Adverse Events Following Immunisation

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Waterford, Aug. 25, 2016

Abbreviations

- **ADR**-adverse drug reaction
- **AE-** adverse event
- **AEFI**-adverse event following immunisation
- **SAE-** serious adverse event
- **SUSAR**-suspected unexpected serious adverse reaction

Definitions

- **Adverse Drug Reaction**
  - A response to a drug which is noxious and unintended, …occurs at doses normally used for the prophylaxis,.. or therapy of disease, …

- **Adverse Event**
  - Any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment

Definitions

Adverse Event Following Immunization (AEFI)

Any untoward medical occurrence which follows immunisation and which does not necessarily have a causal relationship with the usage of the vaccine.

The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.

AEFI

1. Loose definition to encourage reporting
   - does not restrict type of event
   - does not limit the time after immunisation
   - events, not reactions, are reported

2. Belief that immunisation was responsible
   may be correct, incorrect, or impossible to assess

3. Does not imply causality

AEFIs

Mild Reactions

- Common
- Include pain, swelling, fever, irritability, malaise
- Self-limiting, seldom requiring symptomatic treatment

But - important to inform parents about such events so they know about them

Serious Adverse Event

- Fatal
- Life-threatening
- Permanently/significantly disabling
- Requires hospitalisation
- Causes a congenital abnormality
- Requires intervention to prevent permanent impairment or damage

Frequency of Reactions

- Very common…….. >10%
- Common……..1-10%
- Uncommon……1/100-1/1,000
- Rare……..1/1,000-1/10,000
- Very rare……<1/10,000

Known AEFIs

More Common (>1 in 100)	Less Common (<1/100)
• Redness • Swelling, nodule • Pain • Fever, irritability, loss of appetite, nausea, D+V	• Encephalitis • Paralysis • Arthritis • Allergic reaction • Thrombocytopoenia • Febrile seizure • Fainting •Narcolepsy • Death

What is “Less Common”?

Frequency of known injury*	What else is this common?
1/1,000 to 1/100,000 – Fainting or collapse – Febrile seizure – Thrombocytopoenia	Having quadruplets
1/100,000 to 1/1,000,000 – Serious allergic reaction – Arthritis	Getting struck by lightning
>1 in a million – Encephalitis – Paralysis – Death	Winning the lottery

*highest rate for any childhood vaccine

Febrile Seizures and Vaccines

- Influenza, DTaP, PCV vaccines given together - febrile seizures in up to 30/100,000 immunised
- If you vaccinate 1000 children <5 including 300- 500 between 6 and 24 months of age annually
- Expect to see at most 1 febrile seizure every 5 to 10 years
- 30 to 75 of the vaccinated children would get febrile seizure from other causes
- Not vaccinated – may get illnesses

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Febrile Seizures and Vaccines

- Febrile seizures - frightening, sequelae rare
- Giving vaccines simultaneously – less visits, pain, irritability
- Assurance that children fully immunized and protected
- Missed vaccines may never be administered
- Infections may → serious illness, seizures.

What Causes AEFIs?

Vaccine – due to vaccine's inherent properties

Programme, administration

Injection reaction - anxiety or pain of injection

Unknown - cause cannot be determined

AEFIs: potential sources

- Manufacturing potency issues
  - over-attenuation of live vaccines
  - instability over time
  - reconstitution, mixing interferences
- Storage issues
- Administration issues
  - technique
  - concomittant administrations
- Patient profile
  - age, weight
  - immune deficiency e.g. AIDS
- Environmental
  - epidemiology: strain variation

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Timing of Vaccine Reactions

- **Inactivated vaccines**: generally within 48hrs

- **Live vaccines**: according to time for virus to replicate

  MMR:

  -measles (malaise, fever, rash) in 6-11 days

  -rubella (pain, stiffness, arthritis) in 2nd week

  -mumps (parotid swelling) in 3rd week
  (up to 6 weeks)

Pertussis

Pertussis Complications

Condition	%
• Pneumonia (12% in infants <6/12)	5
• Convulsions	1.4
• Encephalopathy	0.2
• Death (83% <3/12)	0.2
Hospitalisation	30

