

Adverse Events Following Immunisation

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Limerick, Sept. 22, 2016

Outline

- Abbreviations, Definitions
- Adverse Event (AE), Adverse Reaction (AR) or coincidence?
- How are AEs recorded?
- How are ARs are identified?
- Frequency of ARs

Abbreviations

- **AE**- adverse event
- **AR**-adverse reaction
- **AEFI**-adverse event following immunisation
- **SAE**- serious adverse event

Definitions

- **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

- **Adverse Drug Reaction**

A response to a drug which is noxious and unintended, ...

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

Immunisation Error-related Reaction

An adverse event following immunisation that is caused by inappropriate vaccine handling, prescribing or administration and thus by its nature is preventable.

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)
<ul style="list-style-type: none">• Redness• Swelling, nodule• Pain• Fever, irritability, loss of appetite• nausea, D+V	<ul style="list-style-type: none">• Encephalitis• Paralysis• Arthritis• Allergic reaction• Thrombocytopenia• Febrile seizure• Fainting• Narcolepsy• Death

What is “Less Common”?

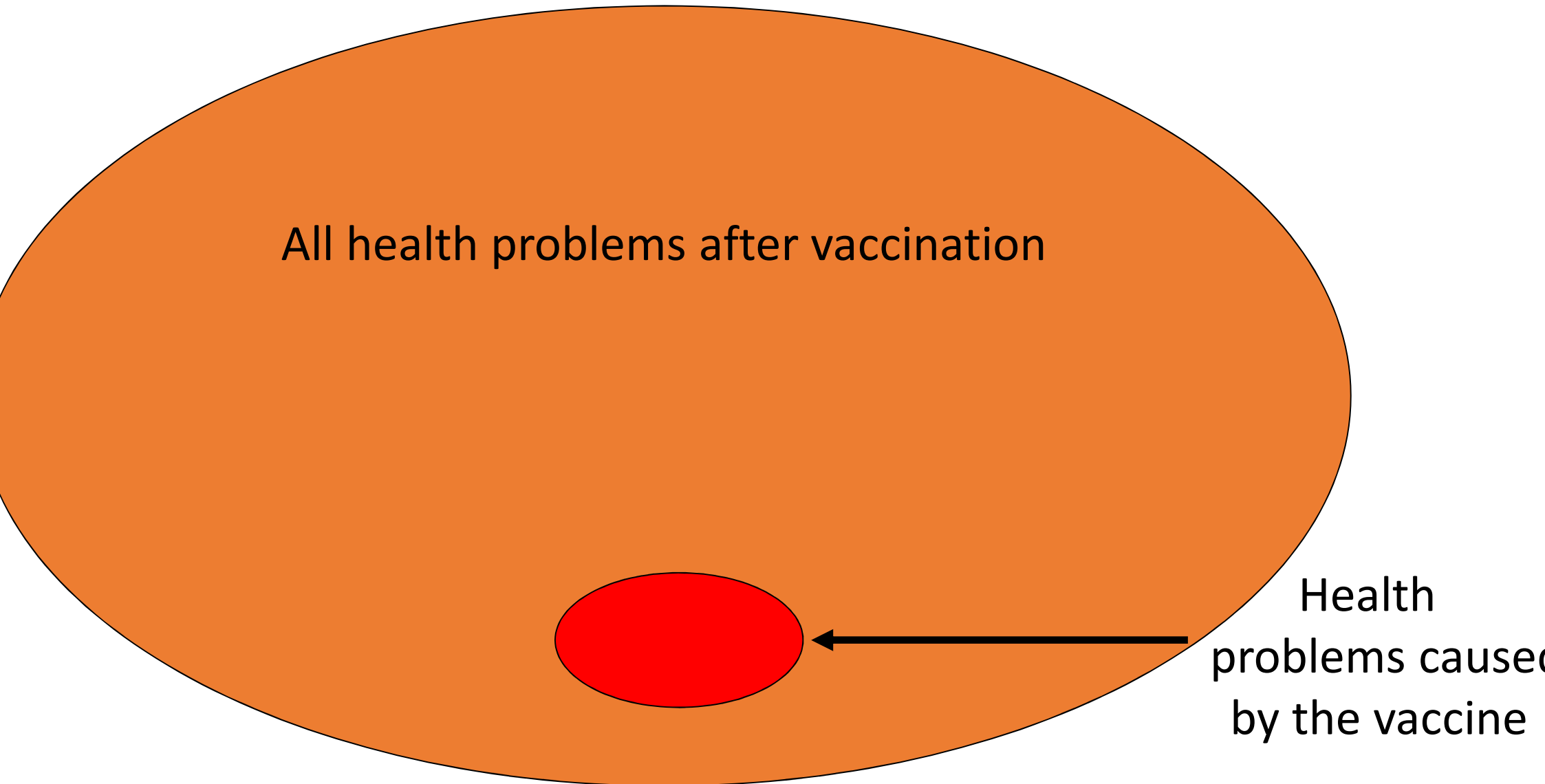
Frequency of known injury*	What else is this common?
1/1,000 to 1/100,000 <ul style="list-style-type: none">– Fainting or collapse– Febrile seizure– Thrombocytopenia	Having quadruplets
1/100,000 to 1/1,000,000 <ul style="list-style-type: none">– Serious allergic reaction– Arthritis	Getting struck by lightning
> 1 in a million <ul style="list-style-type: none">– Encephalitis– Paralysis– Death	Winning the lottery

