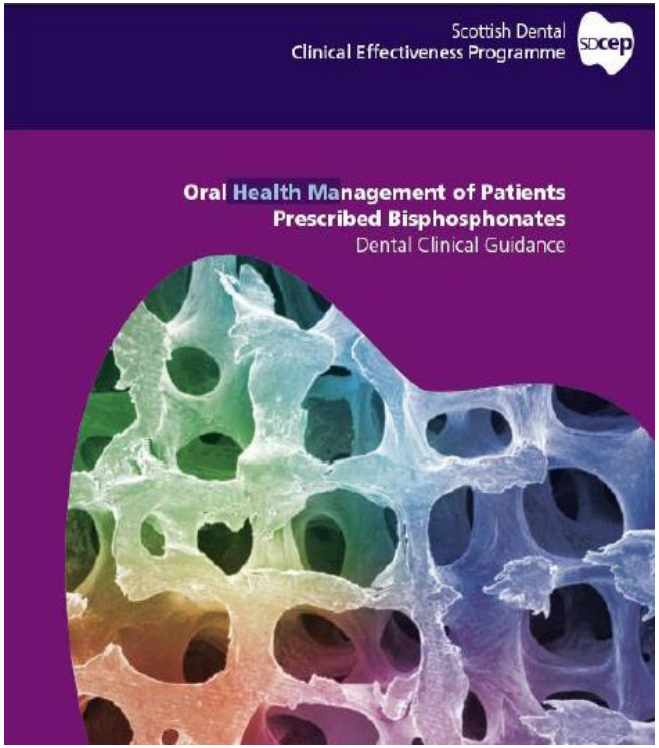
From: Medicines and Healthcare products Regulatory Agency
Published: 20 July 2015
Therapeutic area: Cancer, Dentistry, Endocrinology, diabetology and metabolism, Obstetrics, gynaecology and fertility, and Rheumatology

Patient reminder cards about the risk of osteonecrosis of the jaw are being introduced;

EudraVigilance reporting monitored over time



ONJ & bisphosphonates – HCPs and patients



This reminder card contains important safety information that you need to be aware of before and during treatment with zoledronic acid (Zometa) injections for cancer-related conditions

OSTEONECROSIS OF THE JAW (ONJ)

Your doctor has recommended that you receive zoledronic acid (Zometa) injections to help prevent bone complications (e.g. fractures) caused by bone metastases and/or to reduce the amount of calcium in the blood in adult patients where it is too high due to the presence of a tumour.

A side effect called osteonecrosis of the jaw (ONJ) (bone damage in the jaw) has been reported uncommonly in patients receiving zoledronic acid (Zometa) injections for cancer-related conditions. ONJ can also occur after stopping treatment.

In order to reduce the risk of developing ONJ, there are some precautions you should take:

How strengthen approach to monitoring impact?

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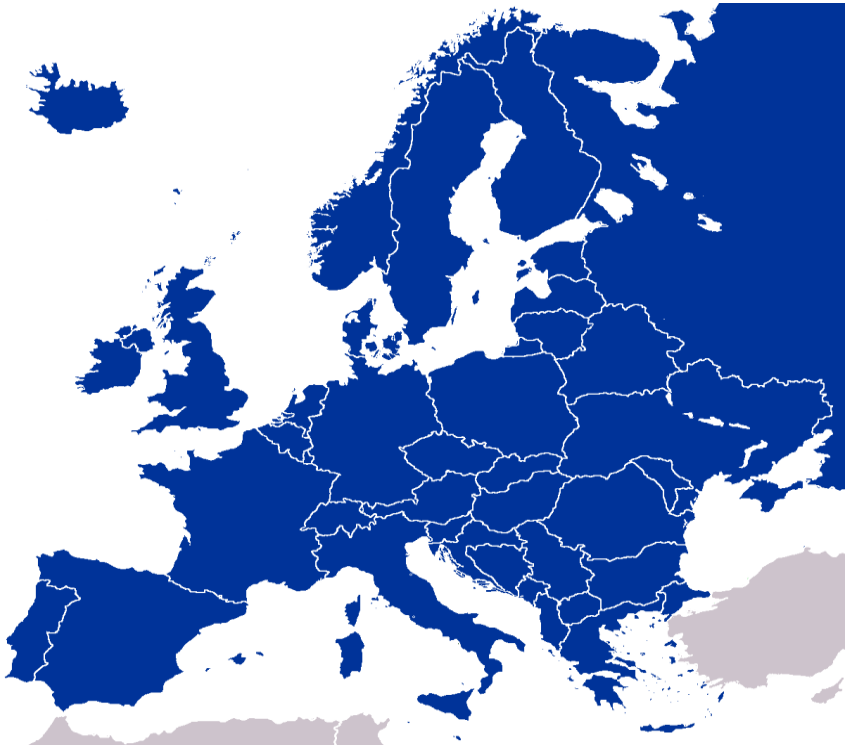
Scientific methodologies development

