Adverse events following Immunisation Common and Uncommon

Dr Anna Clarke

National Immunisation Office

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www.immunisation.ie

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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

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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**

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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

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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

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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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What Causes Adverse Events Following Immunisation

1. Vaccine Product-Related AEFI
2. Vaccine Quality Defect-Related AEFI
3. Immunisation Error-Related Reaction AEFI
4. Immunisation Anxiety-Related Reaction AEFI
5. Coincidental Event AEFI

Vaccine Induced AEFIs

- Local reactions
  - common *(redness and swelling at the injection site)*
- General reactions
  - usually occur within 24-48 hours of vaccination *(fever, irritability, loss of appetite)*
- Anaphylaxis
- Later reactions
  - post MMR (“mini measles” after 7-10 days)

Local reaction

- Not surprising
- Occur within hours of receiving the vaccine
- Usually mild and self limiting
- Reduced by using correct needle length
- **Does not contraindicate** the administration of this vaccine subsequently.

Systemic reaction

Timing varies according to the type of vaccine received.

- Inactivated vaccines: generally within 48 hours - Tetanus containing vaccines - fever within a few hours
- Live vaccines: accorading to time for virus to replicate - MMR vaccine - rash 7-10 days later.

– **Does not contraindicate** the administration of the vaccine subsequently

Management of common reactions

- Inform parents verbally and with information leaflets
  - expected common events post-vaccination
  - Give the tear pad
  - how to treat them.
    - paracetamol or ibuprofen (pyrexia)
    - no aspirin or aspirin-containing medication if under 18 years of age (Reye's syndrome).
- MMR vaccination
  - Local reaction
  - Rash in 6-11 days
  - Swelling in jaw area in 3rd week (up to 6 weeks)

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"

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Why Monitor AEFIs?

- No vaccine is 100% safe
  - Safety profile established in pre-licensure trials
  - Detectable frequency depends on numbers studied
    - 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, Pandemrix, etc
- If in doubt, write one out
- Every report is important

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Reporting of AEFI

- Report all suspected adverse reactions to the Health Products Regulatory Authority (formerly Irish Medicines Board)

  Kevin O' Malley House
  Earlsfort Centre,
  Earlsfort Terrace,
  Dublin 2,

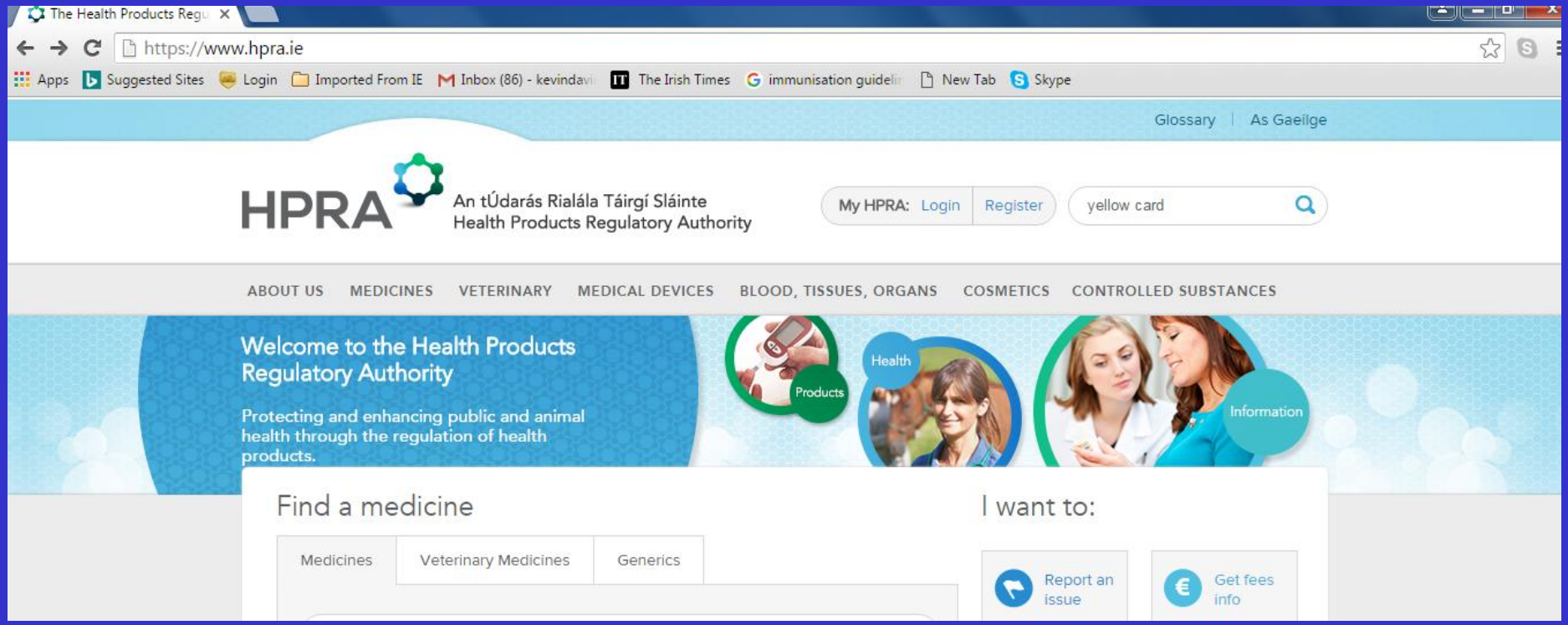
- Use the on-line reporting system at www.hpra.ie