*highest rate for any childhood vaccine

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 will experience no significant adverse reaction

AEFI - Coincidence or Vaccine Injury?



What Causes AEFIs?

Vaccine – due to vaccine's inherent properties

Programme, administration

Injection reaction - anxiety, pain

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
 - concomitant administrations
- Patient profile
 - age, weight
 - immune deficiency e.g. AIDS
- Environmental
 - epidemiology: strain variation

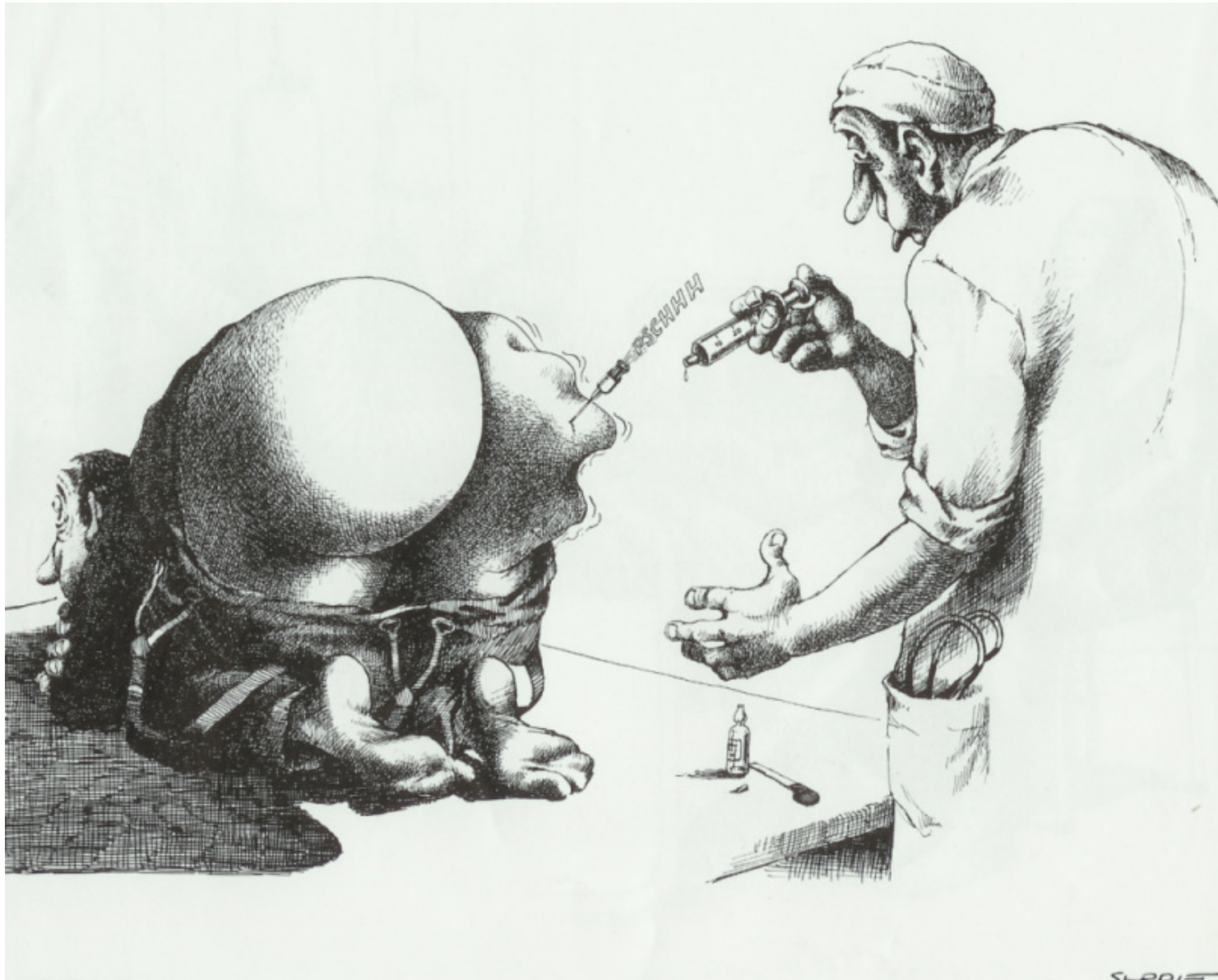
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Is this an AE or an AR?



