

Does my Bias Look Big In This?

David Healy

1



2

GIG GIGI Bendi Iscylt Pffynghol
 CYMRU Betsi Cadwaladr
 NHS University Health Board
 W.A.L.E.S

NORTH WALES BONE DENSITOMETRY/OSTEOPOROSIS SERVICE
 Llandudno General Hospital
 Ffordd Ysbyty/Hospital Road
 LLANDUDNO
 CONWY
 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'.

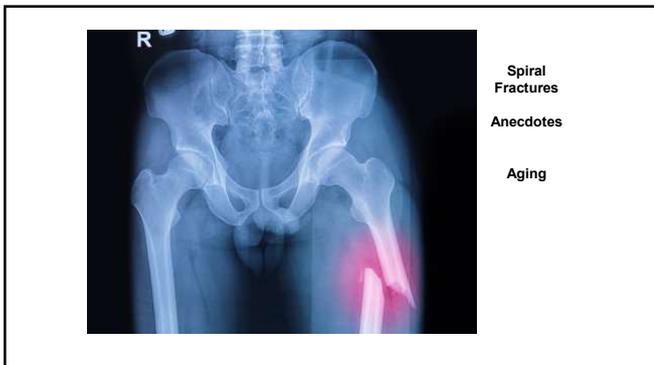
To help us find out more about your broken bone(s) please could you complete the consent form and the questionnaire.

Thank you for taking the time to fill in our questions.

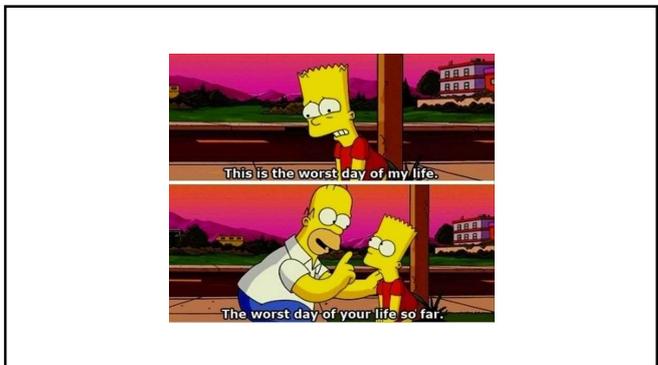
Yours
 The Osteoporosis Team at Llandudno Hospital