Build a sustainable infrastructure for real world monitoring of impact of regulatory action

Systematic incorporation of impact evaluation in regulatory guidance and procedures

Evaluation of performance of regulatory “tools” eg patient alert cards, materials



Scientific methodologies

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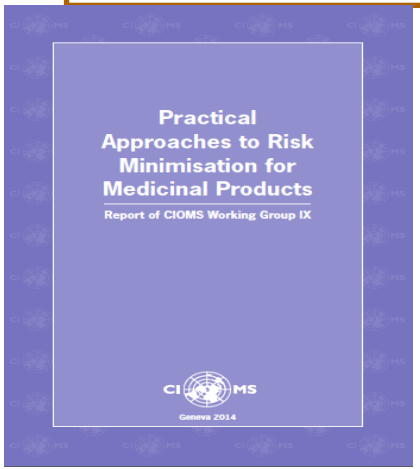
Best use of available scientific methodologies and development of new methodologies

Incorporation of methodologies from behavioural science

Systematic application at time of regulatory action including epidemiological modelling

Routine application in scientific advice to marketing authorisation holders



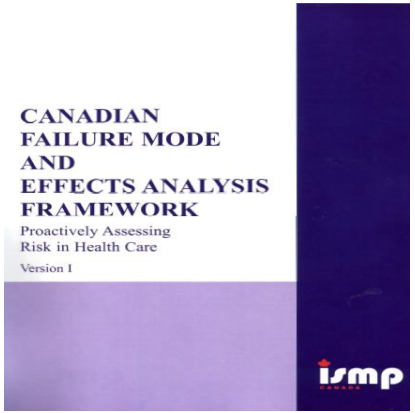