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Timing of Vaccine Reactions

- **Inactivated vaccines:** generally within 48hrs
- **Live vaccines:** according to time for organism to replicate

MMR: - mini-measles 6-11 days (SSPE years)

- rubella 2nd week

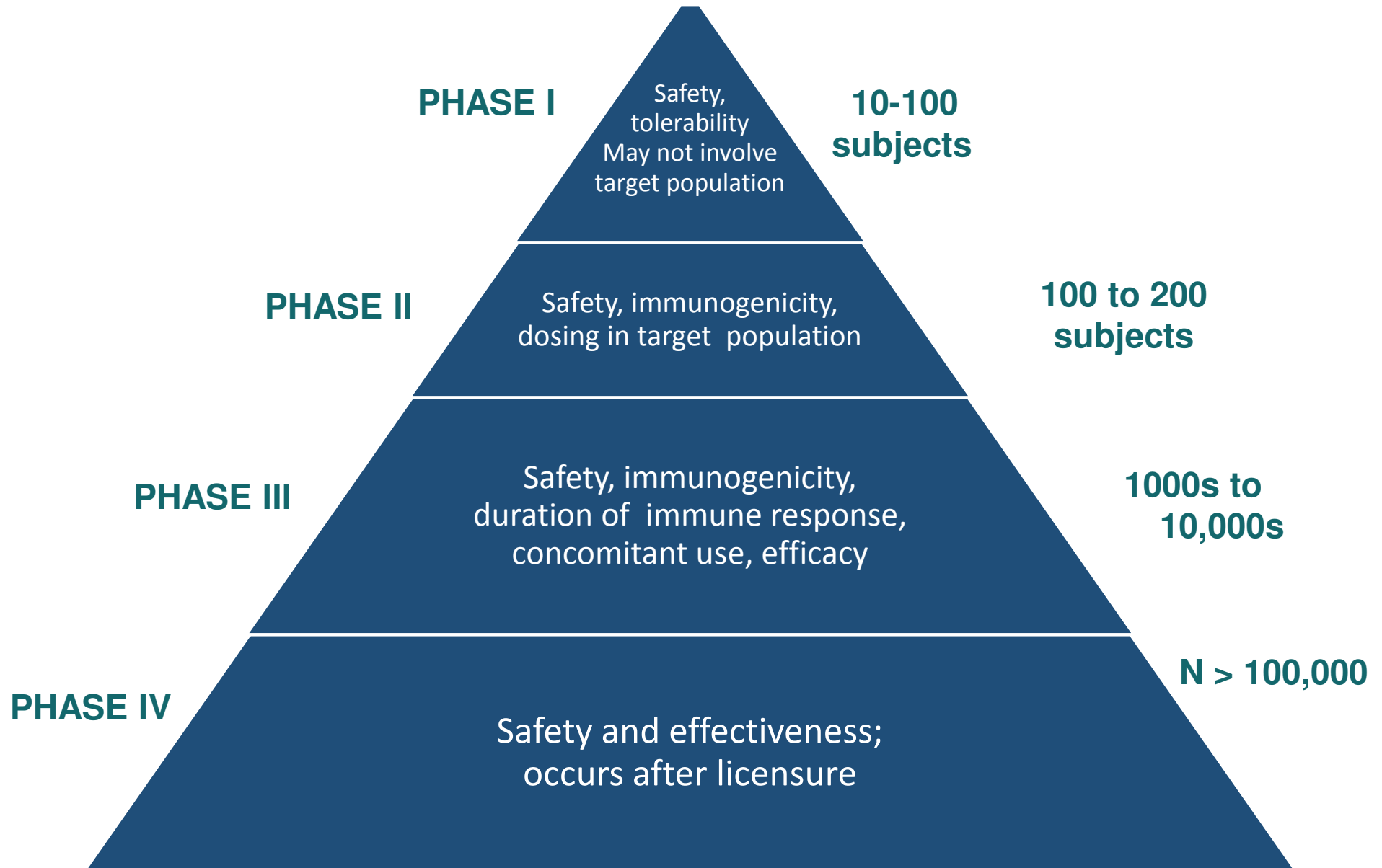
- mumps 3 to 6 weeks

BCG: days - 12 months +

Minimising Errors

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

Vaccine Safety Studies



Why Monitor AEFIs?