3

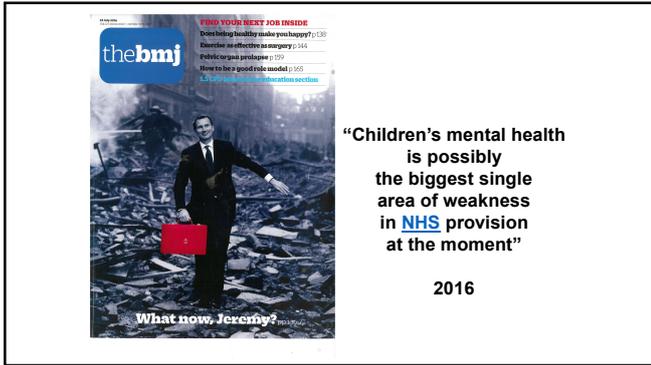
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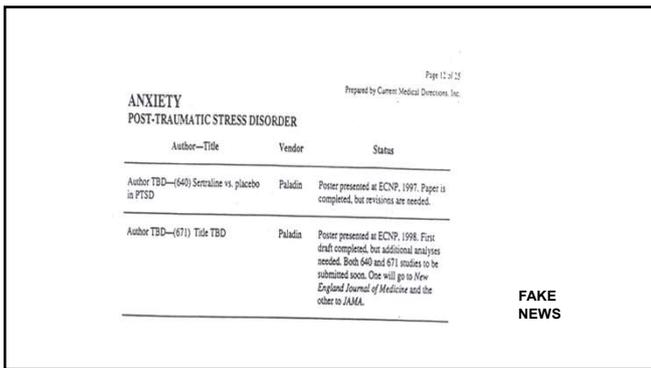
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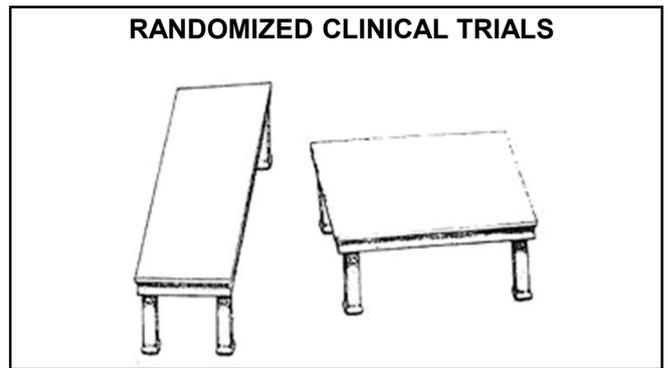
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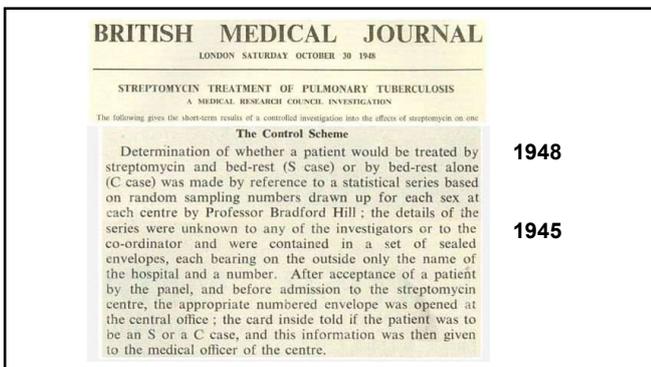
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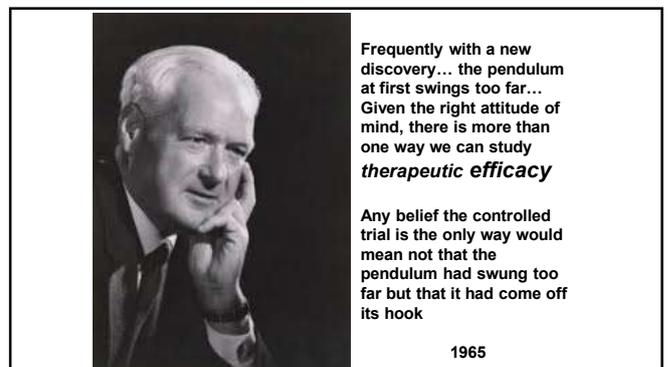
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10



11



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Controlled Trials: Necessity or Necessity?



From The Johns Hopkins University School of Medicine, Department of Medicine, Division of Clinical Pharmacology and Experimental Therapeutics, Baltimore, Md. Vol. 1, No. 4, July 1962, pp. 79-82.

Why do we insist on more than the observation of active drugs. The importance of many studies in clinical trials in the evaluation of therapeutic agents and the value of drugs is well established by careful studies from better experiments. It is important that clinical trials will proceed only if the costs incurred in experimental design are justified.

VERBODENPLAASING: NIETIG OOKER NOTWENDIGHEIT?

Waarom komen wij voortdurend tot de charachteristieke experimentele onderzoekingen toe? Het belang van deze onderzoekingen in het bepalen van de waarde van geneesmiddelen is algemeen bekend. Het is belangrijk dat klinische proeven voortgaan alleen als de kosten daarvan gerechtvaardigd zijn.

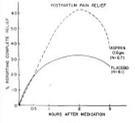


FIGURE 1

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Thalidomide

Randomized Controlled Trials

Efficacy & Safety

1962

14

Reprinted from JOURNAL OF CHRONIC DISEASES, St. Louis, Vol. 11, No. 6, Pages 627-631, June, 1960 (Printed in the U. S. A.) (Copyright © 1960 by The C. V. Mosby Company)



THALIDOMIDE—A NEW NONBARBITURATE SLEEP-INDUCING DRUG

LOUIS LASAGNA, M.D.
BALTIMORE, Md.

From the Departments of Medicine (Division of Clinical Pharmacology), Pharmacology, and Experimental Therapeutics, Johns Hopkins University School of Medicine (Received for publication Dec. 9, 1959)

THALIDOMIDE* is the generic name for N-phthalyl-glutamic acid imide, a compound which has been employed in Europe for several years as a sedative-hypnotic. It is chemically related to glutethimide (Doriden), another sedative-hypnotic, and to bemegride (Megimide), a convulsant anesthetic.

