

Does my Bias Look Big In This?

David Healy

1



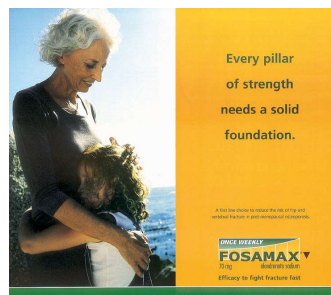
2



Bandod Ischyd Prifysgol
Betsi Cadwaladr
University Health Board
NORTH WALES BONE DENSITOMETRY/OSTEOPOROSIS SERVICE
Llandudno General Hospital
FFORD YSBYTYNOSPITAL ROAD
LLANDUDNO
CONVY
LL30 1LB

Dear Mr David Healy
We are writing to you because you recently attended the Fracture Clinic with a broken bone(s).
We would like to invite you for a scan to look for osteoporosis, this is also known as 'brittle bones'.
To help us find out more about your broken bone(s) please could you complete the consent form and the questionnaire.
Thank you for taking the time to fill in our questions.
Yours
The Osteoporosis Team at Llandudno Hospital

3



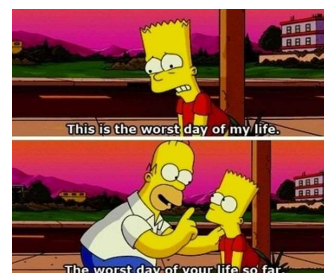
Guidelines
Screening
But
Auditors
Managers
Costs
+
Drugs
Drug Wrecks
Personnel

4

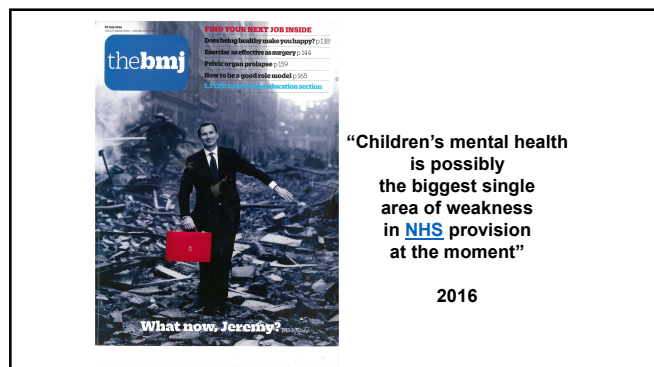


Spiral
Fractures
Anecdotes
Aging

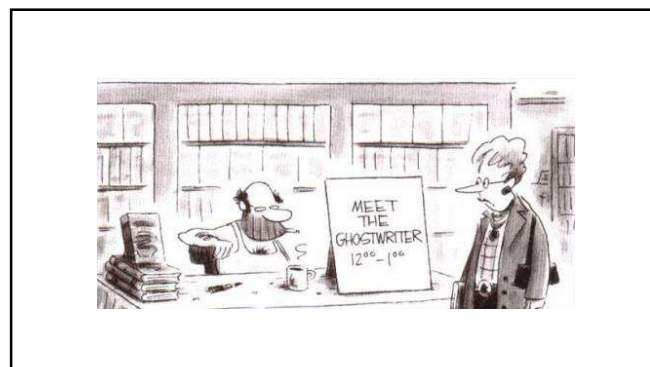
5



6



7



8

Page 12 of 15
Prepared by Current Medical Decisions, Inc.

ANXIETY POST-TRAUMATIC STRESS DISORDER

| Author—Title | Vendor | Status |
|---|---------|--|
| Author TBD—(640) Sertraline vs. placebo in PTSD | Paladin | Poster presented at ECNP, 1997. Paper is completed, but revisions are needed. |
| Author TBD—(671) Title TBD | Paladin | Poster presented at ECNP, 1998. First draft completed, but additional analyses needed. Both (640) and (671) studies to be submitted soon. One will go to <i>New England Journal of Medicine</i> and the other to <i>JAMA</i> . |

FAKE NEWS

9



10

BRITISH MEDICAL JOURNAL
LONDON SATURDAY OCTOBER 30 1948

STREPTOMYCIN TREATMENT OF PULMONARY TUBERCULOSIS
A MEDICAL RESEARCH COUNCIL INVESTIGATION

The following gives the short-term results of a controlled investigation into the effects of streptomycin on one.