- No vaccine is 100% safe
 - Safety profile established in pre-license trials
 - Rare events require huge numbers to detect
- Risk / benefit balance changes over time
 - as incidence falls-e.g. VAPP with oral polio vaccine
 - as society becomes more critical

Pharmacovigilance

Science and activities relating to the detection, assessment, understanding and prevention of adverse effects

Objectives :

- preventing harm from adverse reactions
- promoting safe and effective use of medicinal products

Number needed to test for increased risk of an AE

	Rate In Vaccinated Population		
Background rate in 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
Evans D et al. J Infect Dis. 2009;200:321-8.			

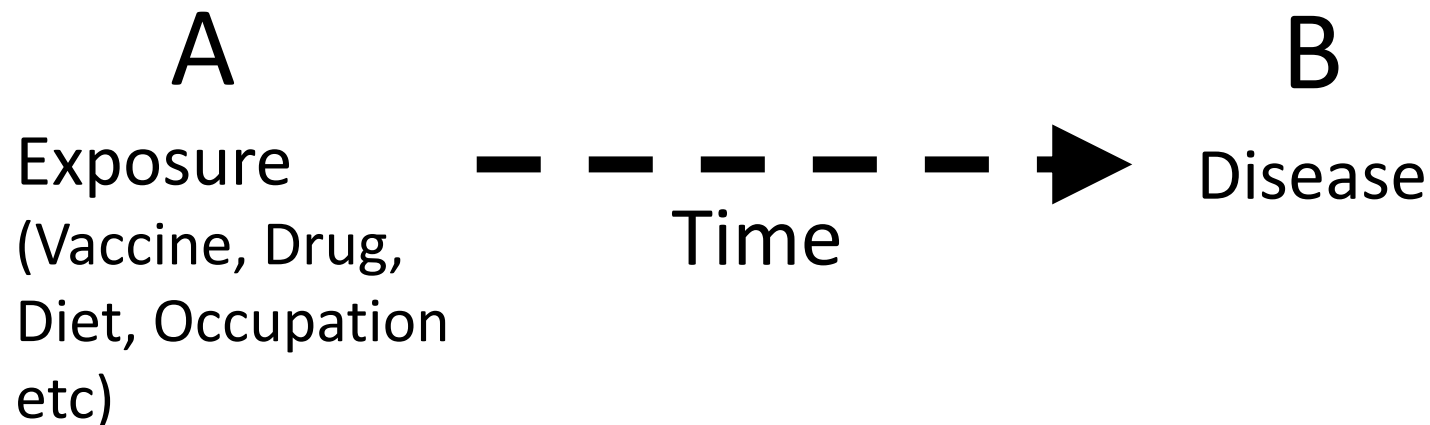
Benefit-risk balance

- Medicines may have unintended, harmful effects.
- Active substance tested in trials
- Licenced only if benefits outweigh risks
- Used in patients who may differ from the study population, e.g. age or additional diseases
- Important to identify any new risk ASAP, and to take measures to minimise risk and promote safe and effective use