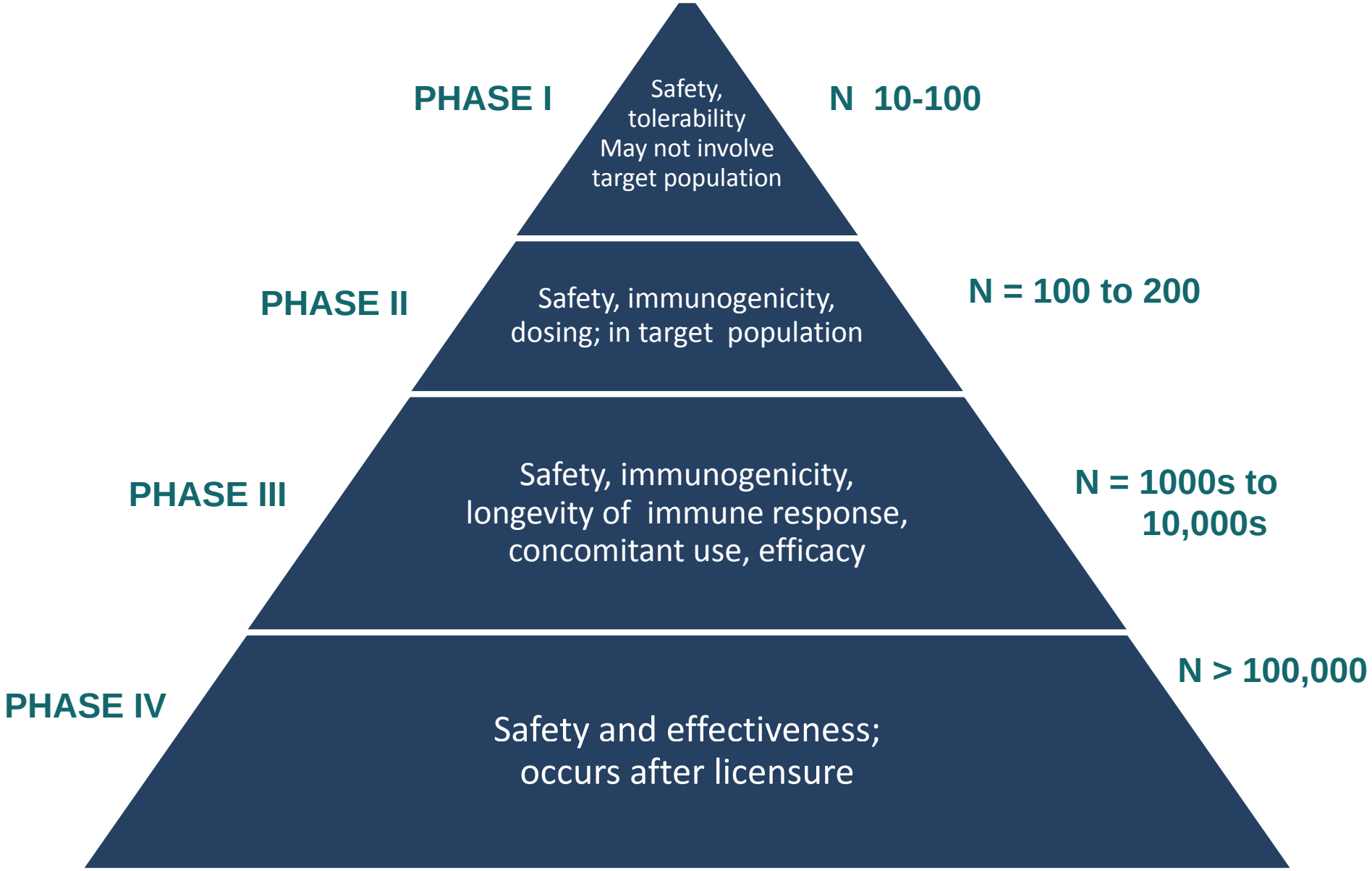
Pertussis Vaccine

Reaction	DTwP	DTaP
• Pain	25	9
• Cry>3 hrs	0.4	0.04
• High fever	0.24	0.04
• Convulsion	0.02	0.007
• Death		0

Presenting Risk Information

1. “A serious reaction occurs about 1 to 3 times per 10,000 doses”
2. “About 1 to 3 children out of 10,000 will experience a serious reaction”
3. “This vaccine rarely causes serious reactions - about 1 to 3 children out of 10,000 who receive it”
4. “This vaccine is very safe - 9,997 children out of 10,000 who receive it will experience no adverse reaction”

Vaccine Safety Studies



Number of subjects needed to test for increased relative risk of an adverse event

	Rate In Vaccinated Population		
Background rate, general population	**2-fold higher**	**10-fold higher**	**100-fold higher**
1 in 10,000	141,000	5,500	500
1 in 100,000	1,238,000	53,500	2,500
1 in 1,000,000	12,951,500	532,500	23,500

Risk always phrased as “less than 1 in X”

Evans D et al. J Infect Dis. 2009;200:321-8.