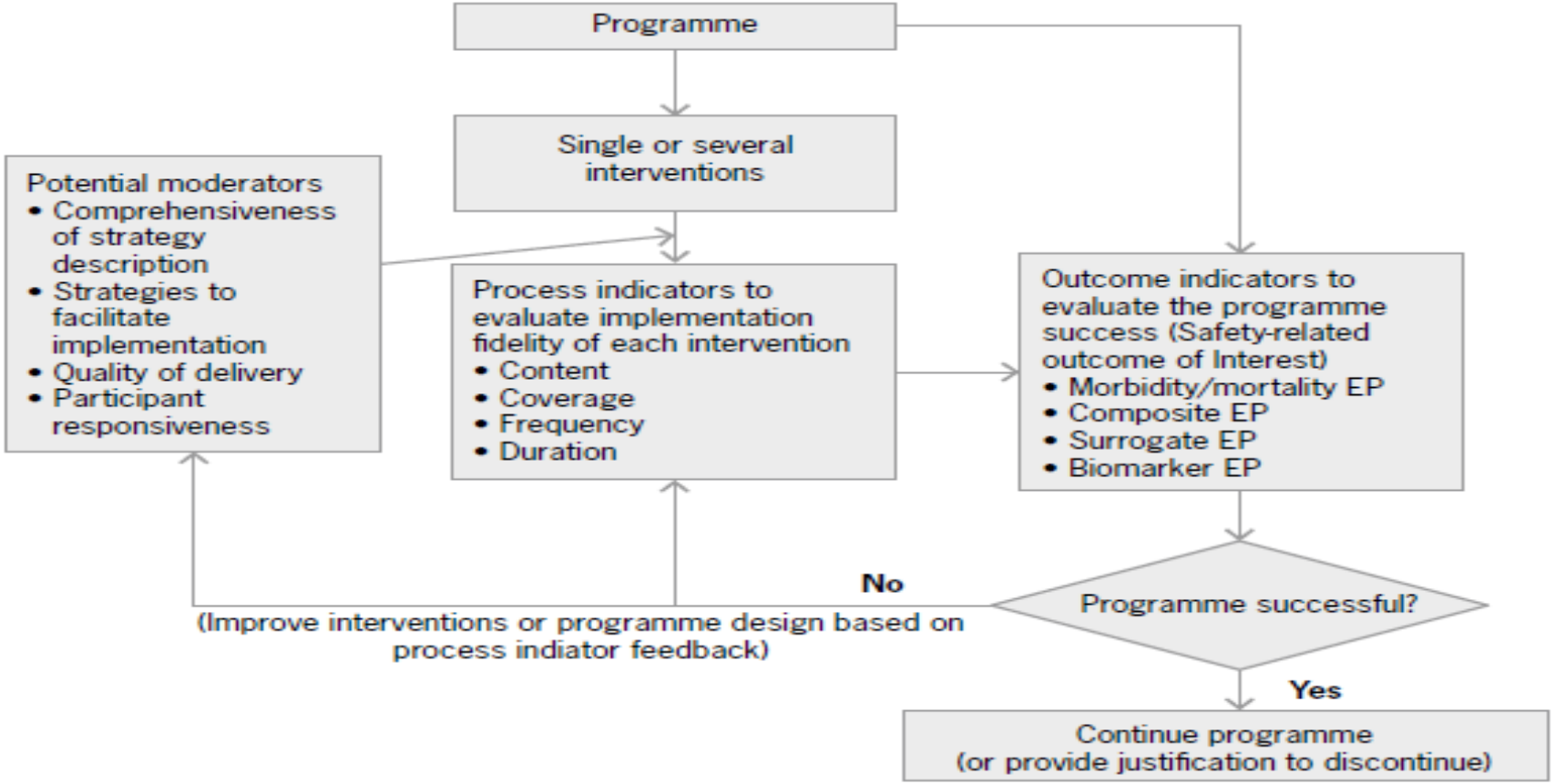


Fig. 5.1: CIOMS IX risk minimisation evaluation framework



Note to Fig. 5.1: EP = endpoint. The 'CIOMS IX risk minimisation evaluation framework' outlines elements to be considered for the evaluation of a risk minimisation programme (modified from Carroll **(25)**.)

Methodological gaps in assessment of RMIs

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2014; 23: 572–579
Published online 24 February 2014 in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/pds.3596

REVIEW

Methodological gaps in the assessment of risk minimization interventions: a systematic review

Inna Gridchyna[1], Anne-Marie Cloutier[1,2], Lenhangmbong Nkeng[1,2], Camille Craig[1,2], Sarah Frise[3,4] and Yola Moride[1,2]*