Pharmacovigilance by Pharmaceutical Companies

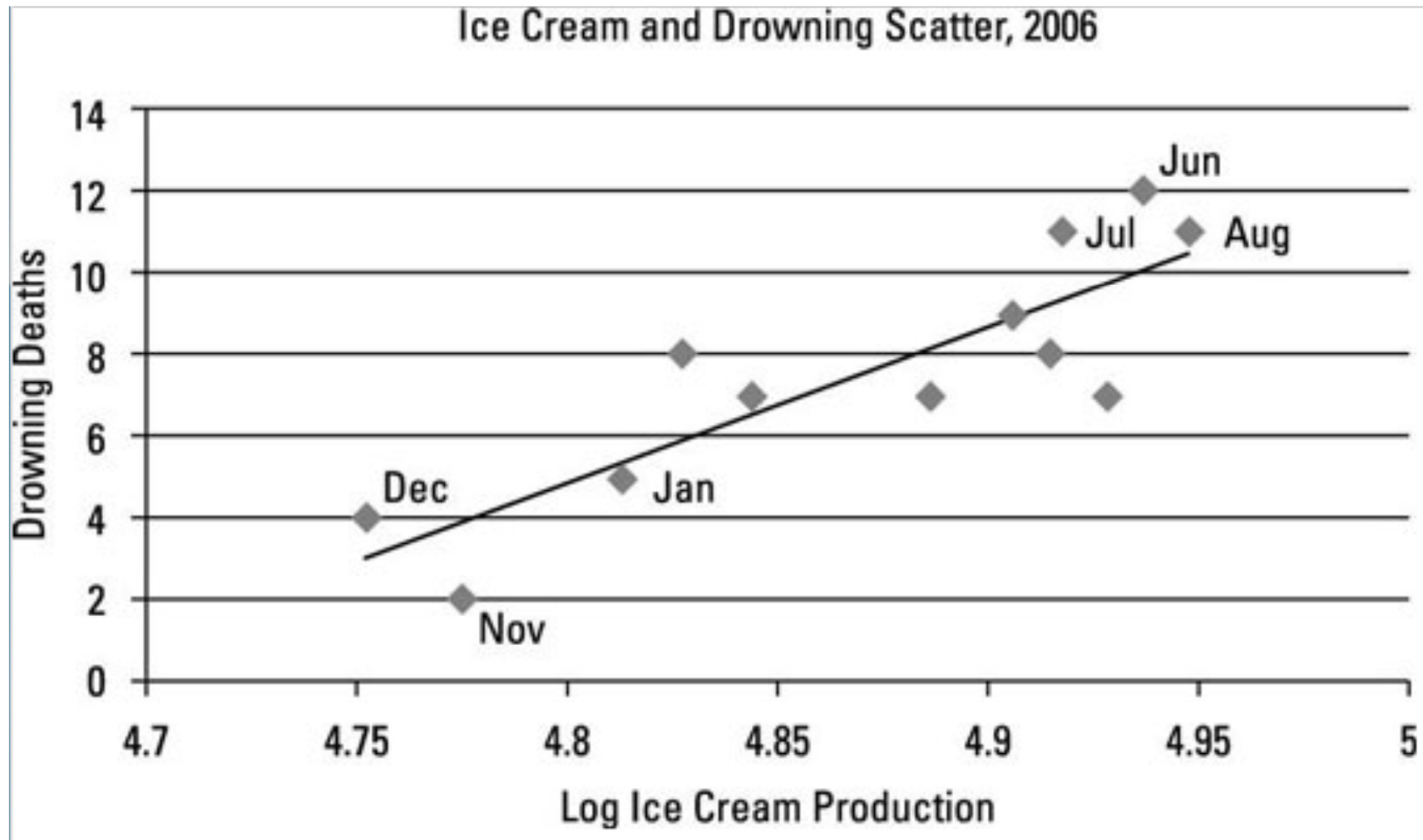
- Legal obligations to continuously collect data and conduct pharmacovigilance
- Data must be sent to authorities within defined timelines
- Any emerging concern about the benefit-risk balance has to be notified immediately.
- Authorities may request further investigations, including formal studies.
- Authorities may update product information and implement other safety measures

Is Sequence Consequence?