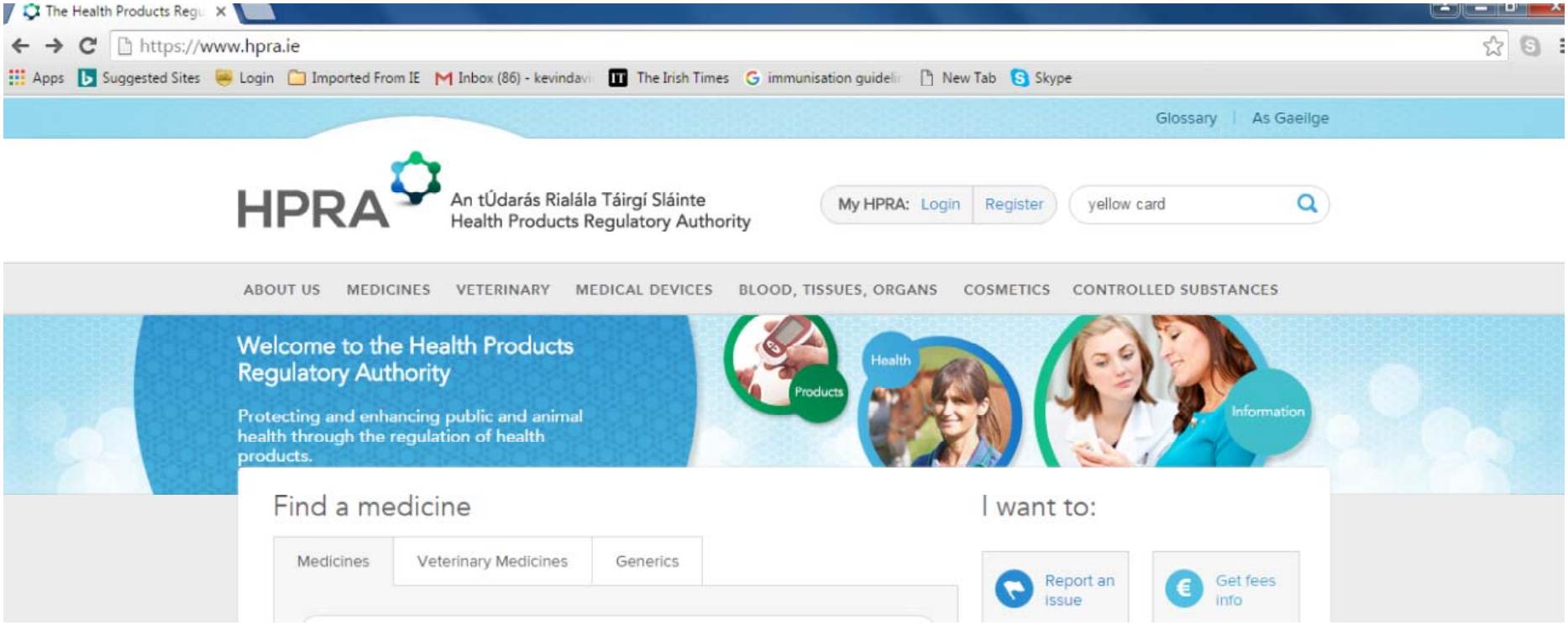
Why Monitor AEFIs?

- No vaccine is 100% safe
  - Safety profile established in pre-licensure trials
  - Detectable frequency depends on numbers studied
    - (rule of 3)
  - Rare events require huge numbers
- Risk / benefit balance changes over time
  - as incidence falls: VAPP
  - as Society becomes more critical

Reporting AEFIs

- 1-10% are reported
- Up to 99% are not reported
- Safety is provisional at time of licencing-
  Rotashield, Vioxx, Pandemrix, HRT, etc
- If in doubt, write one out
- Every report is important

Reporting AEFIs



- How We Regulate
- Our New Name
- Contact Us
- Our Structure
- Standards of Service
- Independence and transparency
- Consultations
- Quality Management
- Recruitment
- Publications & Forms
- Report an Issue
  - Human Medicines

Report an Issue

Reporting Safety and Quality Concerns

If you are concerned that you have had a side effect to a medicine, or experienced a problem with any other type of healthcare product regulated by the HPRA, you may need to contact your healthcare professional who can advise on any treatment that may be needed. They can also report the issue to the HPRA on your behalf.