  - **A downloadable version of the form is also available, which can be filled in manually and sent to the HPRA by freepost.**

  - **By calling the HPRA on (01) 676 4971.**

- Give as much detail as possible – brand name and batch number
- Pharmaceutical companies are obliged to also submit adverse reaction reports to the HPRA.

Reporting AEFIs



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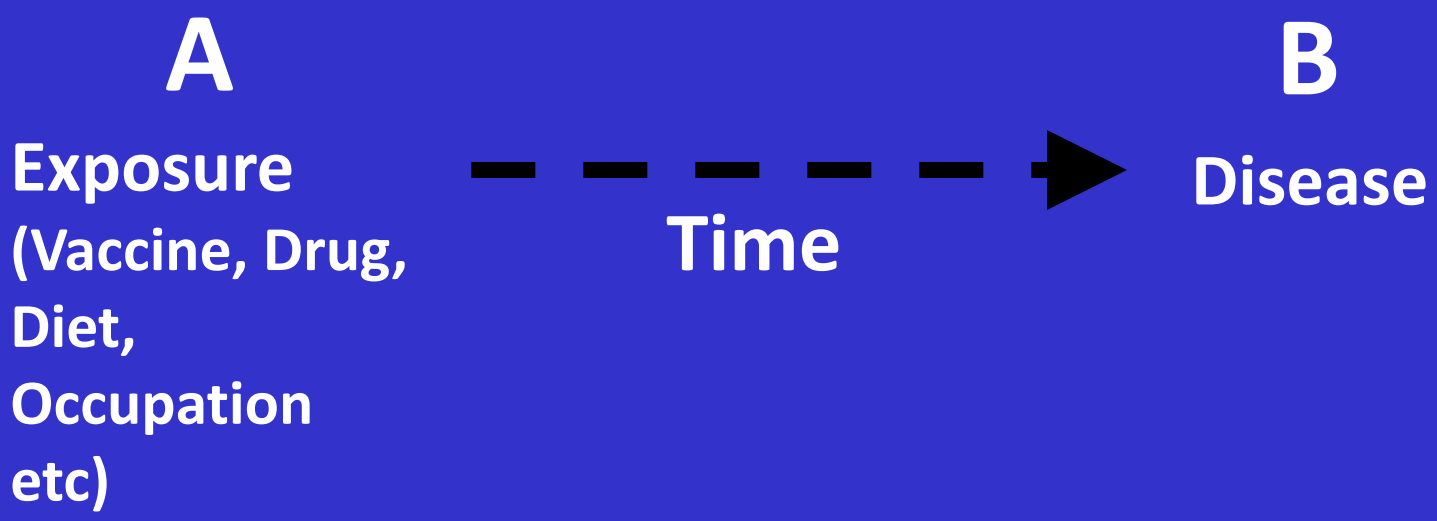
Coincidence or Cause?
Is Sequence Consequence?