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Spontaneous reporting is "the least sophisticated and scientifically rigorous . . . method of detecting new adverse drug reactions"

This may be true in the dictionary sense of sophisticated meaning 'adulterated' . . . but I submit spontaneous reporting is more 'worldly-wise, knowing, subtle and intellectually appealing' than grandiose, expensive RCTs.

1983

16

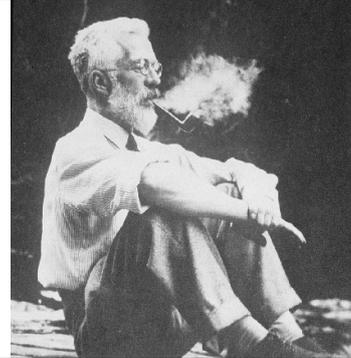
In contrast to my role in the 1950s which was trying to convince people to do controlled trials, now I find myself telling people that it's not the only way to truth.



Louis Lasagna

Evidence Based Medicine has become synonymous with RCTs even though such trials invariably fail to tell the physician what he or she wants to know which is which drug is best for Mr Jones or Ms Smith – not what happens to a non-existent average person

17



R.A. Fisher, Design of Experiments. Edinburgh: 1935.

Randomization

Statistical Significance

18



Statistical Significance means

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

19



Statistical Significance means

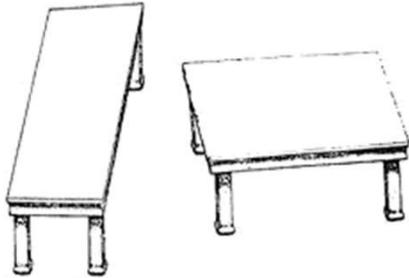
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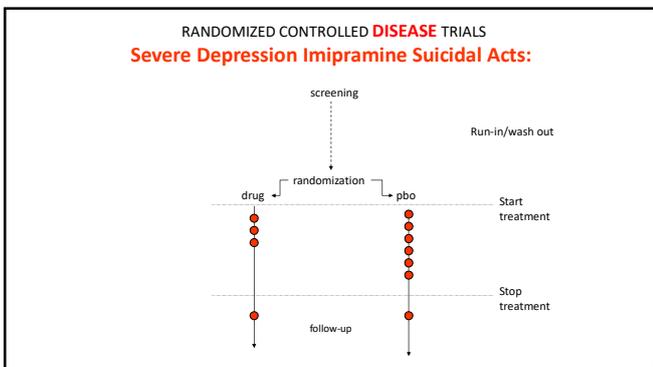


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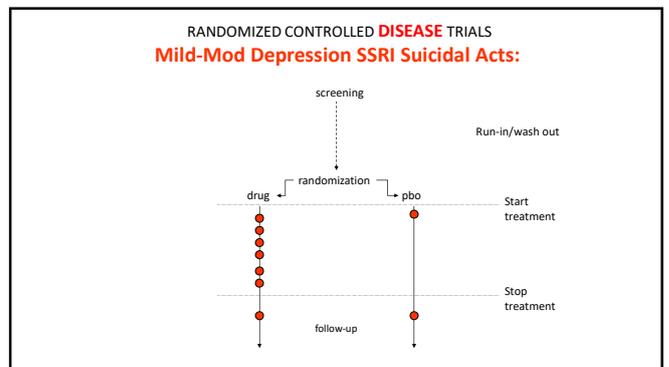
CONFOUNDING



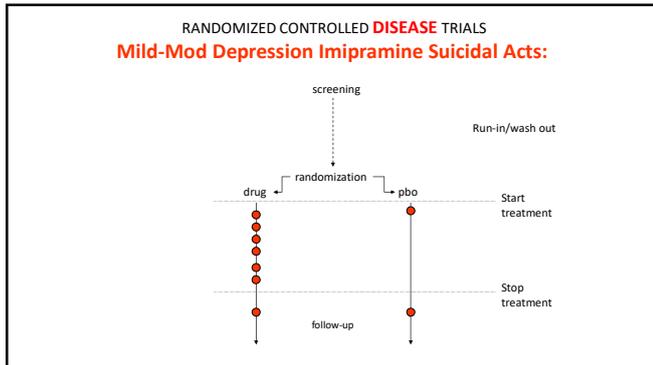
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24



