

# Patient ADR Reporting – UK View

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# Topics to Cover



- ADR Reporting in the UK
- Patient ADR Reporting
- Evaluation of the contribution of patient reporting
- Contribution of patient reports to signals
- Communications with the public
- Future strategies

# Patient reporting in UK



- Yellow Card Scheme (1964, thalidomide tragedy)
  - Voluntary reports submitted of suspicions of ADRs (in confidence) to date >700,000 reports.
- Need for consumer reporting highlighted:
  - Independent Review of access to the Yellow Card Scheme (Metters, 2004)
- Until 2005, only HCPs could report directly
- Patient Reporting Working Group and engagement with patient organisations / charities

# Patient reporting – the beginning



## **When?**

- January 2005 - Pilot scheme for patient reporting introduced

## **How?**

- paper
- internet reporting
- telephone

## **What?**

- all reports welcomed, especially for serious or unlabelled suspected side effects

# Experience from pilot scheme



By end 2007:

- Internal evaluation: Detailed review of reports received during first 6 months of pilot scheme
- 6,000 patient reports received
- Majority received via paper; 31% via the internet
- Similar levels of reports of serious reactions
- Fewer reactions to black triangle drugs
- Less complete reports: but no difference in causality, or proportion of unlabelled reactions
- More information on impact of ADRs on quality of life
- Low levels of consumer awareness of the YC Scheme

# Formal Launch of Patient reporting – 18<sup>th</sup> February 2008



- 6 week campaign, supported by RPSGB
- Community Pharmacies
- Information packs (leaflets, posters)
- Advice & support for patients
- Engaging with patient groups and charities to promote the scheme
- PLUS Media Coverage:
  - - BBC News/Radio
  - - Article in Pharmaceutical Journal

A vertical leaflet for the YellowCard scheme. The top has a yellow header with the 'YellowCard' logo and the tagline 'Helping to make medicines safer'. Below this is a photograph of a blister pack containing several pills. To the right of the photo, the text reads: 'A side effect of your medicine? You can report it using YellowCard'. Below this, it lists reporting methods: 'online at www.yellowcard.gov.uk' and 'or using a Yellow Card form.' It also says 'Pick up a leaflet for more information' and 'This pharmacy supports the Yellow Card Scheme.' At the bottom, it identifies the 'Medicines and Healthcare products Regulatory Agency' and includes the MHRA logo and a small copyright notice: '© Crown Copyright 2008'.

# Updated electronic Yellow Card



- UAT by patient groups
- Easy to complete
- Smart fields
- Registering details (optional)
- Saveable

## Reporting links on:

- NHS Choices
- EMC
- MIMS

# Promotional material



Tear along the dotted line

Confidential

## YellowCard<sup>®</sup> report

Use blue or black ink. Complete all the lines marked with \* and give as much other information as you can

### 1 About the suspected side effect

\* What were the symptoms of the suspected side effect, and how did it happen? If there isn't enough space here, attach an extra sheet of paper.

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

How bad was the suspected side effect? Tick the box that best describes how bad the symptoms were.

\*  Mild  Unpleasant, but did not affect everyday activities  Bad enough to affect everyday activities  Bad enough to see doctor  
 Bad enough to be admitted to hospital  Caused very serious illness  Caused death  Other \_\_\_\_\_

When did the side effect start?

\_\_\_\_\_

How is the person feeling now? Tick the box that best describes whether the person still has symptoms of the suspected side effect.

\*  Better (no more symptoms)  Getting better  Still has symptoms  More seriously ill  Died  Other \_\_\_\_\_

Can you give any more details? For example, did the person take or receive any other treatment for the symptoms? Did they stop taking the medicine as a result of the side effect?

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

### 2 About the person who had the suspected side effect

Who had the suspected side effect?

\*  You  Your child  Someone else

Information about the person Supply as much information as you can, even if you prefer not to give a name.

First name or initials \_\_\_\_\_ Family name \_\_\_\_\_  Male  Female

\* Age \_\_\_\_\_ Weight \_\_\_\_\_  kg  stones/pounds Height \_\_\_\_\_  metres  feet/inches

Any other relevant information? For example, does the person have any medical conditions or allergies?

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Make sure you have completed all the lines marked \*

Please turn over →

### What is the MHRA?

The Medicines and Healthcare products Regulatory Agency (MHRA) is a UK government body. Its principal aim is to protect the public's health. It does this by making sure that medicines and medical devices work properly and are acceptably safe.

When any possible problem is found, the MHRA takes prompt action to protect the public and reduce risk.

For more information about the MHRA:

visit [www.mhra.gov.uk](http://www.mhra.gov.uk)

or telephone 020 7084 2000

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### A side effect of your medicine?

If you have a symptom which you think may be a side effect of your medicine...

- 1 Check the patient information leaflet supplied with the medicine. This lists the known side effects, and advises you what to do.
- 2 Ask your doctor or pharmacist for advice.
- 3 You can report the side effect using Yellow Card, especially if it is not mentioned in the patient information leaflet.

Always talk to your doctor if you have any symptom that worries you.



### How to report a suspected side effect

There are three ways to use the Yellow Card Scheme:

- use the online Yellow Card at [www.yellowcard.gov.uk](http://www.yellowcard.gov.uk)  
This is the easiest way to make a report, if you have access to the Internet.
- ask your pharmacist for a Yellow Card form which you can complete and post
- call the Yellow Card hotline on 0808 100 3352

You can report suspected side effects of any medicine or herbal remedy, whether it was prescribed by your doctor or bought without a prescription.