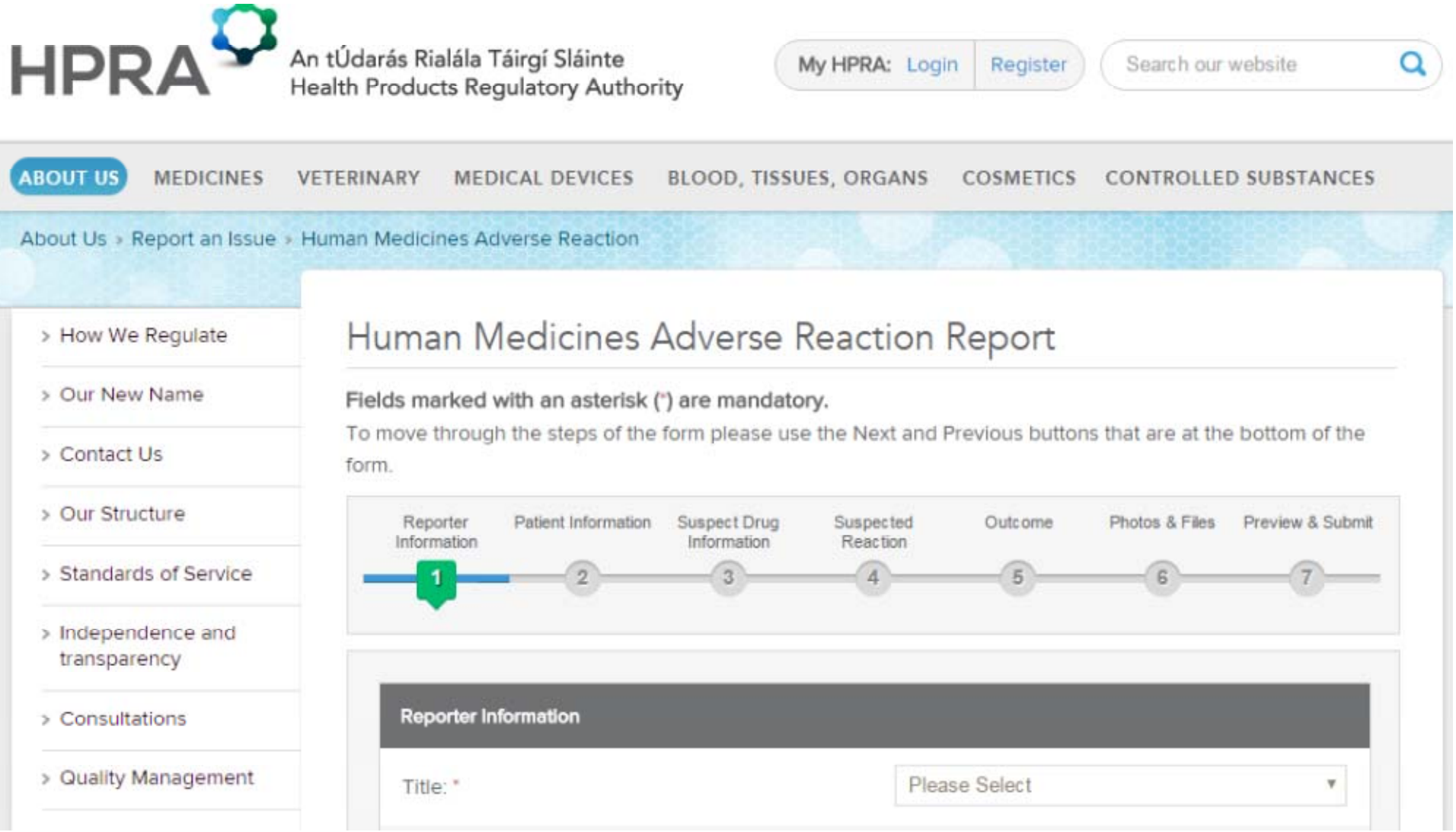
If you wish to directly report issues relating to the use or quality of healthcare products you can use the HPRA's online reporting service. Anyone can report issues relating to the safety and quality of healthcare products to the HPRA. This includes patients, carers, other members of the public and healthcare professionals.

Please note that in completing a report form, we understand that you are consenting to the information provided, including your contact details, to be stored securely by the HPRA. Your contact details will be used solely for the purposes of interaction with you regarding the report submitted. For the purposes of complying with our statutory and legal reporting requirements, summary details of this report (excluding personal information) may be shared with other bodies also involved in monitoring activities in accordance with HPRA obligations and data protection requirements. This ensures that the information is available to all relevant parties. The right exists to request a copy of personal data held by the HPRA and to have any inaccuracies in such data corrected or deleted.