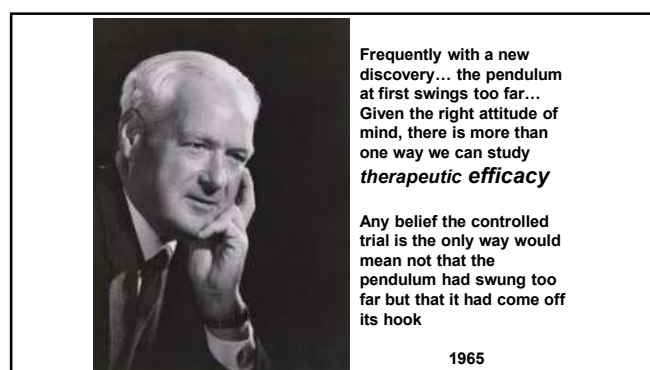
The Control Scheme

Determination of whether a patient would be treated by streptomycin and bed-rest (S case) or by bed-rest alone (C case) was made by reference to a statistical series based on random sampling numbers drawn up for each sex at each centre by Professor Bradford Hill; the details of the series were unknown to any of the investigators or to the co-ordinator and were contained in a set of sealed envelopes, each bearing on the outside only the name of the hospital and a number. After acceptance of a patient by the panel, and before admission to the streptomycin centre, the appropriate numbered envelope was opened at the central office; the card inside told if the patient was to be an S or a C case, and this information was then given to the medical officer of the centre.

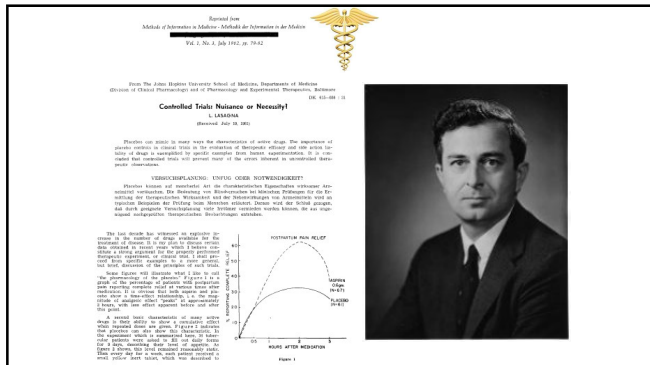
1948

1945

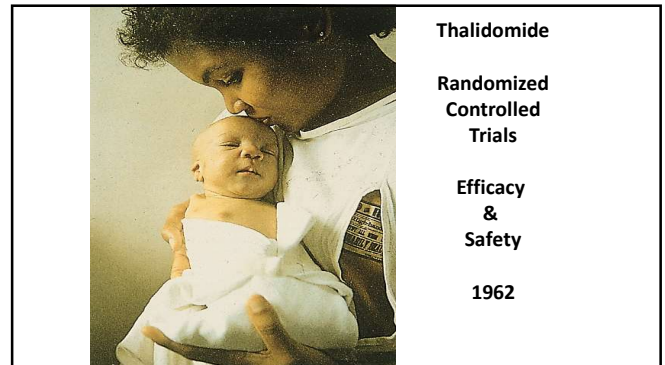
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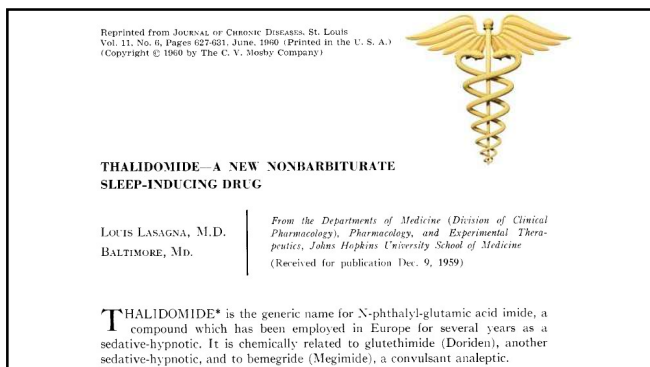
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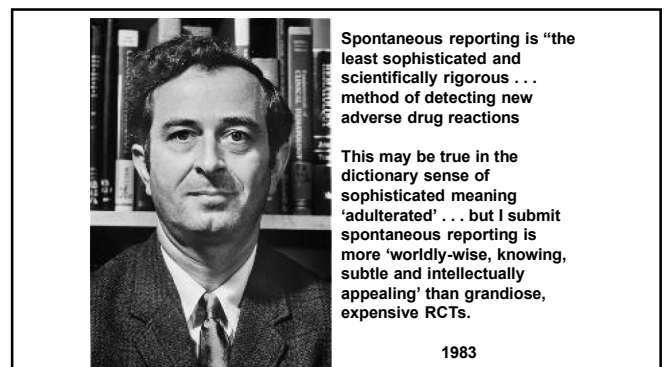
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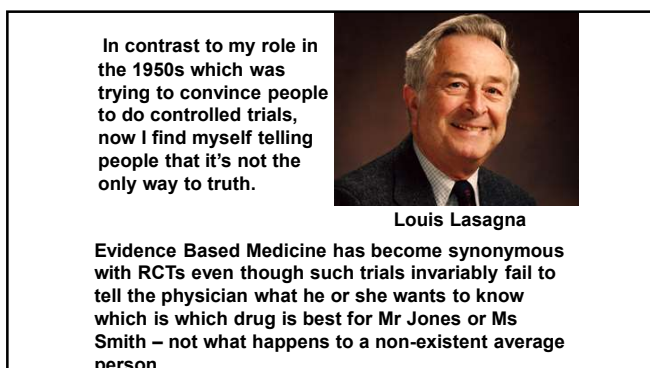
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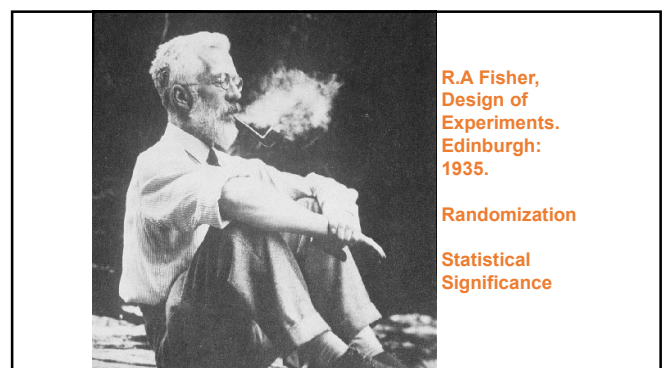
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16