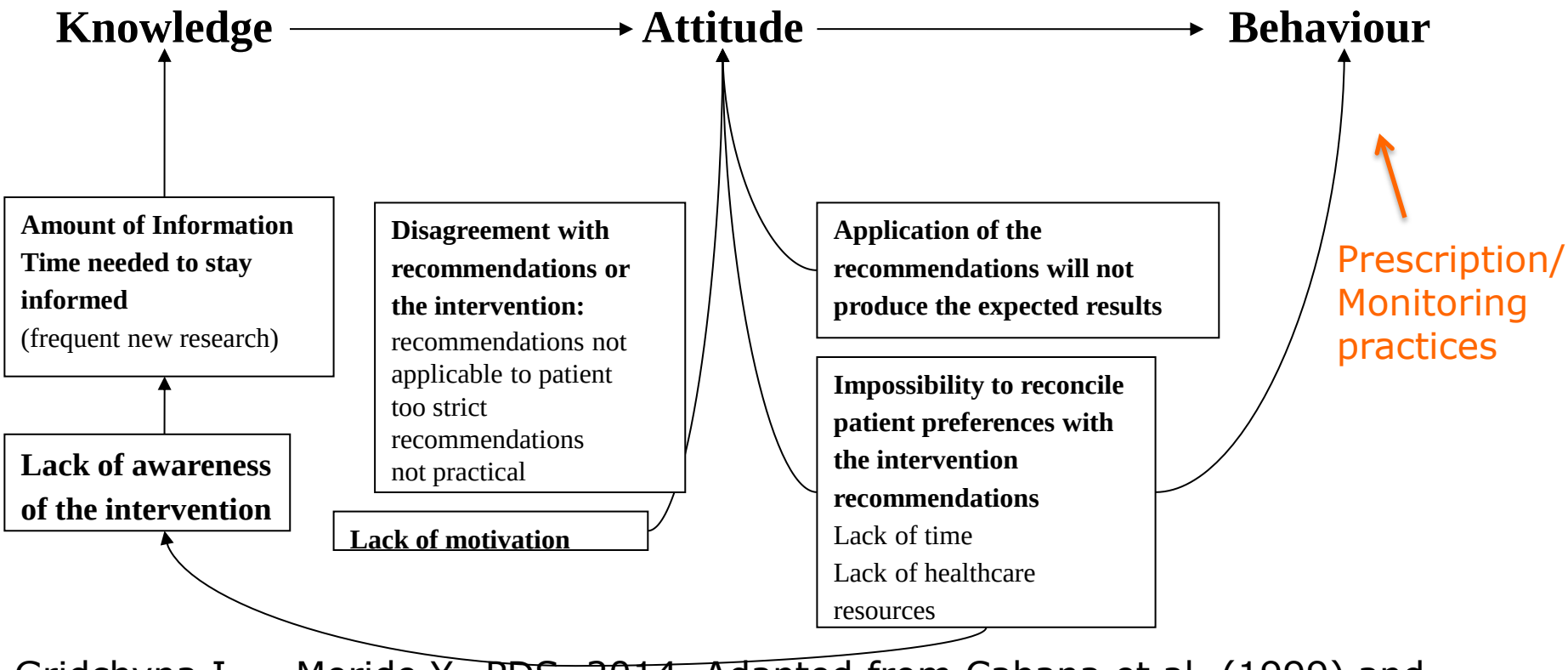
[1] Faculty of Pharmacy, Université de Montreal, Montreal, Quebec, Canada
[2] Pharmacoepidemiology Unit, Research Center, University of Montreal Hospital Center (CRCHUM), Montreal, Quebec, Canada
[3] Department of Patient Safety and Medical Information, AstraZeneca Canada, Mississauga, Ontario, Canada
[4] Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada

In one third of studies, the effectiveness measure did not correspond to aim of intervention