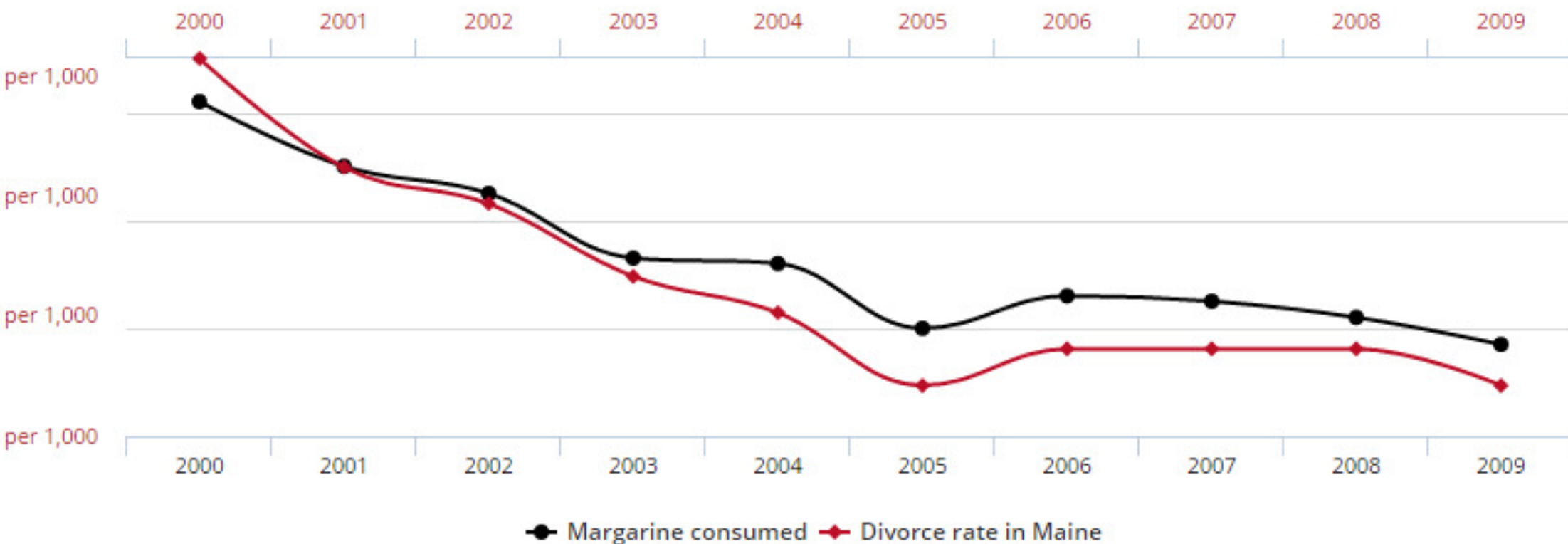
- Direct and only cause?
- One of multiple potential causes?
- Co-factor/indirect cause, trigger?
- Coincidental?

Correlation is not Causation



Divorce rate in Maine correlates with Per capita consumption of margarine

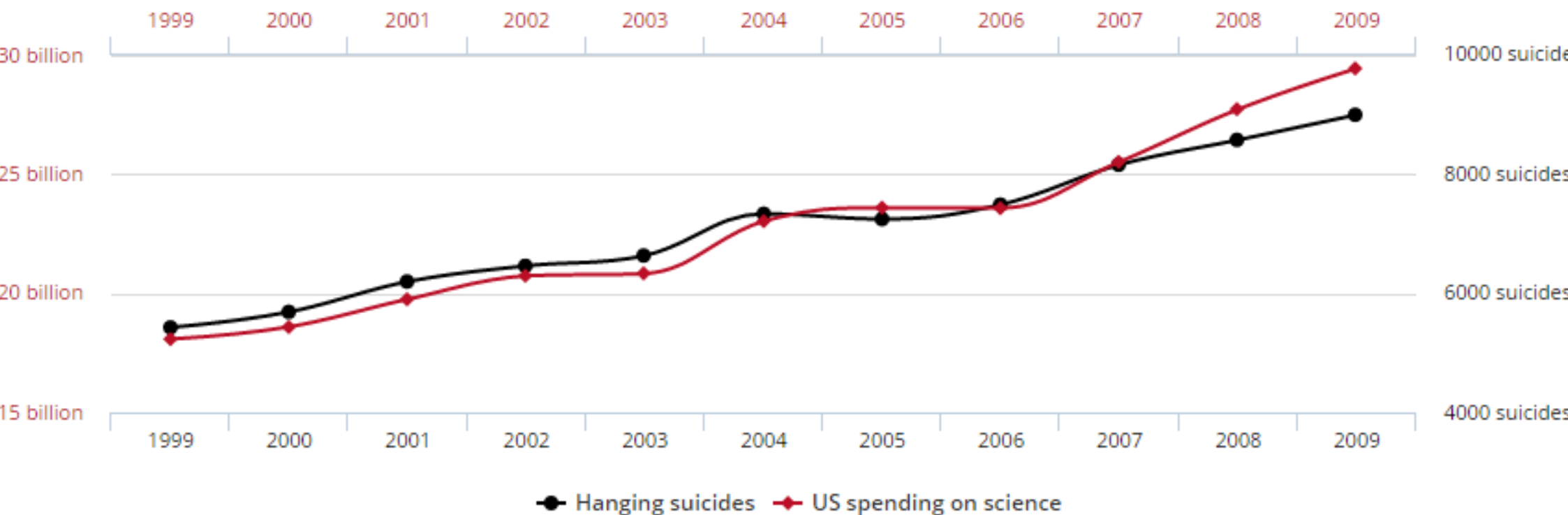
Correlation: 99.26% ($r=0.992558$)



es: National Vital Statistics Reports and U.S. Department of Agriculture

US spending on science, space, and technology correlates with Suicides by hanging, strangulation and suffocation