### What happens to Yellow Card reports?

The MHRA (*see overleaf*) collects Yellow Card reports from people taking medicines, as well as from healthcare professionals such as doctors, pharmacists and nurses.

These reports are used to identify side effects and other problems which might not have been known about before. If a new side effect is found, the MHRA will review the way that the medicine can be used, and the warnings that are given to people taking or using it.

The information you provide will be kept safe, secure and confidential. No details that could identify you will be passed on without your permission.

# YellowCard<sup>®</sup>

Helping to make medicines safer



# Increased accessibility

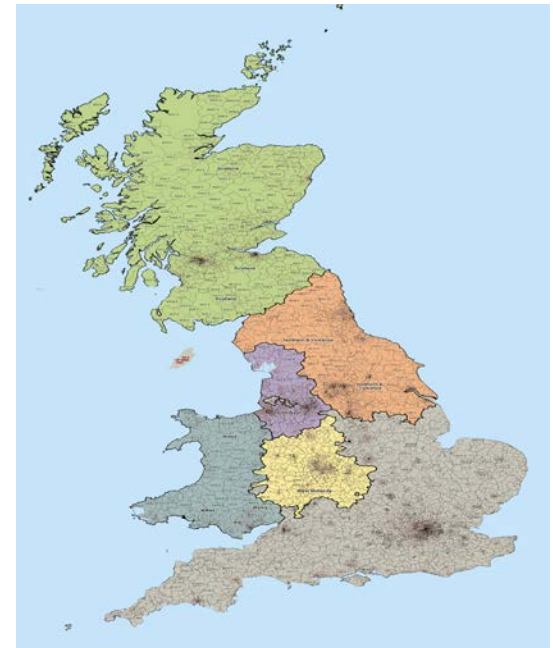


- TV advert for some GP surgeries
- Poster campaign
- Nationwide Leaflet Distribution
- Translation into 10 languages
  
- 5 Regional Centres for promotion
  - Scotland (Edinburgh)
  - Wales (Cardiff)
  - West Midlands (Birmingham)
  - Northern and Yorkshire (Newcastle)
  - North West (Liverpool)
- Education / awareness - patient groups
- Conferences

**YellowCard**  
Helping to make medicines safer

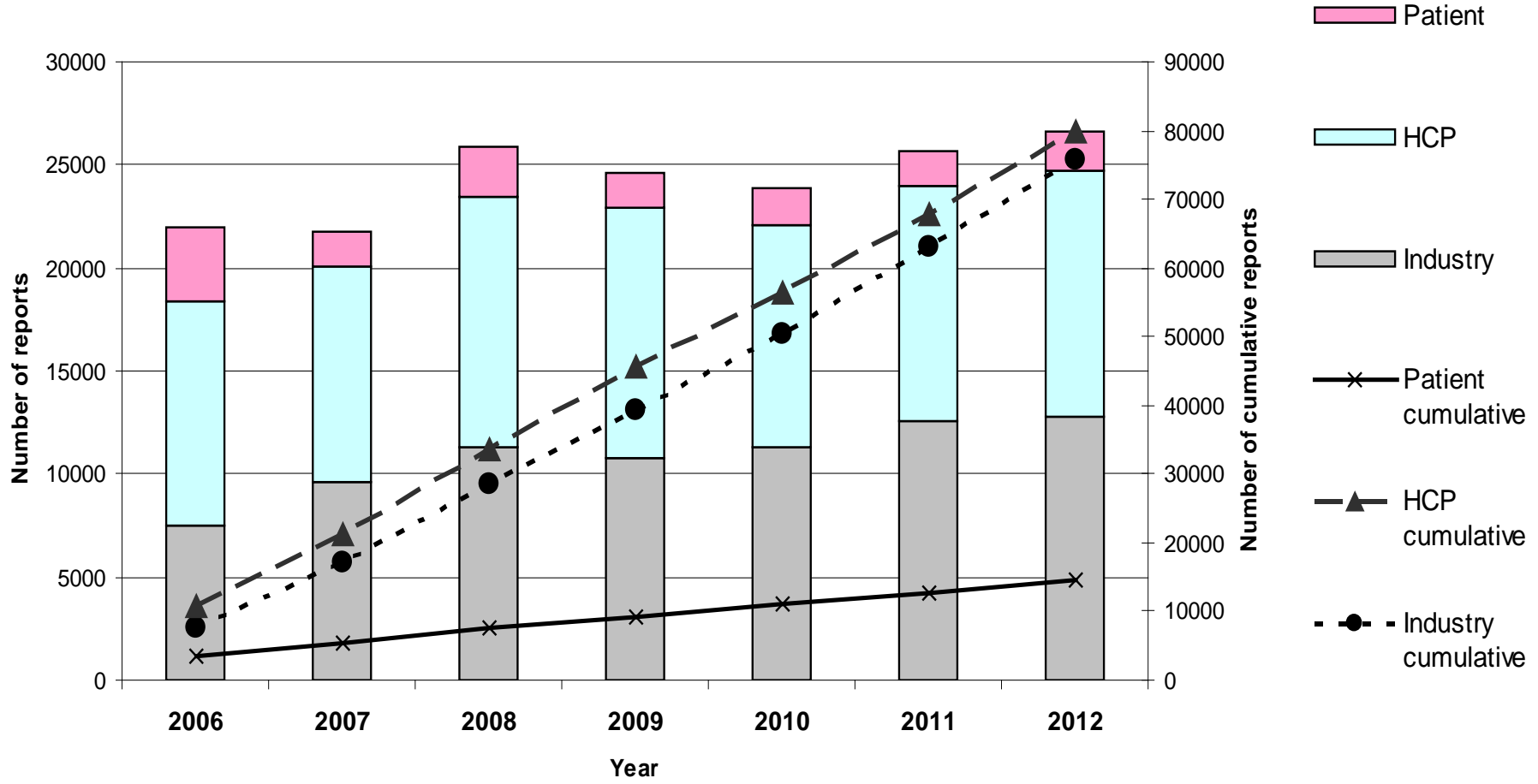
Information in other languages:

<a href="#">Cymry</a>	<a href="#">العربية</a>	<a href="#">বাংলা</a>	<a href="#">官话</a>	<a href="#">čeatina</a>	
<a href="#">Polski</a>	<a href="#">Português</a>	<a href="#">ਪੰਜਾਬੀ</a>	<a href="#">Русско</a>	<a href="#">Slovincina</a>	<a href="#">أردو</a>



# Overall ADR Reporting trends (2006 to 2012) MHRA

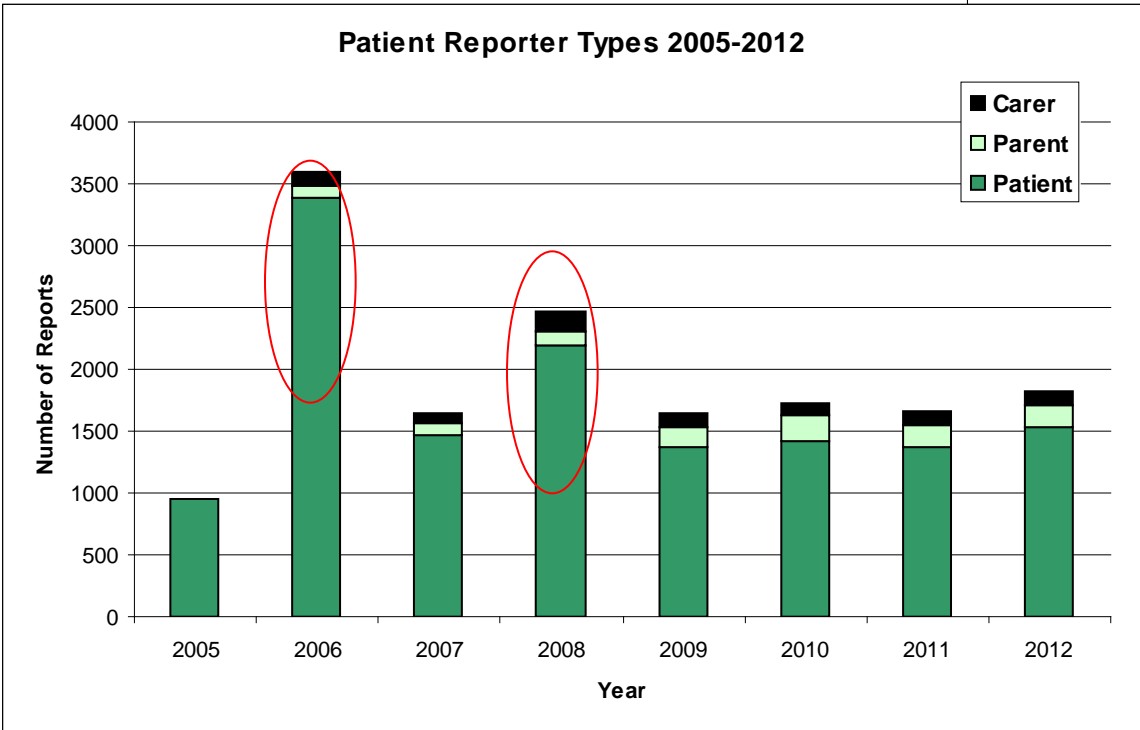
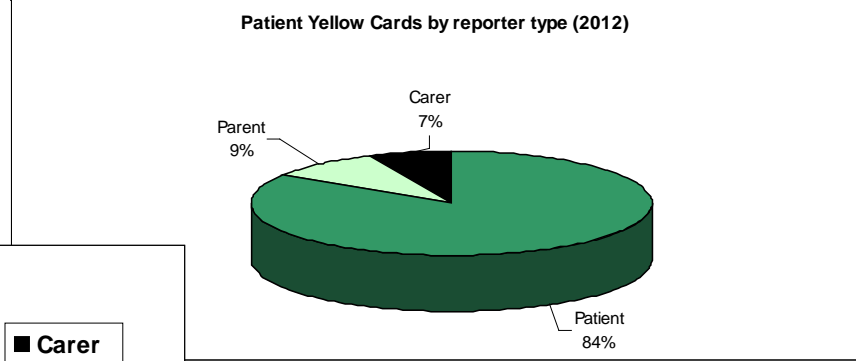
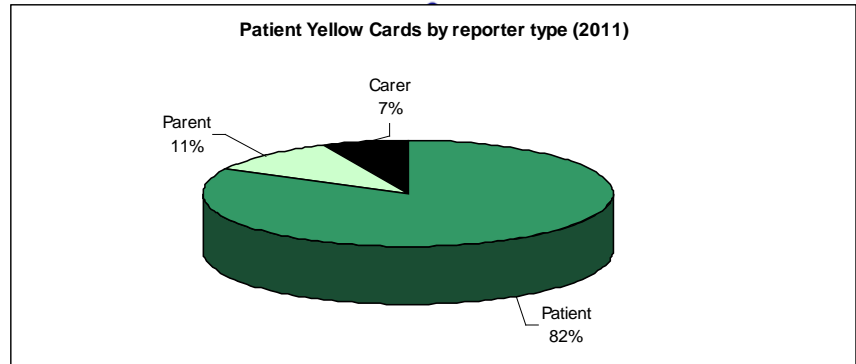
Spontaneous ADR reporting by source 2006-2012