Study not supported by theoretical framework

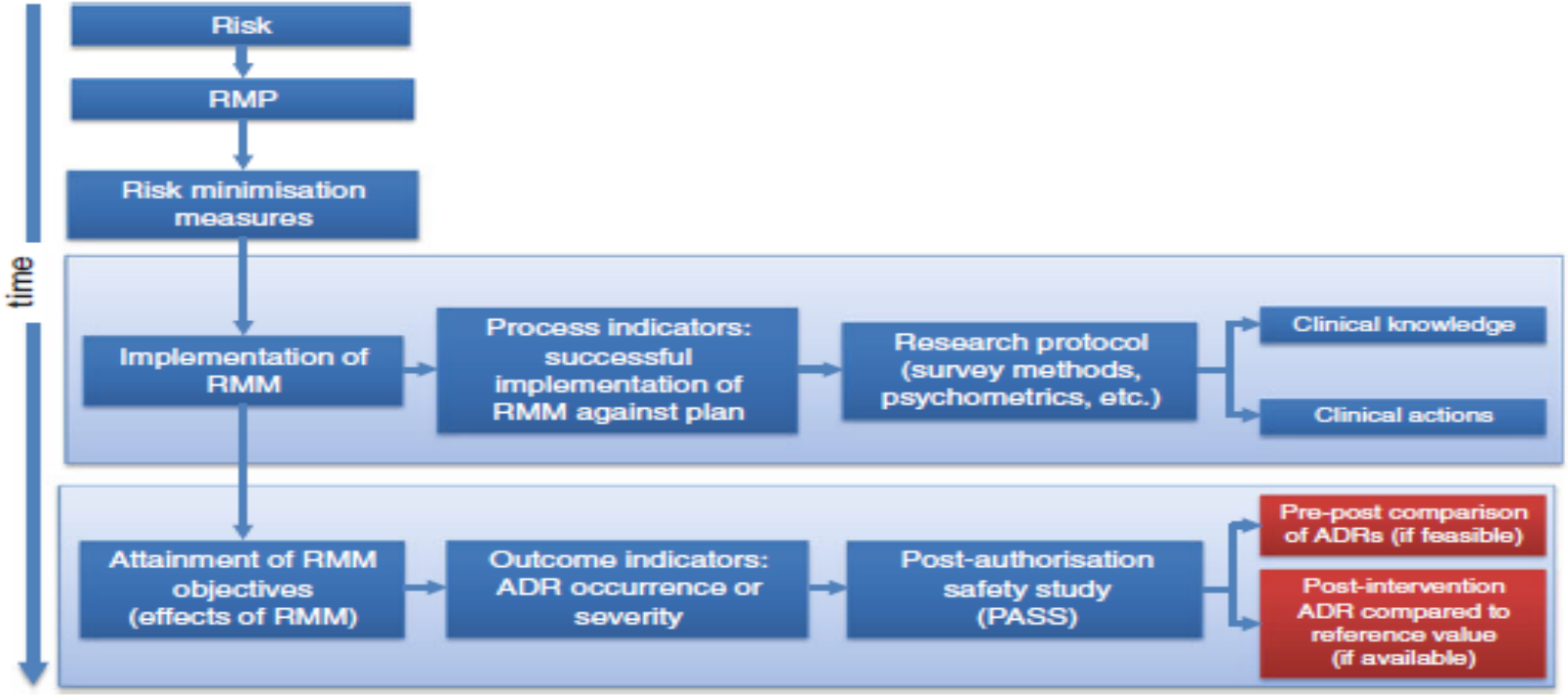
Lack of robust designs

Theoretical framework



Gridchyna I,…, Moride Y., PDS, 2014. Adapted from Cabana et al. (1999) and Hudon et al. (2004)