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**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

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

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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

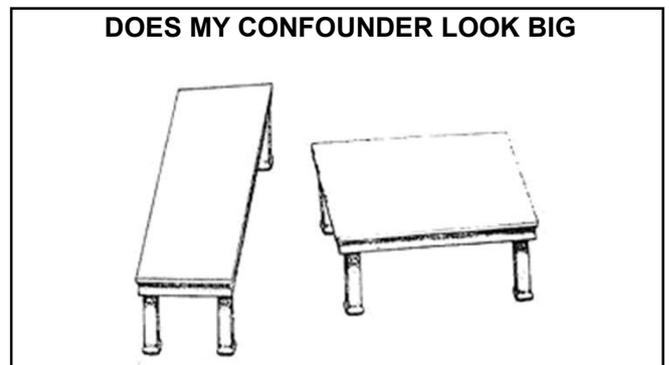
GSK - 2006

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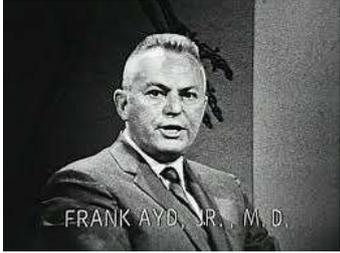
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Paroxetine Suicidal Acts 47 v 35 Placebo Suicidal Acts
N = 3090 N = 1818
RR < 0.80

29



30

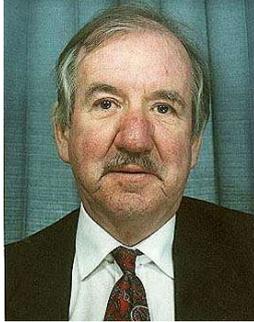


FRANK AYD, JR., M.D.

AMITRIPTYLINE

1960

31



GEORGE BEAUMONT

CLOMIPRAMINE

1970s

32



“Fools”, but sometimes is wise...

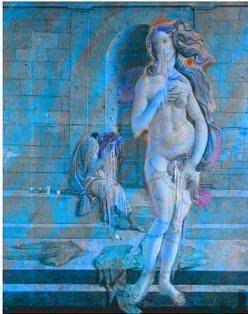
SELECTIVE SEROTONIN REUPTAKE INHIBITORS SSRIs

1990

Sex - 5% or 50+%

Risk
MAKING MEDICINES SAFER FOR ALL OF US

33



Post SSRI Sexual Dysfunction PSSD – 1991 - 2006

**Genital Numbing
Loss of Function
Loss of Libido**

Post-Finasteride Syndrome PFS – 2011

Post Retinoid Syndrome PRSD - 2014

Risk
MAKING MEDICINES SAFER FOR ALL OF US

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thebmj

Question over child obesity claims p 174
The case search for albatross p 182
Painkiller row: do patients care? p 191
Responsibility for GP's p 199
GoD home in the education section