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

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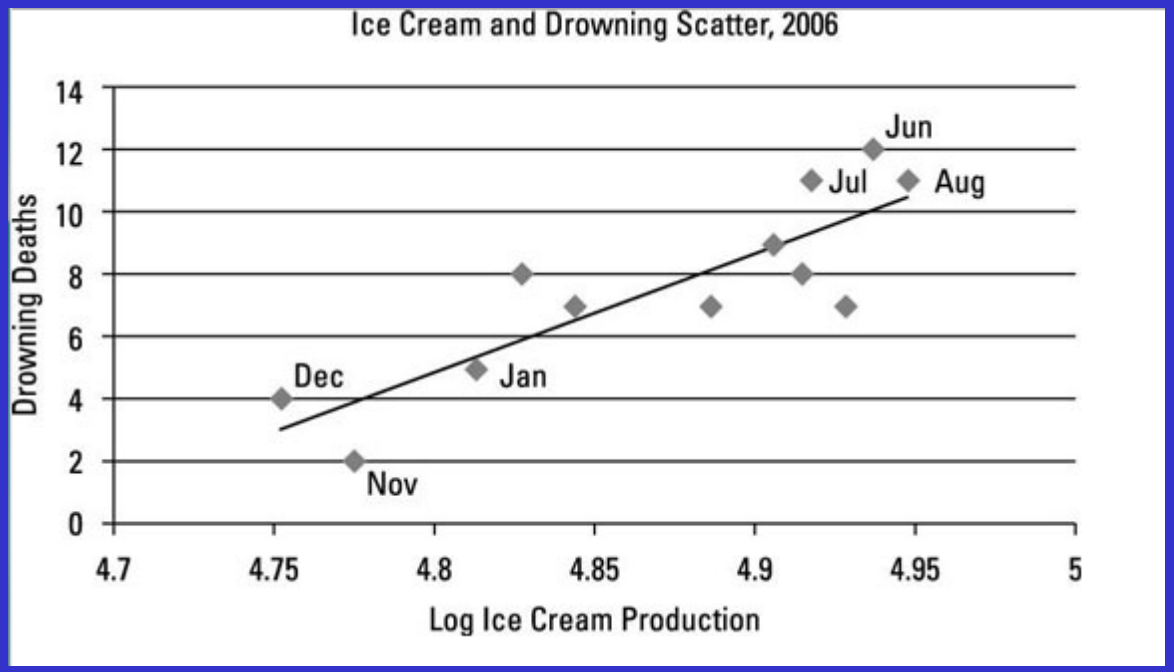
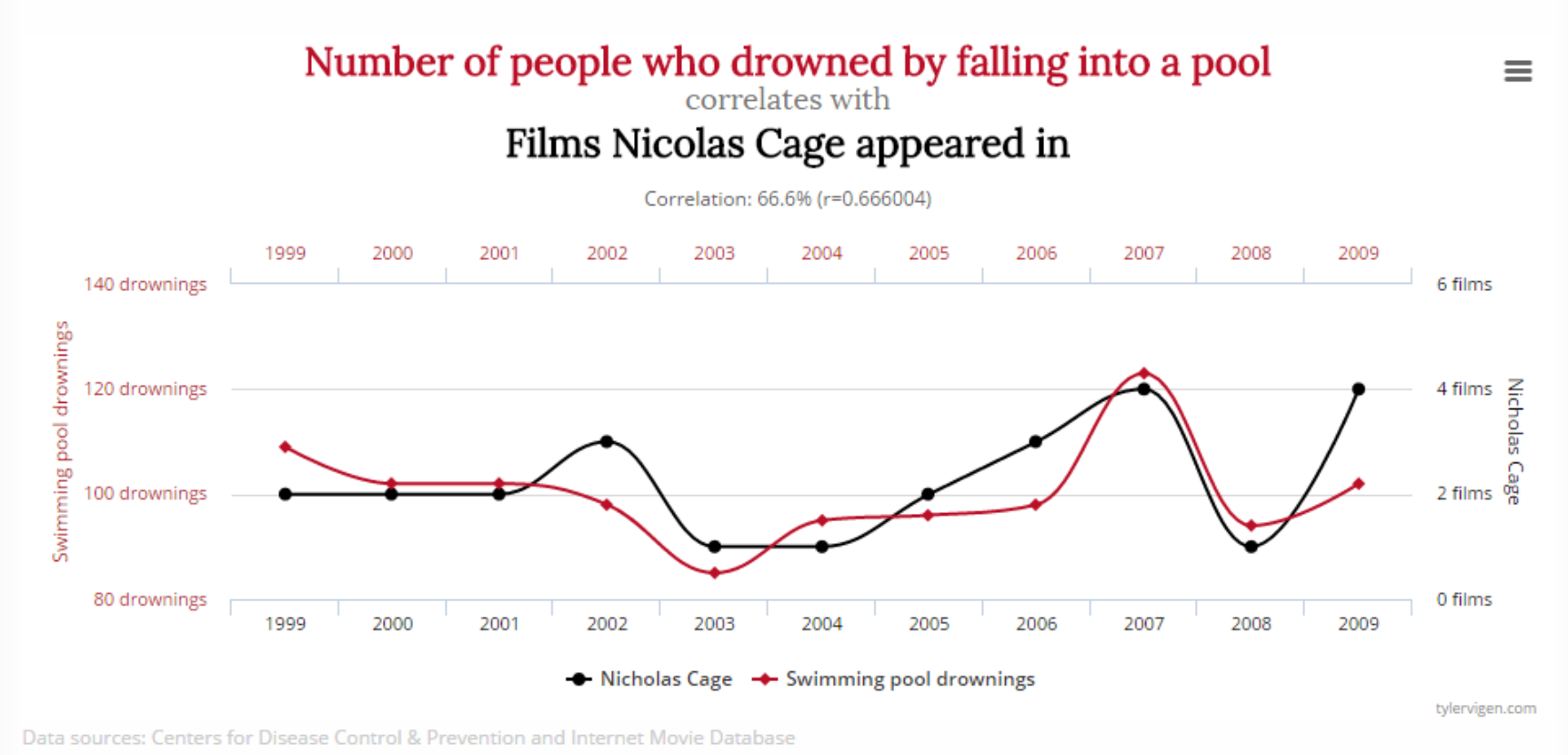
Vaccine Scares