Integrating different evidence sources



Prieto et al 2012 Drug Safety 21(8) 896-9

Scientific resources –ENCePP

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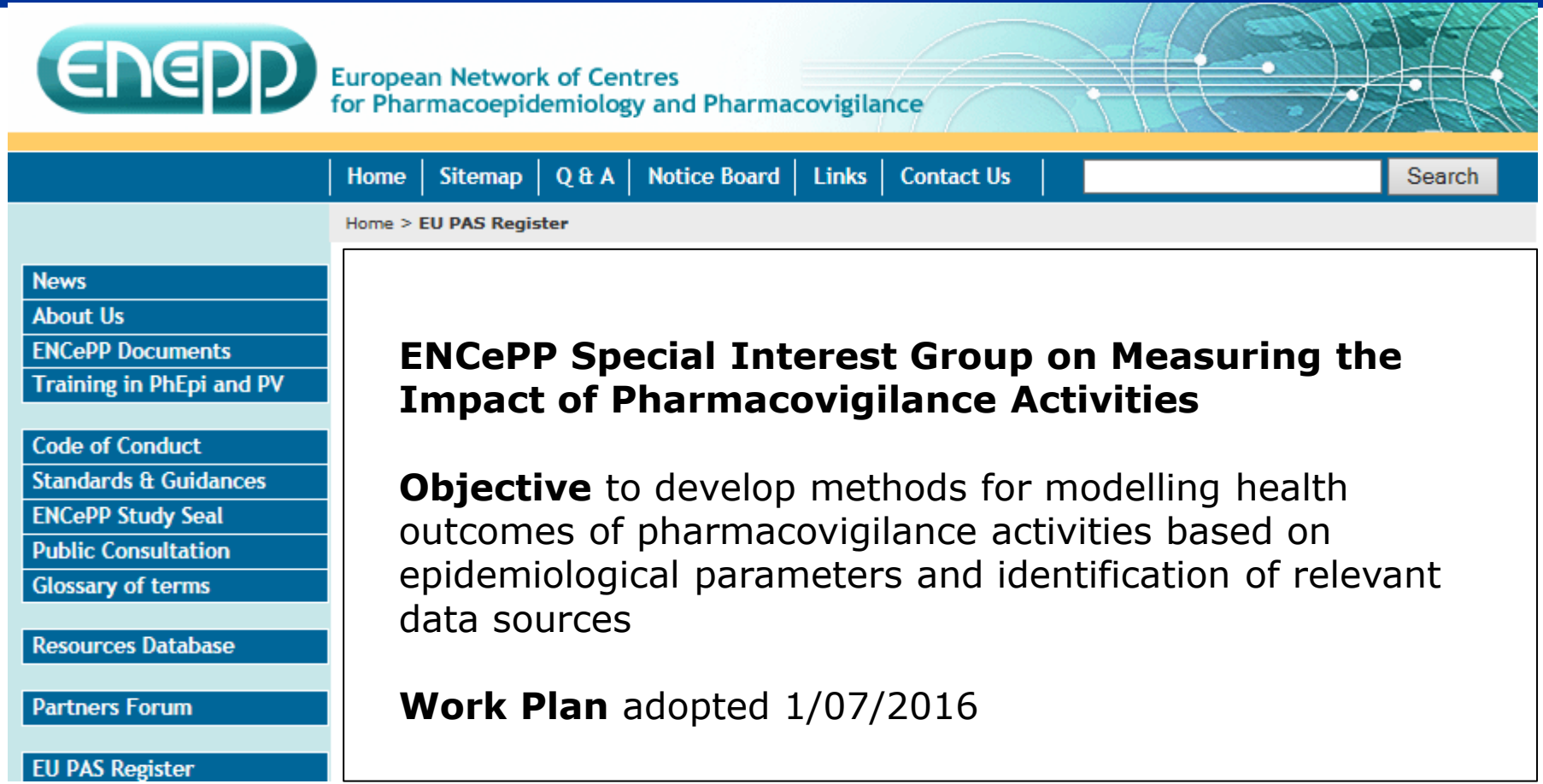

ENCePP Special Interest Group on Measuring the Impact of Pharmacovigilance Activities

Objective to develop methods for modelling health outcomes of pharmacovigilance activities based on epidemiological parameters and identification of relevant data sources

Work Plan adopted 1/07/2016

Patient Alert Card

Infections

Before treatment with Remicade

- Tell your doctor if you have an infection, even if it is a very minor one.
- It is very important that you tell your doctor if you have ever had TB, or if you have been in close contact with someone who has had TB. Your doctor will test you to see if you have TB. Ask your doctor to record the type and date of your last screening(s) for TB on the card.
- Tell your doctor if you have hepatitis B or if you know or suspect you are a carrier of the hepatitis B virus.