Online Report Forms

The following forms can all be completed using the HPRA online reporting system:

Human Medicine Adverse Reaction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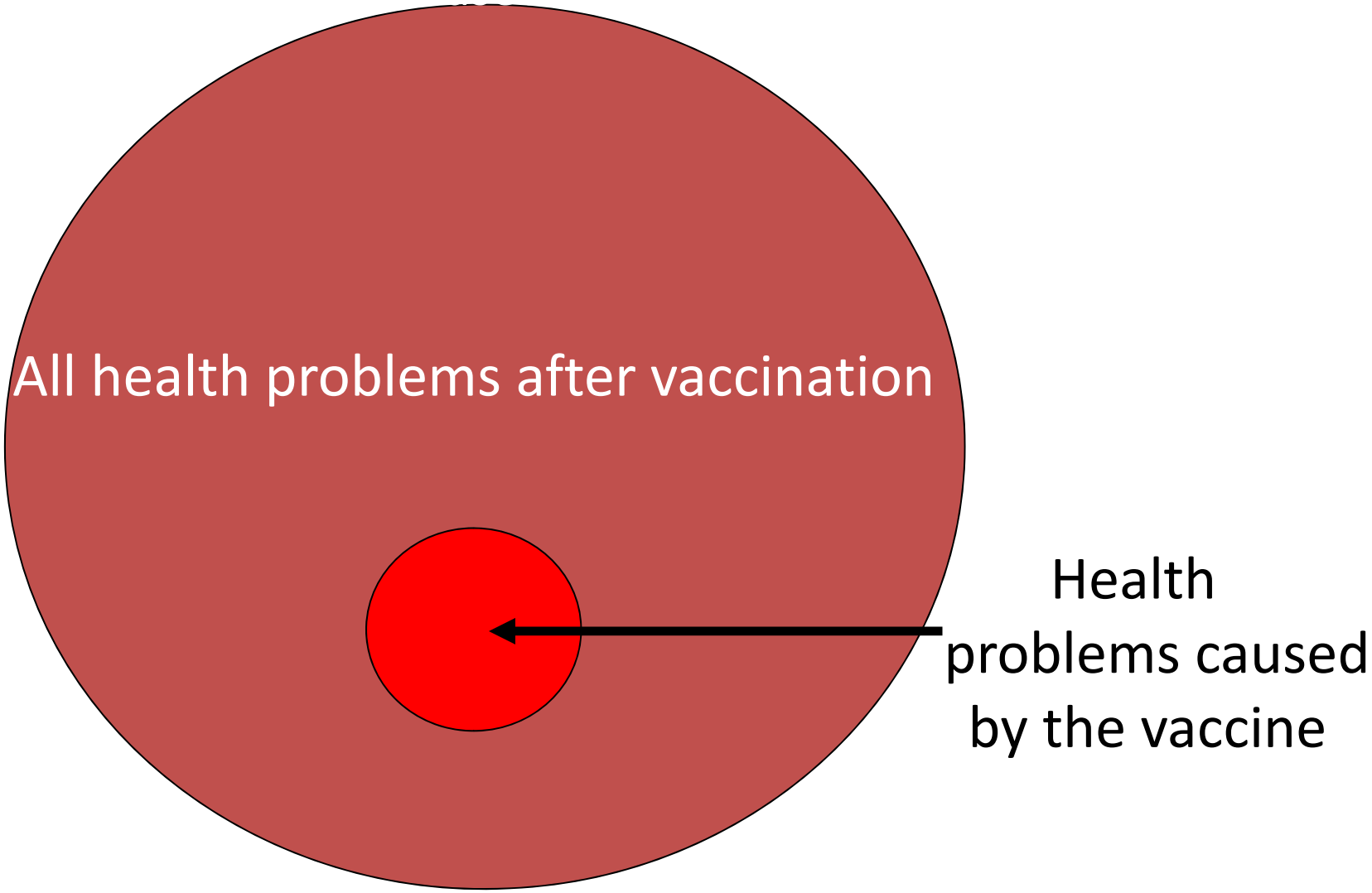
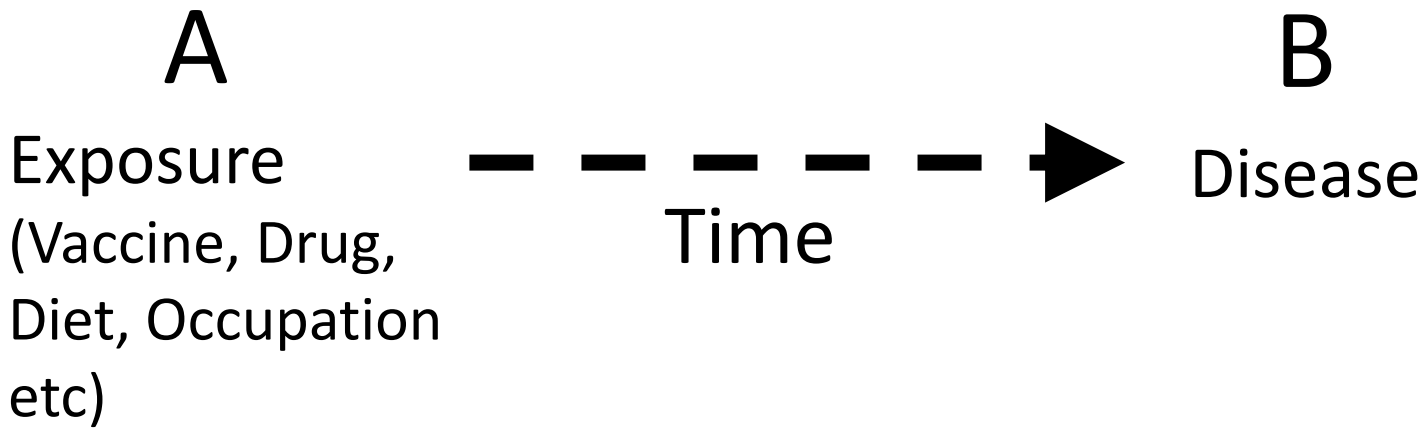
How We Regulate
Our New Name
Contact Us
Our Structure
Standards of Service
Independence and transparency
Consultations
Quality Management
Human Medicines Adverse Reaction Report
Fields marked with an asterisk (*) are mandatory.
To move through the steps of the form please use the Next and Previous buttons that are at the bottom of the form.
Reporter Information
Patient Information
Suspect Drug Information
Suspected Reaction
Outcome
Photos & Files
Preview & Submit
1
2
3
4
5
6
7
Reporter Information
Title: *
Please Select