Antidepressants & Sex

BMJ May 2019

Declining sex in Britain

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PETITION

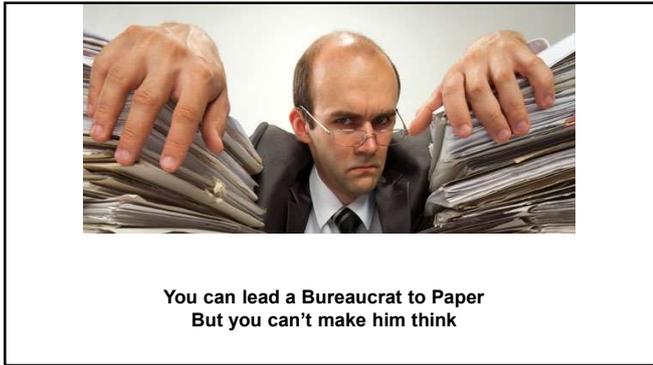
Ridicule

Cure

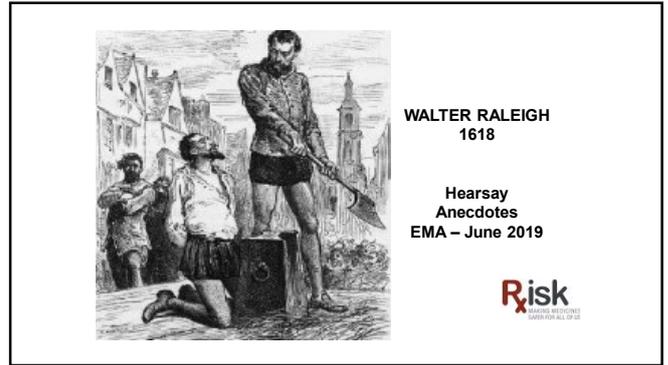
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Risk
MAKING MEDICINES SAFER FOR ALL OF US

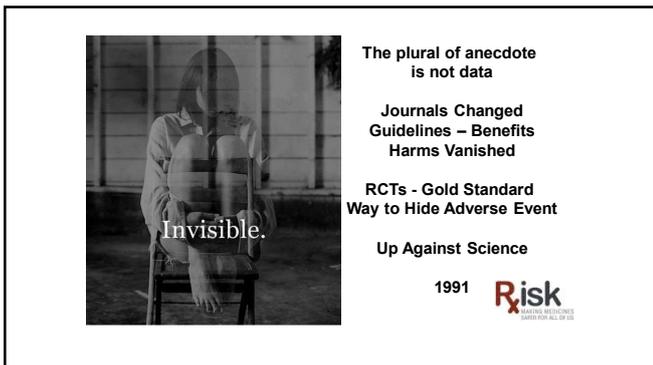
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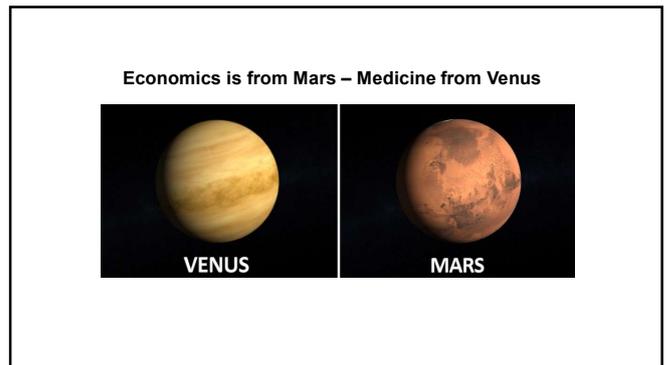
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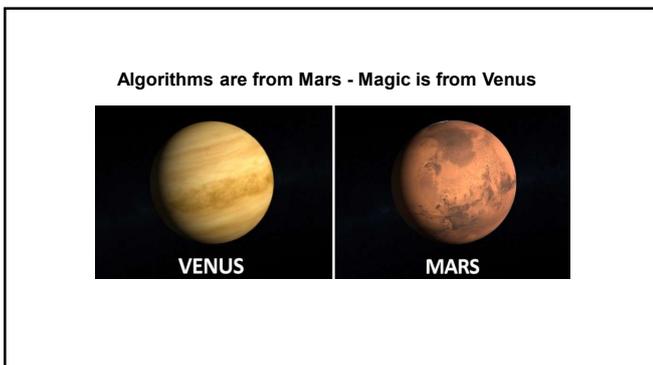
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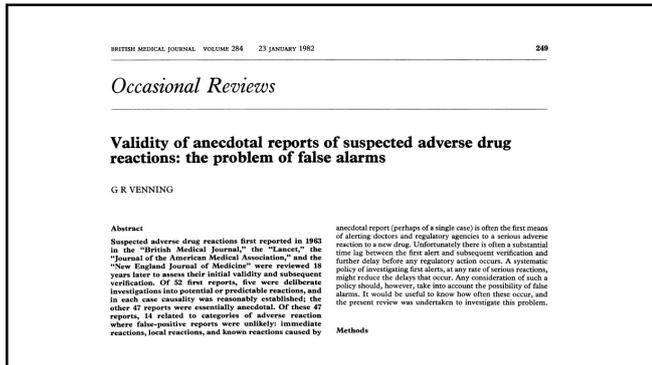
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