During treatment with Remicade

- Tell your doctor straight away if you have signs of an infection. Signs include a fever, feeling tired, (persistent) cough, shortness of breath, weight loss, night sweats, diarrhoea, wounds, dental problems, burning sensation when urinating, or 'flu-like' symptoms.

Heart failure

Before treatment with Remicade

- Tell your doctor if you have any heart problems, such as mild heart failure.

During treatment with Remicade

- Tell your doctor straight away if you notice signs of a heart problem. Signs include shortness of breath, swelling of the feet or changes in your heartbeat.

Please make sure you also have a list of all other medicines that you are using with you at any visit to a healthcare professional.

Keep this card with you for four months after your last dose of Remicade. Side effects may occur a long time after your last dose.

09-15 GAST-1095635-0000
Date of preparation: September 2013

This Alert Card contains important safety information that you need to be aware of before and during treatment with Remicade.

Show this card to any doctor involved in your treatment.

Please read the Remicade 'Package Leaflet' carefully before you start using this medicine.

Date of Remicade therapy initiation: _____

Current administrations: _____

When starting a new card, please keep this card as a reference for four months after this date.

Ask your doctor to record the type and date of last screening(s) for TB below:

Test: _____
Date: _____
Result: _____

List of allergies: _____

List of other medicines: _____

Patient Alert Card

Patient: _____

Doctor: _____

Telephone: _____

Patient Alert Card - infliximab

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Percentage of specialist physicians responding "true" to statement *"HCPs should hand Patient Alert Card to patient before treatment"*

Data from all countries surveyed - 2012			
Rheumatologists	**Dermatologists**	**Gastroenterologists**	**All specialties**
(n=225)	(n=237)	(n=225)	(n=678)
80%	81%	63%	75%
Data from the UK - 2012			
Rheumatologists	**Dermatologists**	**Gastroenterologists**	**All specialties**
(n=30)	(n=30)	(n=30)	(n=90)
87%	80%	77%	81%

EC Shortcomings Report on product information

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Focus on **improvement of PIL** rather than on the SmPC

Guidelines should be revised

Further strengthen **patient input** during PIL development

Showcase **best practice** examples of leaflet design

Explore use of **electronic media**

Consider countries with more than one official language in electronic media strategy