AEFI-Coincidence or Vaccine Injury?



Coincidence or Cause?
Is Sequence Consequence?

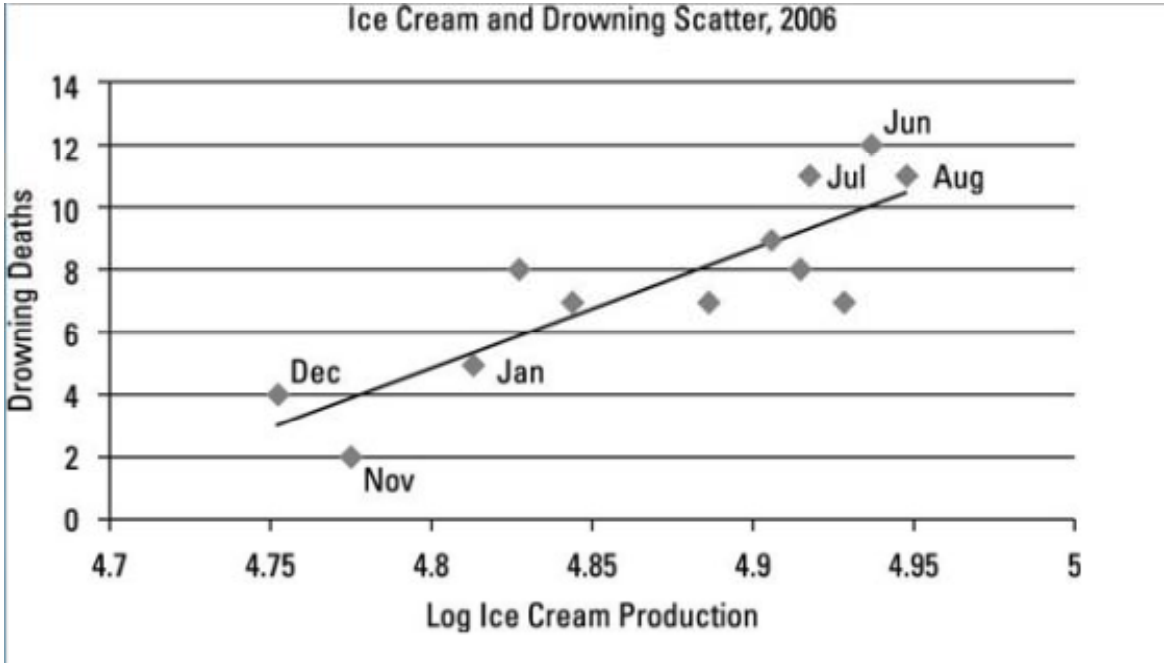


- Direct and only cause?
- One of multiple potential causes?
- Co-factor/indirect cause, trigger?
- Coincidental?