Yellow Card Statistic	2011	2012	Trend
Total number of reports	25,691	26,568	↑
Serious reports	87%	87%	↑
Fatal reports	6%	7%	↑
Industry reports	49%	48%	↓
Patient reports	6%	7%	↑
Direct reports	51%	52%	↑
Direct serious reports	83%	84%	↑
Direct electronic reports	58%	67%	↑
Most reported drug	Clozapine (15%)	Clozapine (10%)	-
Most reported vaccine	HPV (44%)	HPV (38%)	-
Most reported drug & reaction pair	Clozapine / neutropenia (1%)	Clozapine / neutrophil count decreased (1%)	-
Reports in <18s	10.6%	9.2%	↓
Gender: M:F:unknown	41% : 54% : 5%	41% : 53% : 6%	- male ↓ female ↑ unknown
Most reported age group	55-64 years	65-74 years	↑ in age group

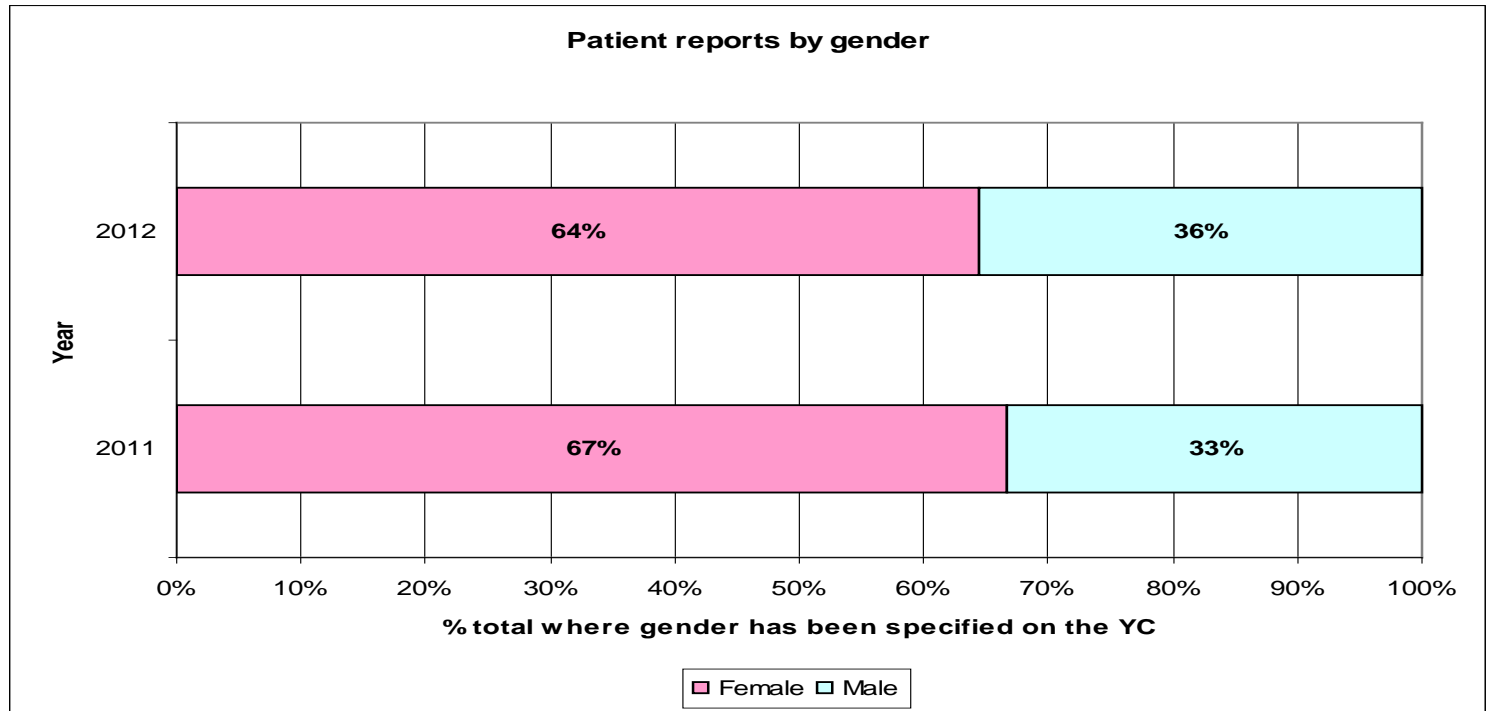
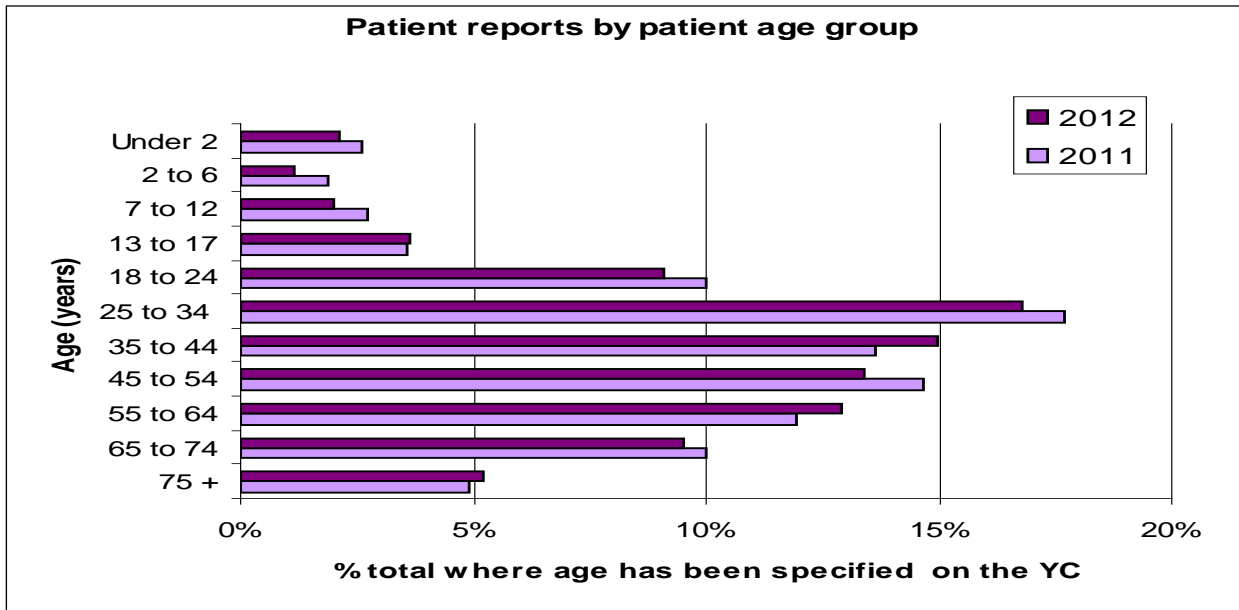
# Patient reporting