Public engagement

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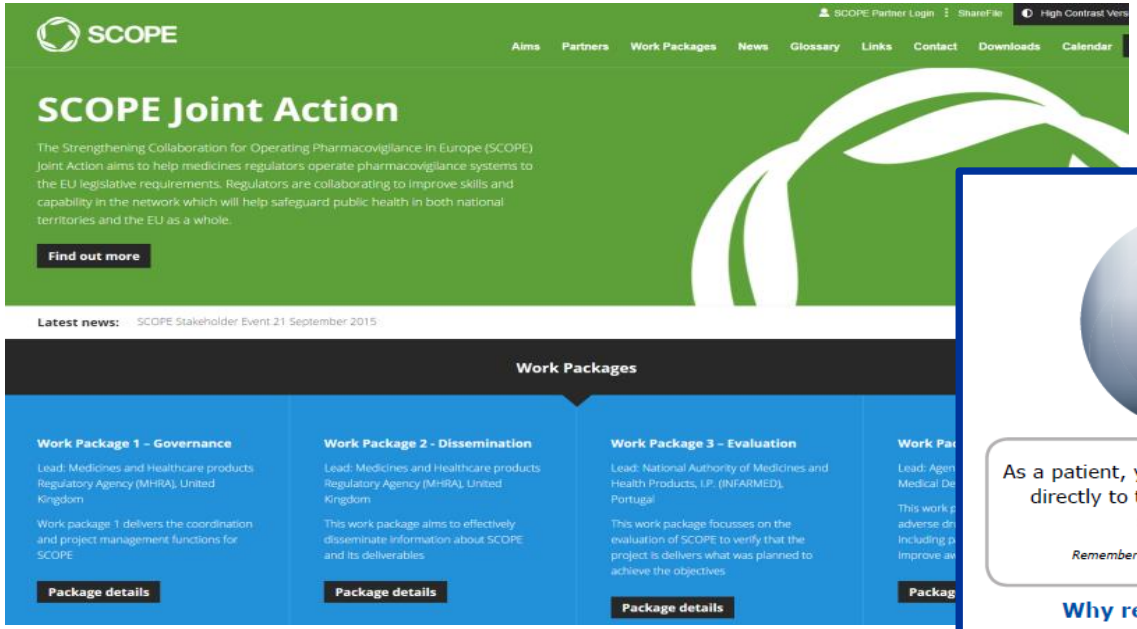
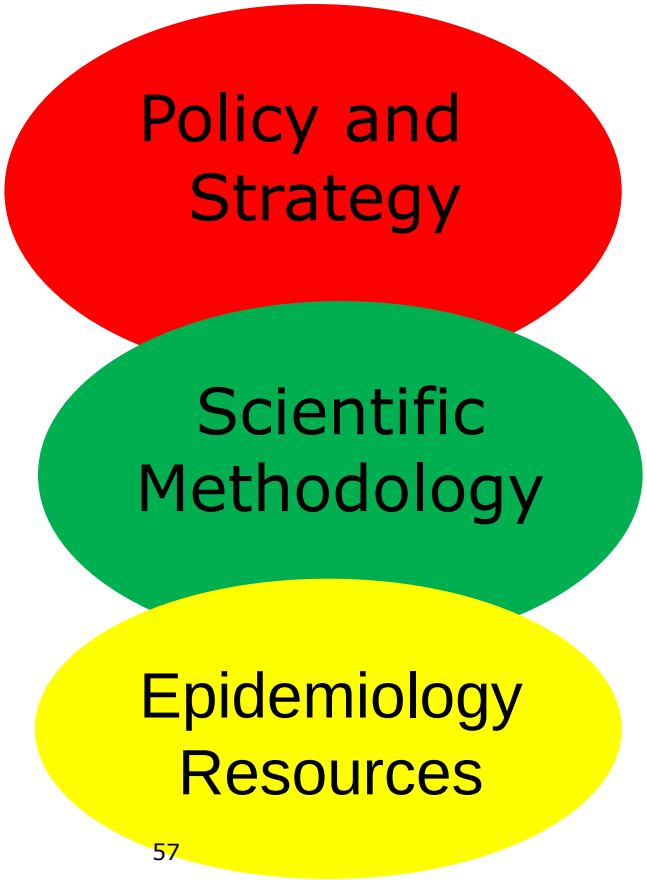
EU ADR Awareness Week 7 -11 November

HMA
Heads of Medicines Agencies



Strengthening Collaborations for Operating Pharmacovigilance in Europe

Measuring impact of regulatory action - conclusion?



Substantial accrued experience in measuring impact of regulatory action

PRAC has a strategic plan to take forward

leveraging existing resources

Methodological and strategic questions remain to be addressed

Stakeholder co-ordination and collaboration essential to progress

Today's regulatory role

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Monitoring benefit risk throughout medicinal product life-cycle

Taking action on safety issues in clinical use to manage and minimise risk

Communicating updated information to healthcare professionals and patients

Systematically monitoring impact of regulatory action

Let’s move forward in collaboration

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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

11 January 2016
EMA/790863/2015
Pharmacovigilance Risk Assessment Committee

PRAC strategy on measuring the impact of Pharmacovigilance activities

Adopted