17



18



Statistical Significance means

- You know what you are doing
- You get the same result each time

19



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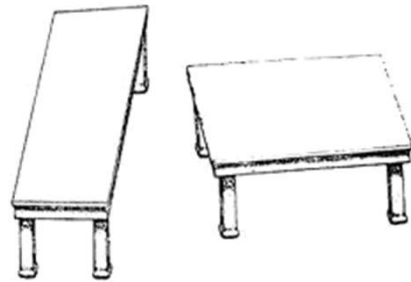


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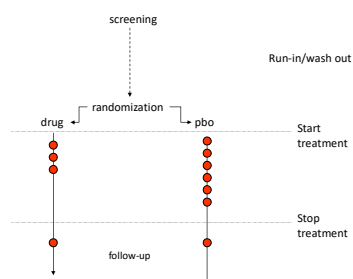
21

CONFOUNDING



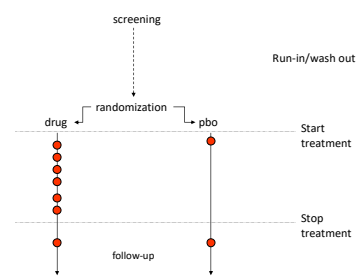
22

RANDOMIZED CONTROLLED **DISEASE** TRIALS Severe Depression Imipramine Suicidal Acts:



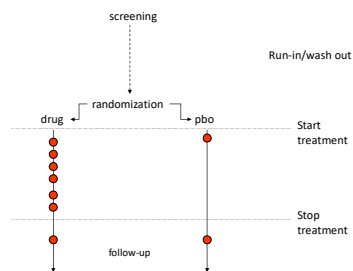
23

RANDOMIZED CONTROLLED **DISEASE** TRIALS Mild-Mod Depression SSRI Suicidal Acts:



24

RANDOMIZED CONTROLLED **DISEASE** TRIALS Mild-Mod Depression Imipramine Suicidal Acts:



Every Time Drug & Illness Produce the same Outcome

| | |
|------------------|------------------------------|
| Anti-arrhythmics | Arrhythmias |
| Anti-asthmatics | Wheezing |
| Rosiglitazone | Diabetes – heart attacks |
| Byetta – Januvia | Diabetes – pancreatitis |
| Tamiflu | Nearly Everything |
| Antidepressant | Libido Suicide Benefit |

25

26

GlaxoSmithKline - 2006

Table 1. Summary of Events of Suicidal Behavior by Study Population, Treatment Group, and Age Band* (5)

| Group | 18-24 year olds | | | 25-64 year olds | | |
|----------------------------|-----------------|---------------|----------------|-----------------|-----------------|----------------|
| | PAR | PBO | OR (95% CI) | PAR | PBO | OR (95% CI) |
| All Indications | 17/776 (2.19%) | 5/542 (0.92%) | 2.4 (0.9, 7.3) | 32/7543 (0.42%) | 34/5000 (0.68%) | 0.6 (0.4, 1.0) |
| Major Depressive Disorder† | 3/230 (1.30%) | 0/104 (0.00%) | Inf (0.3, Inf) | 8/2713 (0.29%) | 0/1567 (0.00%) | Inf (1.3, Inf) |