- Proportion of total reports:
- 6% 2011 & 7% (2012)
  
- Proportion of serious reports: 84% (2011 and



> 81% report themselves

# Patient reporting



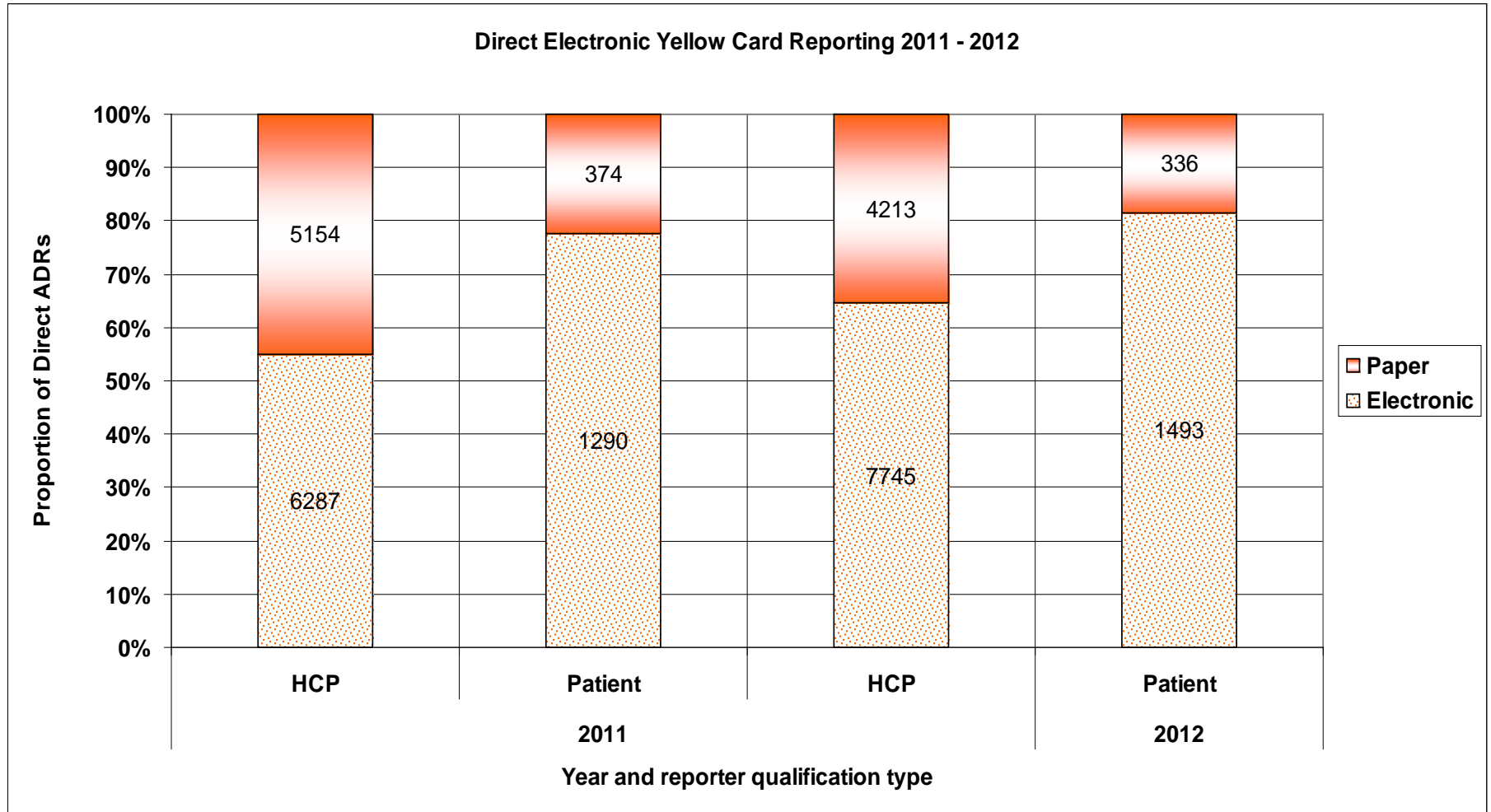
**Gender**

# Electronic reporting



82% eYC patient reports in 2012; 4% ↑

62% direct eHCP reports– 10% ↑

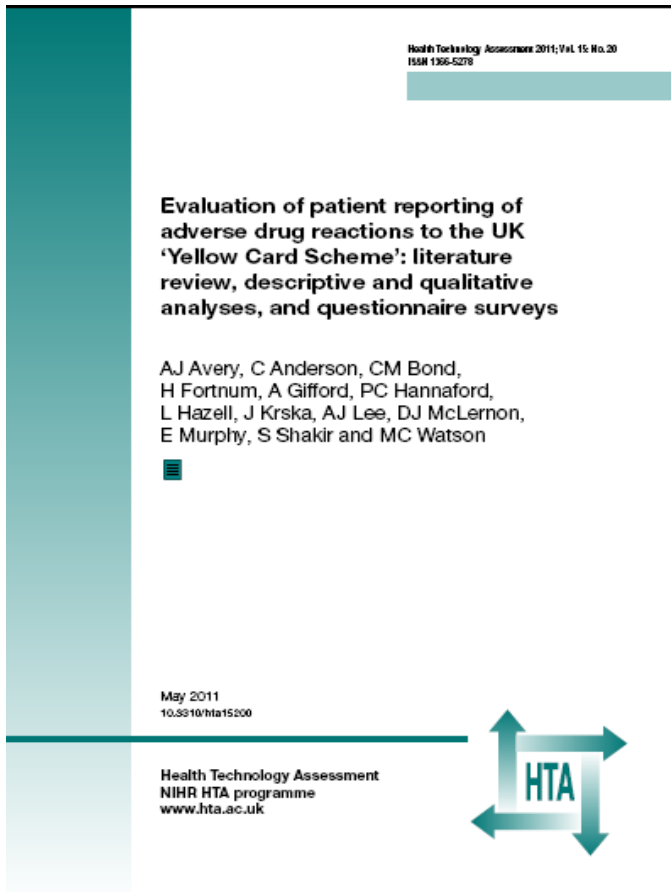


# Drug-Reaction Combinations MHRA 2012

HCP Drug-Reaction combinations				Patient Drug-Reaction combinations			
Drug substance	ADR term (*Serious PT)	No. reports	% Total HCP reports	Drug substance	ADR term (*Serious PT)	No. reports	% Total patient reports
Sevoflurane	Procedural vomiting	214	1.6	Varenicline	Depression*	23	1.3
HPV	Dizziness	164	1.2	HPV	Fatigue	23	1.3
Propofol	Procedural vomiting	164	1.2	HPV	Headache	22	1.2
Codeine	Constipation	142	1.0	Desogestrel	Depression**	19	1.0
Morphine	Pruritus	124	0.9	Levothyroxine	Fatigue	18	1.0
Morphine	Procedural vomiting	111	0.8	Levothyroxine	Product substitution issue	17	0.9
Varenicline	Nausea	104	0.8	HPV	Dizziness	15	0.8
Varenicline	Depressed mood *	102	0.7	Desogestrel	Anxiety	13	0.7
Nitrous Oxide	Procedural vomiting	100	0.7	Varenicline	Nausea	13	0.7
HPV	Headache	91	0.7	Co-cyprindiol	Depression*	13	0.7

**Vaccines: make up 7% all reports in 2012; 9% patient reports**

\* - serious PT; \*\*Signal – RMS - Sweden



- Higher median number of ADRs per patient report than HCPs and more detailed description
- Similar proportion of “serious” reports
- More signals when combined HCP and patient reports - 47 new serious  
Some signals in HCP only set were lost but fewer than those gained
- Different patterns of drugs and reactions reported by patients

- *Avery et al 2011 HTA; vol 15; no 20*



# Signal Detection Methodology



Empirica Signal used for analysis and data provision:

- Empirical Bayes Geometric Mean (EBGM) routine statistic of disproportionate reporting (SDR) since 2006. PRR used since 1996, and still computed alongside EBGM.
- Statistic calculated and analysed weekly for all products
- Drugs/ Vaccines analysed separately
- Patient & HCP reports analysed together

# Timelines for signal review



## **2011/2012 Agency Signal target:**

- Ensure all potential UK signals (relating to medicines and vaccines) from whatever source are acted on promptly: 80% initially evaluated within 5 working days

Evidence based tools for further evaluation of signals:

## **Impact Analysis**

- This is a tool to prioritise possible signals and decide the next step that should be taken. This takes into consideration the strength of evidence as well as the public health implications of the signal.

