REAL WORLD EVIDENCE: CAN WE REALLY EXPECT IT TO HAVE MUCH INFLUENCE?

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What is Real World Data and Evidence?

- “Data regarding the usage, or the potential benefits or risks, of a drug derived from sources other than traditional clinical trials.”
  - Federal Food, Drug and Cosmetic Act Section 505F (b)
- “RWE is clinical evidence regarding the usage, and potential benefits or risks, of a medical product derived from analysis of RWD.”
  - CDRH. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices: Guidance for Industry and Food and Drug Administration (FDA) Staff (CDRH Guidance)

RWE Strengths

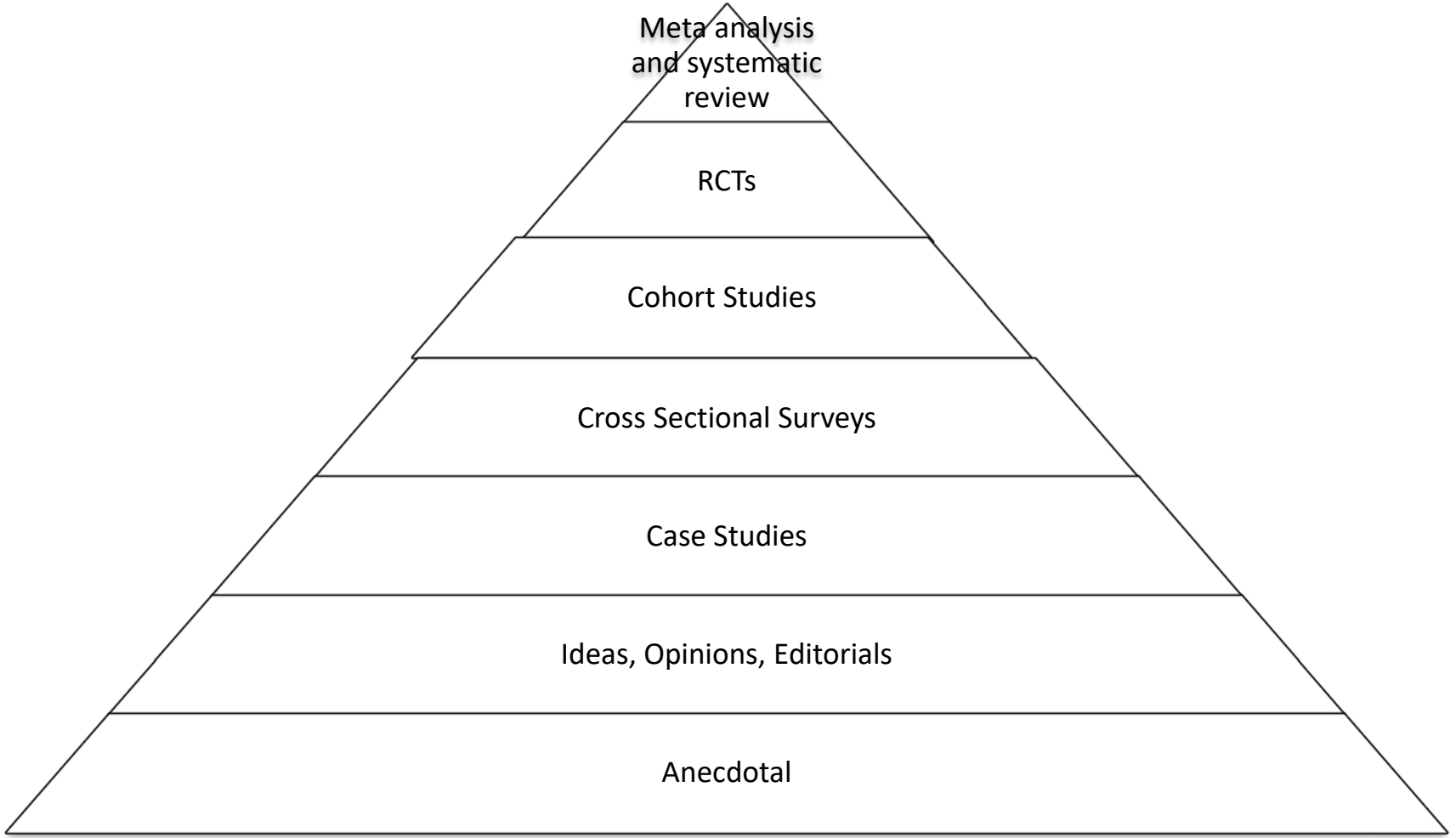
- 85% of clinical interventions are not covered by guidelines
- It has many applications
  - Pre-development phase
  - Market access phase
  - Market usage phase
- RWE can cover diverse or specific sub-populations
- Easy to gather[1] and generalize from
- Its really not that new[2]
- We have used it successfully in healthcare already[3]