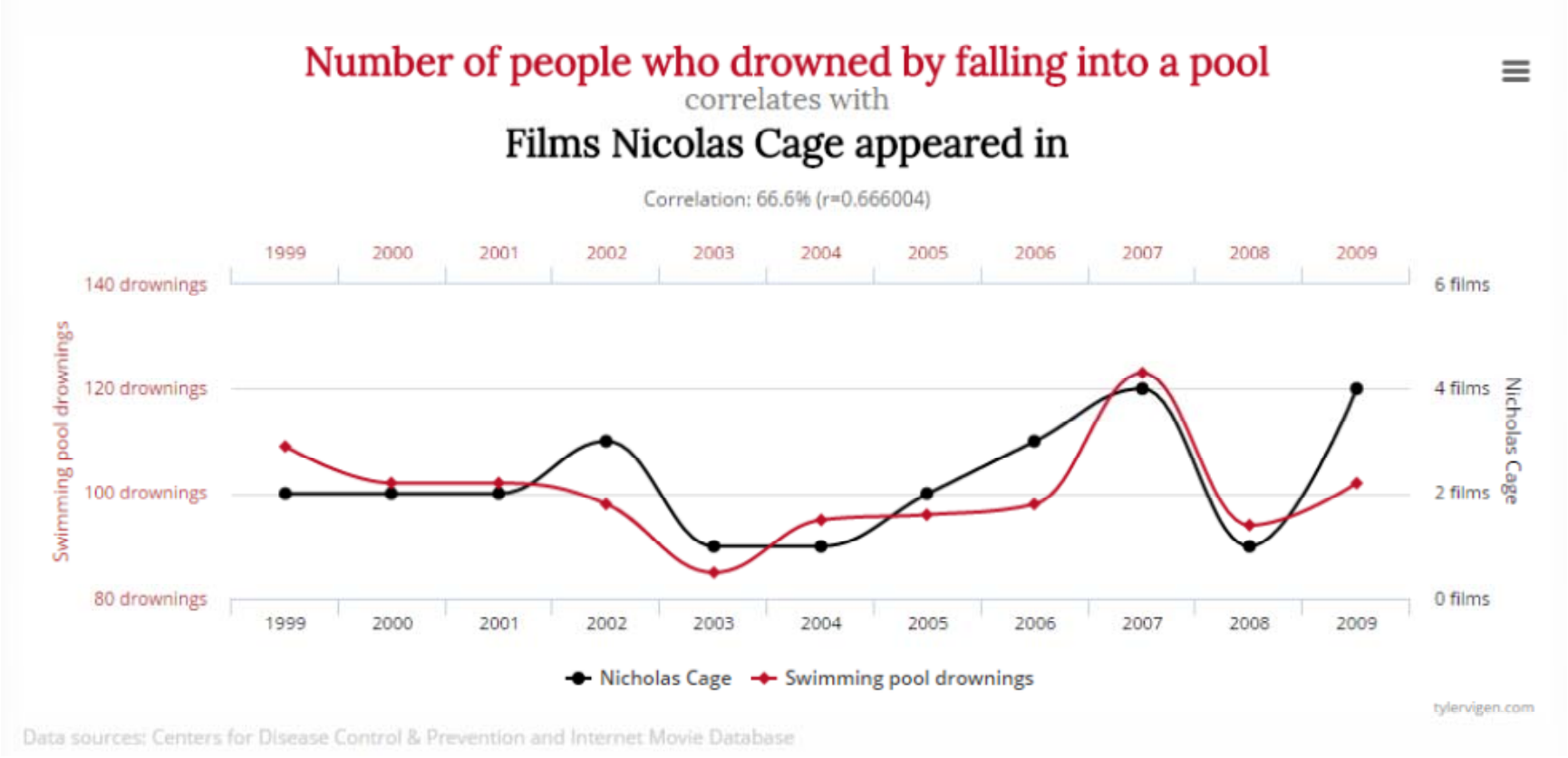
Vaccine Scares

“Punch” and Smallpox vaccine
Kulenkampff and Pertussis vaccine
Wakefield and MMR
Nigeria and OPV
POTS, CRPS, CFS and HPVV