## **RPPS**

- The Regulatory Pharmacovigilance Prioritisation System. This is further signal prioritisation also taking into account public perception of the ADR and Agency obligations.

# Signals investigated in 2011 & 2012



- In 2011 - 138 signals identified
- In 2012 - 68 signals identified
  
- In total 69 ADR reports from the members of the public contributed towards all signals raised in 2011 & 2012.
  
- 11 of these signals were initiated after receiving a report by a member of the public
  
- Some examples include:
  - Leuprorelin & injection site reactions
  - Varenicline & epilepsy
  - Erlotinib & pancreatitis
  - Saxagliptin & anaphylactic reaction
  - Panitumumab & folliculitis

# Regulatory Action & Communication



- Updating product information (SPC/PIL)
- Restrict indications / introduce new contra-indications / reduce the recommended dose
- Warnings in Drug Safety Update
- Inform rapporteur/RMS
- Raise in PSURs



Latest advice for medicines users

The monthly newsletter from the MHRA and its independent advisor, the Commission on Human Medicines

Volume 6, Issue 9, April 2013

## Contents

Drug safety advice	Insulin degludec (Tresiba ▼): available in additional higher strength than existing insulins—care needed to minimise risk of error, including training for patients	A1
	Cilostazol (Pletal): risks of cardiovascular and bleeding events—indication restricted to second-line treatment and contraindicated with some cardiovascular conditions and medicines	A2
Hot topic	Recent drug-name confusion: please be vigilant as life-threatening errors may occur	H1
Stop press	Strontium ranelate (Protelos): risk of serious cardiac disorders—restricted indications, new contraindications, and warnings	S1

- Most importantly: Who should receive any communications?
- Proactive communication?

*Article 107*

1. Marketing authorisation holders shall record all suspected adverse reactions in the Union or in third countries which are brought to their attention, whether reported spontaneously by patients or healthcare professionals, or occurring in the context of a post-authorisation study
2. Marketing authorisation holders shall not refuse to consider reports of suspected adverse reactions received electronically or by any other appropriate means from patients and healthcare professionals.