1. Department of Health (2005). *Chief Executive's report to the NHS: December 2005.* http://webarchive.nationalarchives.gov.uk/20071204134909/http://www.dh.gov.uk/prod_consum_dh/idcplg?IdcService=GET_FILE&dID=11878&Rendition=Web
2. Gnanalingham MG, Robinson SG, Hawley DP*, et al* A 30 year perspective of the quality of evidence published in 25 clinical journals: Signs of change? Postgraduate Medical Journal 2006;82:397-399.
3. European Medicines Agency (2016). *EMA Annual Report* www.ema.europa.eu/docs/en_GB/document_library/Annual_report/2017/05/WC500227334.pdf

RWE Weaknesses

- The data
  - Quality
  - Bias
  - Ownership/Privacy
- Regulation
- 50+ years of RCTs
- 30+ years of the hierarchy of evidence

The Hierarchy of Evidence



RWE Weaknesses

- The data
  - Quality
  - Bias
  - Ownership/Privacy
- Regulation
- 50+ years of RCTs
- 30+ years of the hierarchy of evidence
- Lack of knowledge
  - “If you cannot explain this process to clinicians in a way that confirms its accuracy..you will find that, to them, such data has no value.”[1]

1. Looney. Real-World Evidence: From Volume to Value. (2016) Pharmaceutical Executive Volume 36, Issue 10

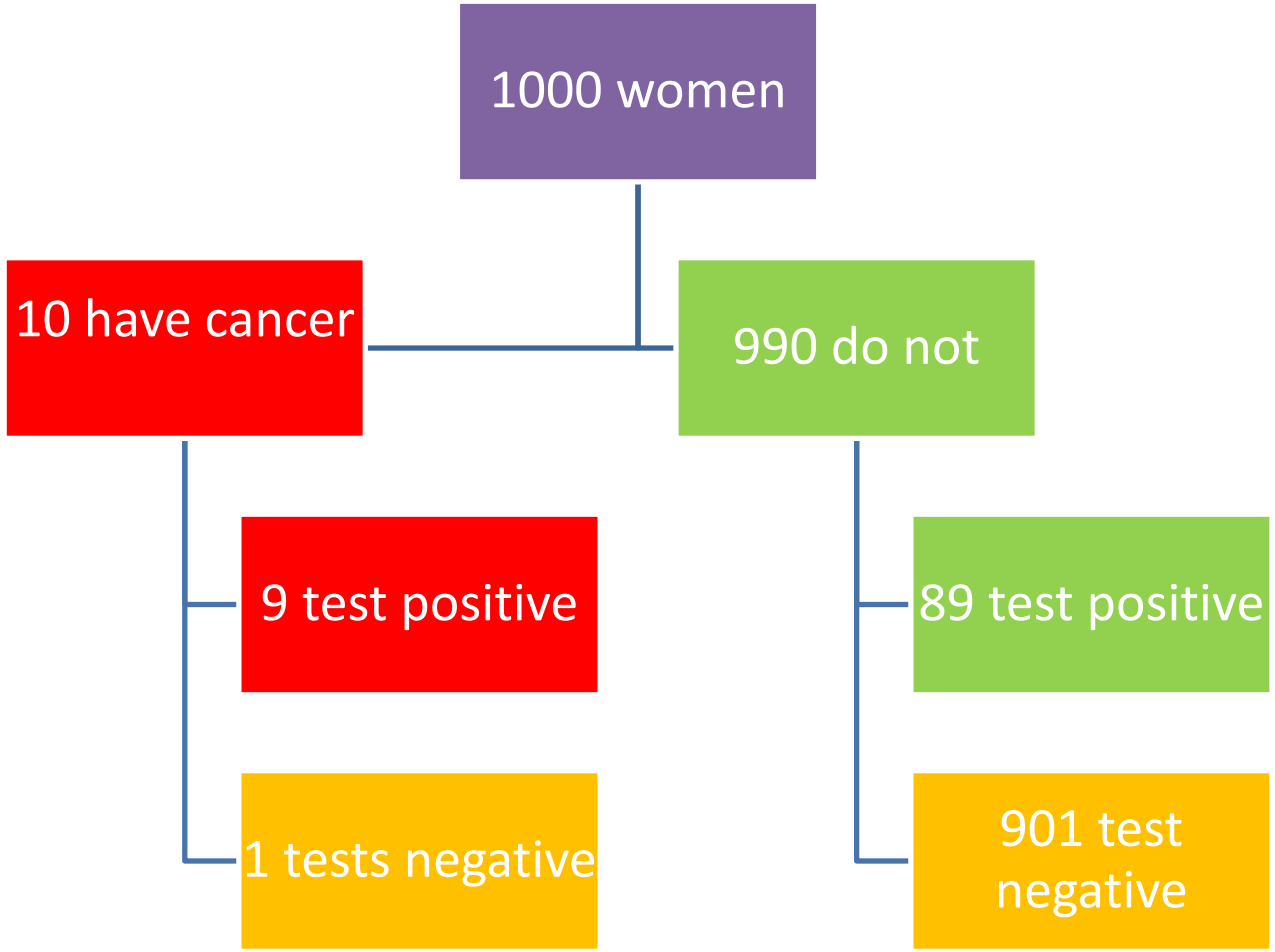
Interactive Question 1

- The probability that a woman has breast cancer is 1% ("prevalence")
- If a woman has breast cancer, the probability that she tests positive is 90% ("sensitivity")
- If a woman does not have breast cancer, the probability that she nevertheless tests positive is 9% ("false alarm rate")

How many women who test positive actually have breast cancer?

A. Nine in 10
B. Eight in 10
C. One in 10
D. One in 100

Easier to understand?