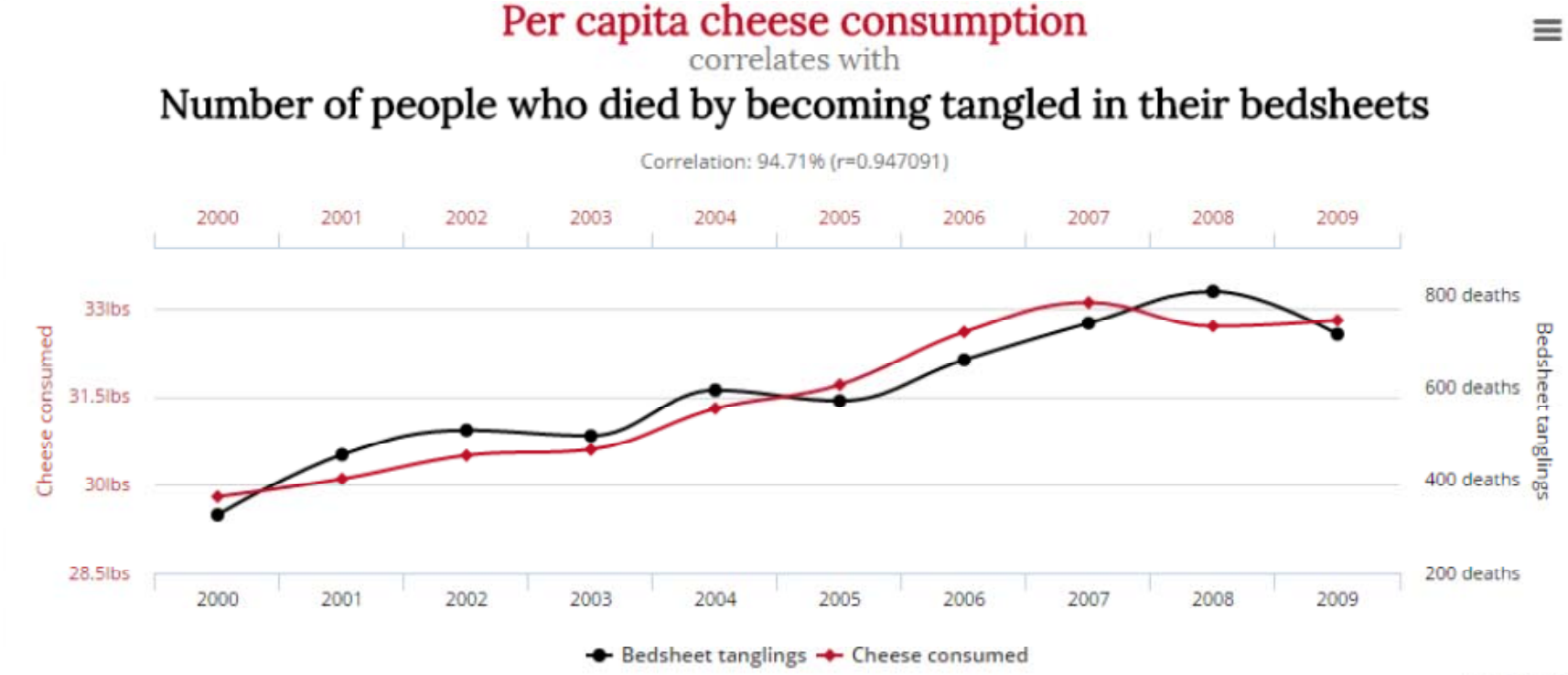
Correlation between Ice Cream Consumption and Drowning



Correlation is not Causation



Per capita cheese consumption
correlates with
Number of people who died by becoming tangled in their bedsheets



Data sources: U.S. Department of Agriculture and Centers for Disease Control & Prevention

Causal Relationship

(Bradford Hill Criteria)

1. Temporal relationship
2. Strength of the association
3. Biologic plausibility
4. Dose–response relationship
5. Replication of the findings
6. Effect of removing the exposure
7. Alternate explanations considered
8. Specificity of the association
9. Consistency with other knowledge

Problems with Beliefs

- Sampling, recall, susceptibility bias
- Symptoms collated
- Verification of symptoms
- Incidence of CSF before and after introduction of HPV vaccines
- EMA assessment

- Incidence of HPV-related cancers
- Effectiveness of HPV vaccine

- One is entitled to one's beliefs and feelings, but not to one's own science
- The overwhelming body of scientific evidence is that there is no causative association between HPV vaccines and POTS, CFS or CRPS

Minimising Errors

- Right patient
- Right vaccine and diluent
- Right time (age, interval, expiry)
- Right dose
- Right site
- Right route
- Right documentation