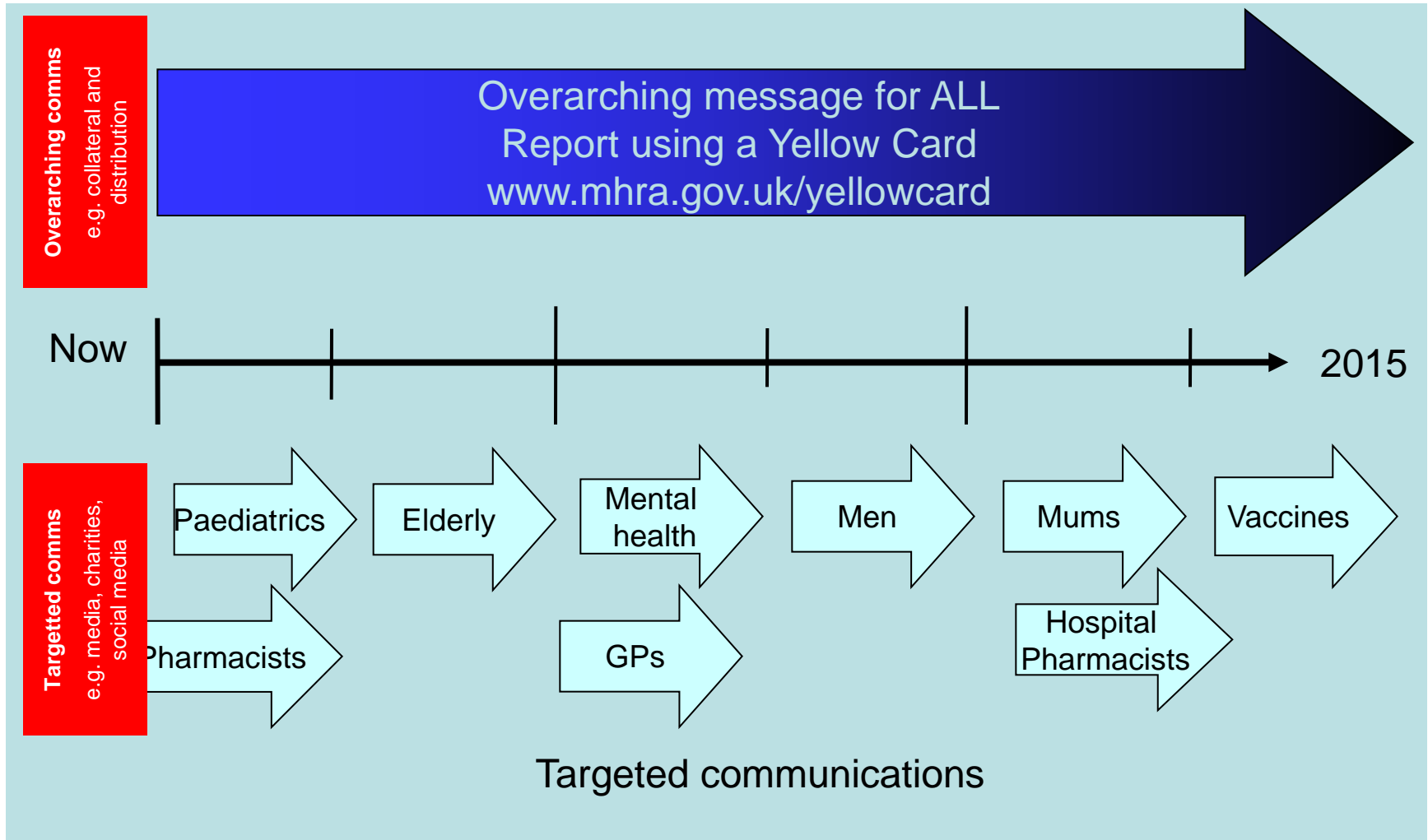
# Encouraging reporting



- *Article 102*
- The Member States shall:

- (a) take all appropriate measures to encourage patients, doctors, pharmacists and other healthcare professionals to report suspected adverse reactions to the national competent authority; for these tasks, organisations representing consumers, patients and healthcare professionals may be involved as appropriate;

# Overarching strategy





# Yellow Card Paediatric Strategy



- Targeted messages around importance of understanding ADRs in Children
- Targeted to where children are the focus of healthcare i.e. paediatricians; paediatric nurses; specialist hospitals
- Use specialist channels to relay messages i.e. mums.net; CharityChoice
- Strengthen messages through academic & professional bodies i.e. RCPCH; BPSU; MCRN

Initiatives under consideration:

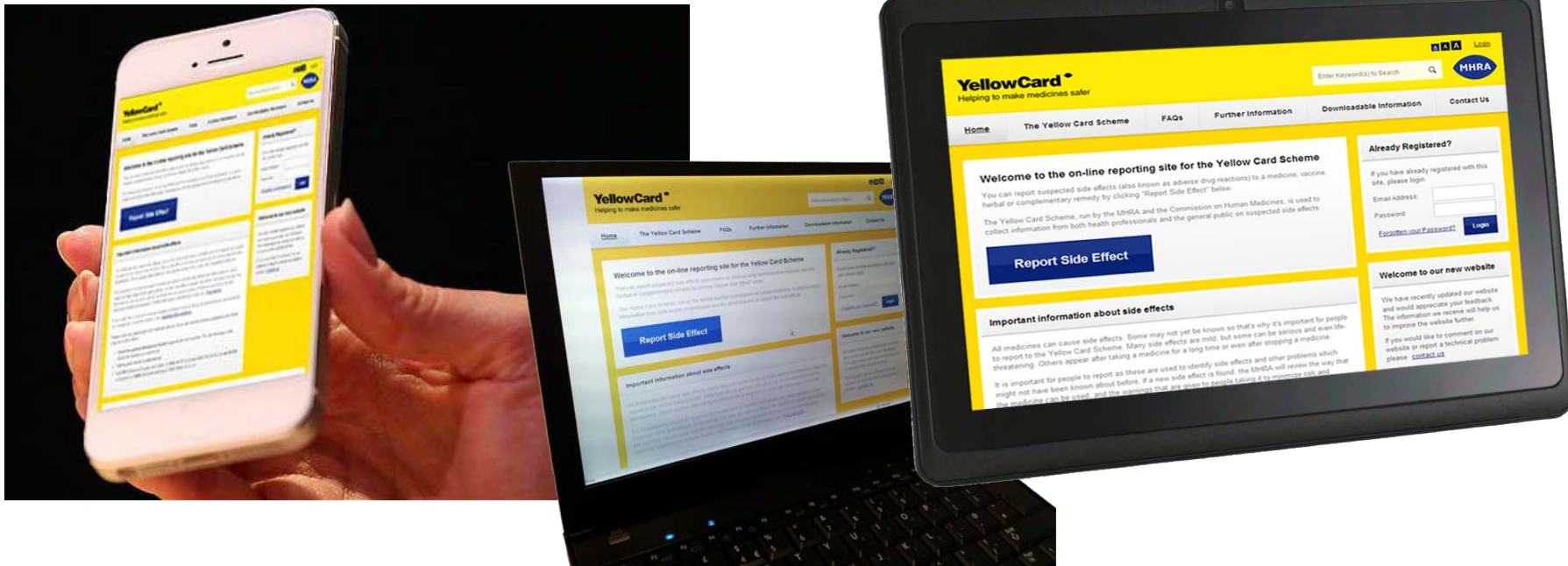
- Children's ADR reporting portal
- Focus on ADRs in children in Drug Safety Update and DSU for the public
- Yellow Card champions in all Trusts & a focus on paediatrics

# Yellow Card App



–Facilitation of Yellow Card reporting through development of Apps

- Initial development of website formatted for smart phones and tablets
- Development of Yellow Card mobile app



# Summary



- Every Yellow Card submitted is important to us
- Numbers of patient reports very encouraging– 100% increase since 05
- Promotion directly impacts on reporting
- Excellent move towards electronic reporting (82%)
- High quality – descriptive reporting, impact on patient QoL
- Positive contribution to signal detection

# Questions

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