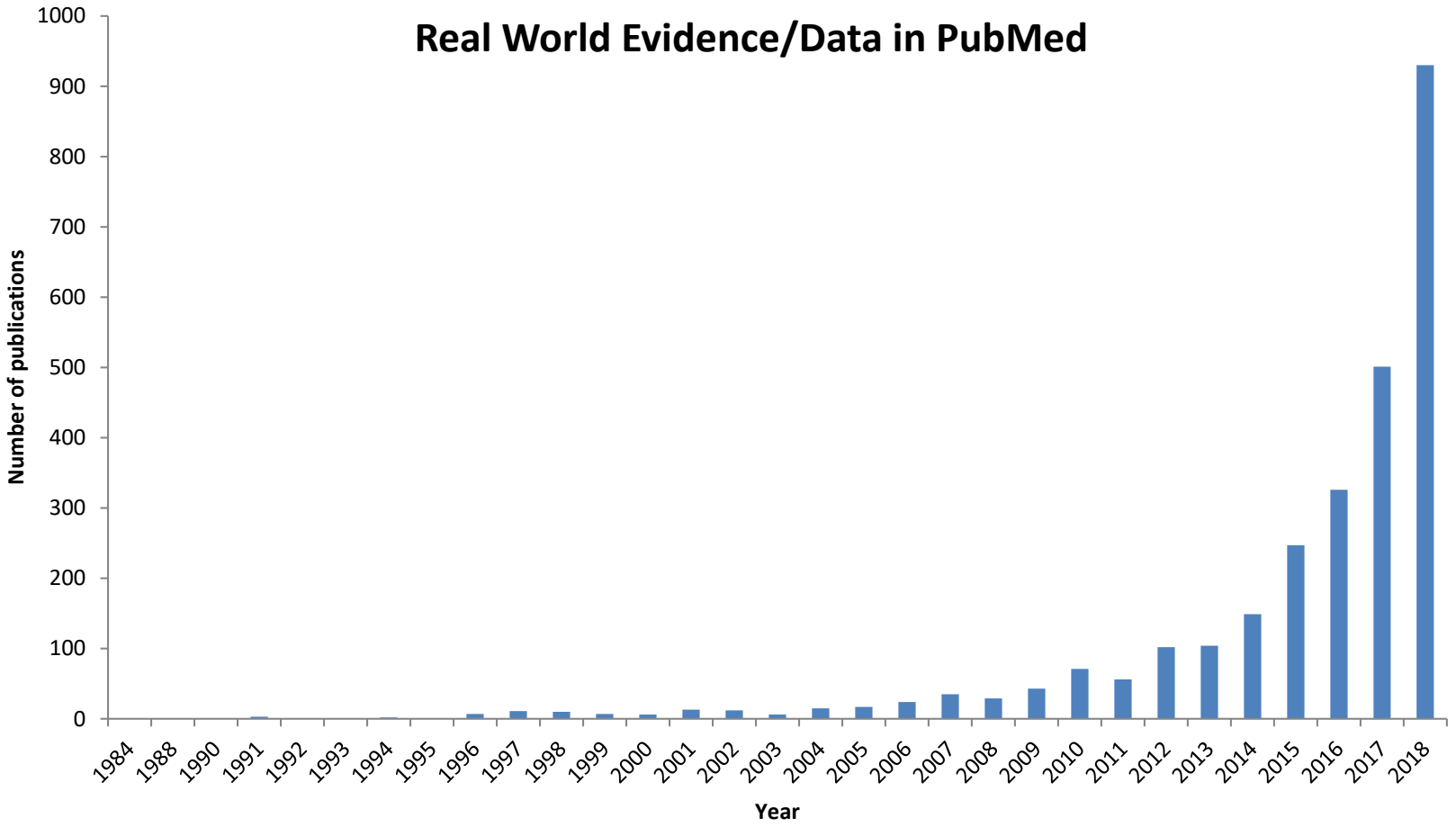


How does pharma plan to measure success in using RWE?

- Number of publications
- Use in HTA
- Decreased use of external vendors
- Sales
- Clinical development activity
- Use in regulatory submissions
- Use in value-based contracting

Source: Deloitte Insights. Mission Critical http://learn.deloitte.com/rwe-survey-deloitte-insights

Successful?


Real World Evidence/Data in PubMed
Number of publications
1000
900
800
700
600
500
400
300
200
100
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1984
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..or not?

- 6% of HTA decision making involved RWE[1]
- ASCO/NCCN reject formal role for RWE in clinical guidelines. Few other guidelines incorporate RWE
- In a study of decision makers use of RWE evidence in the US[2]
  - 60% of respondents reported that RWE delivered information in diverse populations only 'sometimes'
  - Not widely using in P&T decisions
  - 24% were confident in their ability to interpret results
  - 29% were aware of two recent RWE studies in JAMA and NEJM

1. **Does real world evidence matter in Health Technology Assessments? https://pharmaphorum.com/articles/does-real-world-evidence-matter-in-health-technology-assessments/**
2. **Malone et al. Real World Evidence: Useful in the Real World of US Payer Decision Making? How? When? And What Studies? (2018) Value in Health 21; 326-333.**

What can we do to improve things?

- Short term
  - Data visualisation
  - Publish the protocol
  - Publish non-study materials on RWE
- Longer term
  - Forget the old ‘hierarchy of evidence’
  - We are looking to complement NOT compete
  - How RWE can be helpful
  - How we minimise bias