Correlation: 99.79% ($r=0.99789126$)

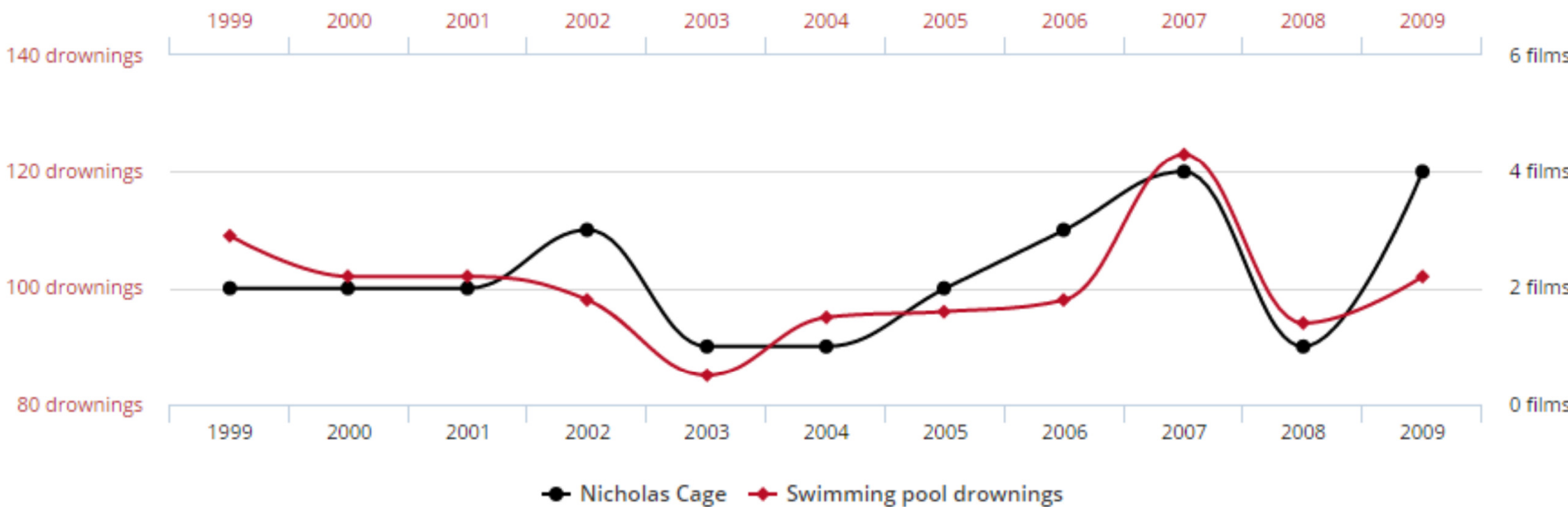


Sources: U.S. Office of Management and Budget and Centers for Disease Control & Prevention

tylervij

Number of people who drowned by falling into a pool correlates with Films Nicolas Cage appeared in

Correlation: 66.6% ($r=0.666004$)