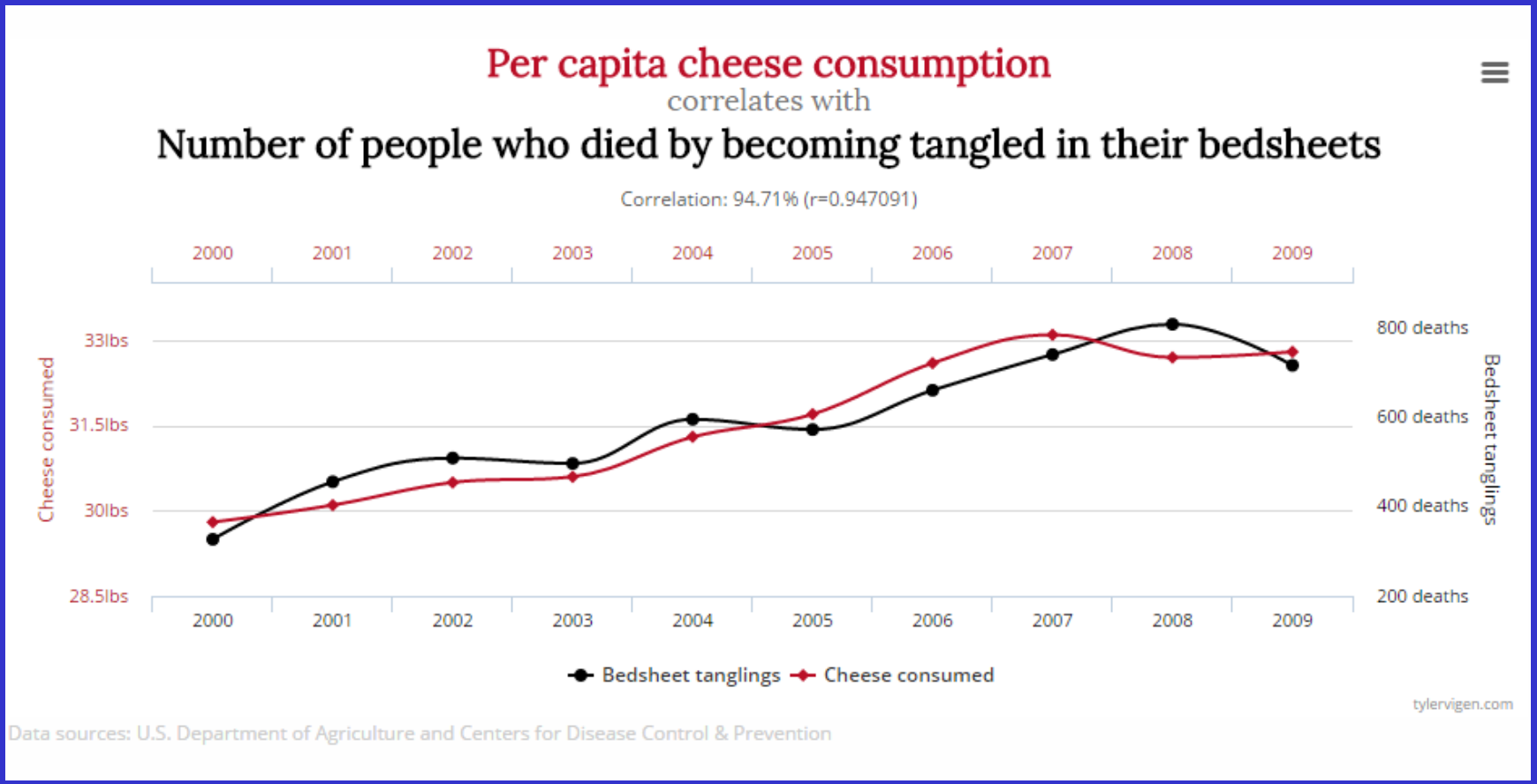
"Punch" and Smallpox vaccine
Kulenkampff and Pertussis vaccine
Wakefield and MMR
Nigeria and OPV
POTS, CFS and HPV

Correlation between Ice Cream Consumption and Drowning



Correlation is not Causation





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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

Minimising Errors

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

Useful Resources

- Health Products Regulatory Authority www.hpra.ie
- Ewan P.W. ABC of allergies: Anaphylaxis. BMJ1998 (316) 1442-1445
- Royal College of Physicians of Ireland. Immunisation Guidelines for Ireland 2013 and updates. Available at www.immunisation.ie
- World Health Organisation. Adverse events following immunisation http://www.who.int/immunization_safety/aefi/en/
- American Academy of Paediatrics. 2015 Report of the Committee on Infectious Diseases – The Red Book.
- https://redbook.solutions.aap.org/redbook.aspx
- Department of Health UK. November 2013. Immunisation against infectious disease. https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book
- SmPCs available at www.medicines.ie

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