Paroxetine Suicidal Acts 11 v 0 Placebo Suicidal Acts
N = 2943 N = 1671

27

GlaxoSmithKline - 2006

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| Intermittent Brief Depression | 10/35 (28.57%) | 5/38 (13.61%) | 2.6 (0.8, 9.4) | 22/112 (19.64%) | 30/113 (26.55%) | 0.7 (0.4, 1.3) |

Paroxetine Suicidal Acts 11 v 0 Placebo Suicidal Acts
N = 2943 N = 1671

Paroxetine Suicidal Acts 36 v 35 Placebo Suicidal Acts
N = 147 N = 147

28

GSK - 2006

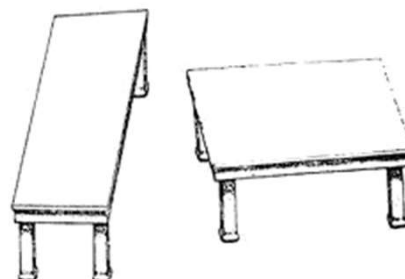
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Paroxetine Suicidal Acts 47 v 35 Placebo Suicidal Acts
N = 3090 N = 1818
RR < 0.80

29

DOES MY CONFOUNDER LOOK BIG



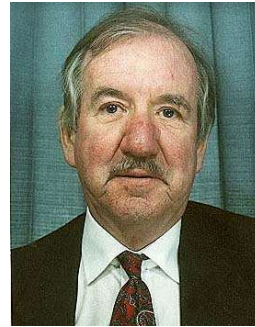
30



AMITRIPTYLINE

1960

31



GEORGE BEAUMONT

CLOMIPRAMINE

1970s

32

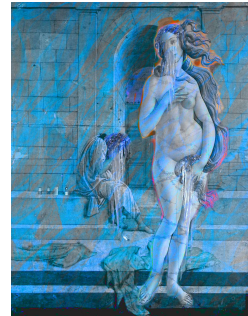
Selective Serotonin
Reuptake Inhibitors
SSRIs

1990

Sex - 5% or 50+%

Risk
MAKING MEDICINES
WORK FOR ALL OF US

33

Post SSRI Sexual Dysfunction
PSSD – 1991 - 2006Genital Numbing
Loss of Function
Loss of LibidoPost-Finasteride Syndrome
PFS – 2011
Post Retinoid Syndrome
PRSD - 2014
Risk
MAKING MEDICINES
WORK FOR ALL OF US

34

Antidepressants
& Sex

BMJ May 2019

35



PETITION

Ridicule

Cure

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH
Risk
MAKING MEDICINES
WORK FOR ALL OF US

36



**You can lead a Bureaucrat to Paper
But you can't make him think**

37



**WALTER RALEIGH
1618**

**Hearsay
Anecdotes
EMA – June 2019**

Risk
MANAGING MEDICINES
UNUSUAL ALL OF US

38



**The plural of anecdote
is not data**

**Journals Changed
Guidelines – Benefits
Harms Vanished**

**RCTs - Gold Standard
Way to Hide Adverse Event**

Up Against Science

1991 Risk
MANAGING MEDICINES
UNUSUAL ALL OF US

39

Economics is from Mars – Medicine from Venus



40

Algorithms are from Mars - Magic is from Venus



41

42

*Occasional Reviews***Validity of anecdotal reports of suspected adverse drug reactions: the problem of false alarms**

G R VENNING

Abstract

Suspected adverse drug reactions first reported in 1963 in the "British Medical Journal," the "Lancet," the "Journal of the American Medical Association," and the "New England Journal of Medicine" were reviewed 18 years later to assess their initial validity and subsequent verification. Of 52 first reports, five were deliberate investigations into potential or predictable reactions, and in each case causality was reasonably established; the other 47 reports were essentially anecdotal. Of these 47 reports, 14 related to categories of adverse reaction where false-positive reports were unlikely: immediate reactions, local reactions, and known reactions caused by

anecdotal report (perhaps of a single case) is often the first means of alerting doctors and regulatory agencies to a serious adverse reaction to a new drug. Unfortunately there is often a substantial time lag between the first alert and subsequent verification and further delay before any regulatory action occurs. A systematic policy of investigating first alerts, at any rate of serious reactions, might reduce the delays that occur. Any consideration of such a policy should, however, take into account the possibility of false alarms. It would be useful to know how often these occur, and the present review was undertaken to investigate this problem.

Methods

43

AERS v ASRS

44