Sources: Centers for Disease Control & Prevention and Internet Movie Database

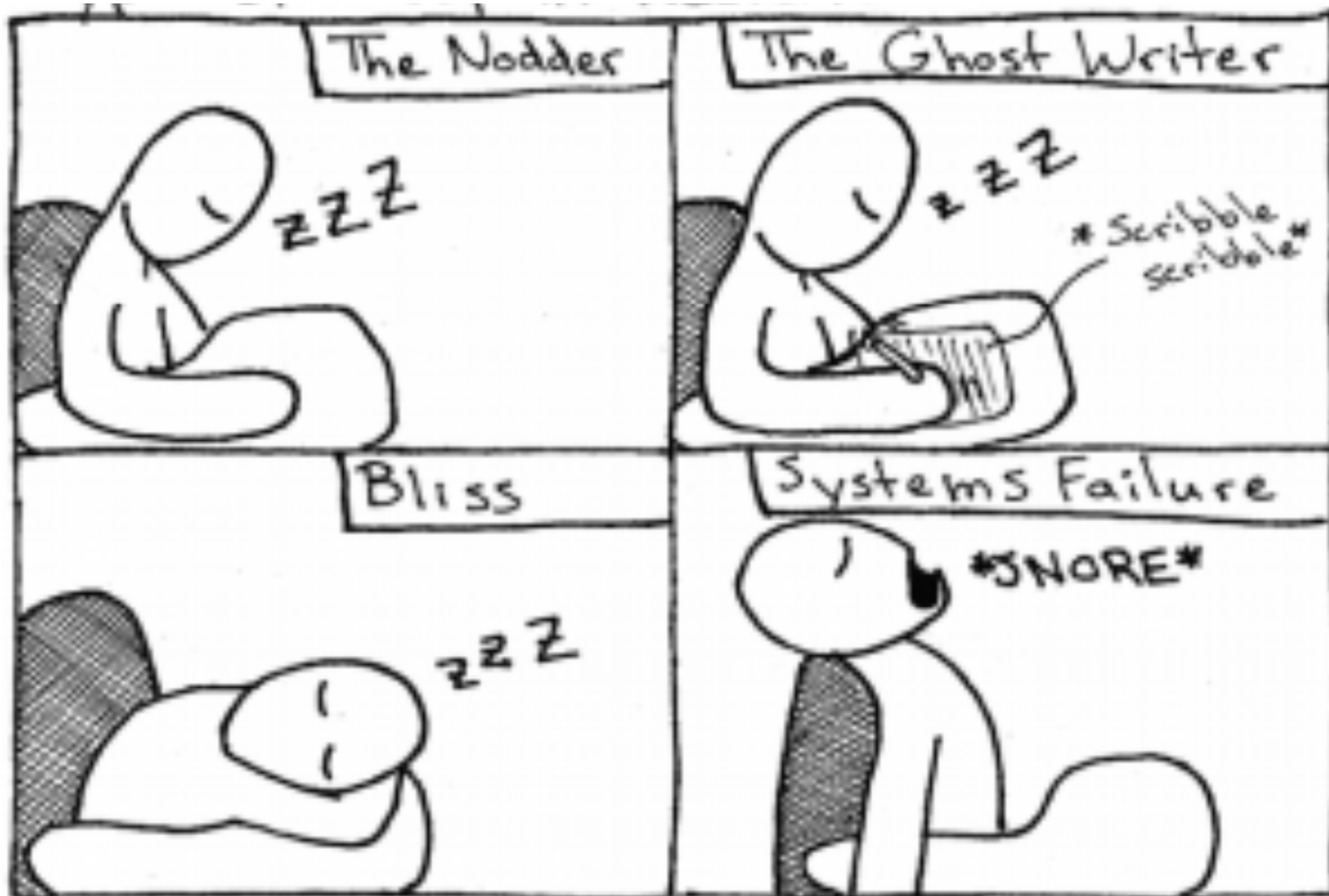
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Criteria of Causality (Bradford Hill)

The Bad Dog Ate the Cat

- Temporality - occurs after, change in incidence over time
- Biological Plausibility - biological mechanism can make causality more plausible
- Dose - Response Relationship
- Association (strength of) - measured using RRs and ORs
- Consistency - similar results from different studies, researchers, populations, times

Adverse Reaction to Lectures



Reporting AEFIs

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

Report an Issue

www.hpra.ie/homepage/about-us/report-an-issue

Suggested Sites Login Imported From IE Inbox (86) - kevin.davi IT The Irish Times immunisation guidelin New Tab Skype NRC Homepage

HPRA

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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

EN

10:59
23/09/2016

R.E.G.R.E.T.

**“Reactions and effects of Gardasil resulting in
extreme trauma”**

“R.E.G.R.E.T. set up by parents of Irish teenage girls who have developed serious health problems after entering secondary school. These parents are certain that the HPV vaccine (Gardasil) is the cause of their daughters' otherwise unexplained illness.”

One is entitled to one's beliefs and feelings, but not
to one's own science

Problems with REGRET'S Beliefs

- Sampling, recall, susceptibility bias
- Incidence of CFS in population, in trials,
after introduction of HPV vaccines
- EMA, WHO assessment

The overwhelming body of scientific evidence is that there is
no causative association between HPV vaccines and
POTS, CFS or CRPS

Remember.....

Incidence of HPV-related cancers

Effectiveness of HPV vaccine

Estimated Impact of HPV Vaccination

In the 9 years since HPV vaccine introduced:

➡ HPV Genital infection reduced by 64 - 85%¹

➡ CIN2 + 3 reduced by 75% ²

¹ US, Australia

² 3m. girls, Sweden, 2006-13, vaccinated <17yrs. International Journal of Cancer (2016).

Estimated Impact of no HPV Vaccination

- ➡ Currently 500,000 girls <15 in Ireland; if none are vaccinated:

- ➡ 3,500 will develop cervical cancer

- ➡ 1,000 will die from cervical cancer

- ➡ **80% uptake would prevent 1600 cases of cancer and 500 deaths**

The End

Unsure if applause is because I was good

?



or because I have shut-up