MHeNs TRANSLATIONAL NEUROSCIENCE LECTURE | 2019

SECOND LECTURE: Professor David Healy, Professor of Psychiatry, Bangor University, United Kingdom Title: Responsibility Care and Neuroscience

Wednesday 13 March 2019 - 16 hrs. | Lecture | Location: Universiteitssingel 50 (UNS50), Blauwe zaal 0.402 17 hrs. | Discussion |





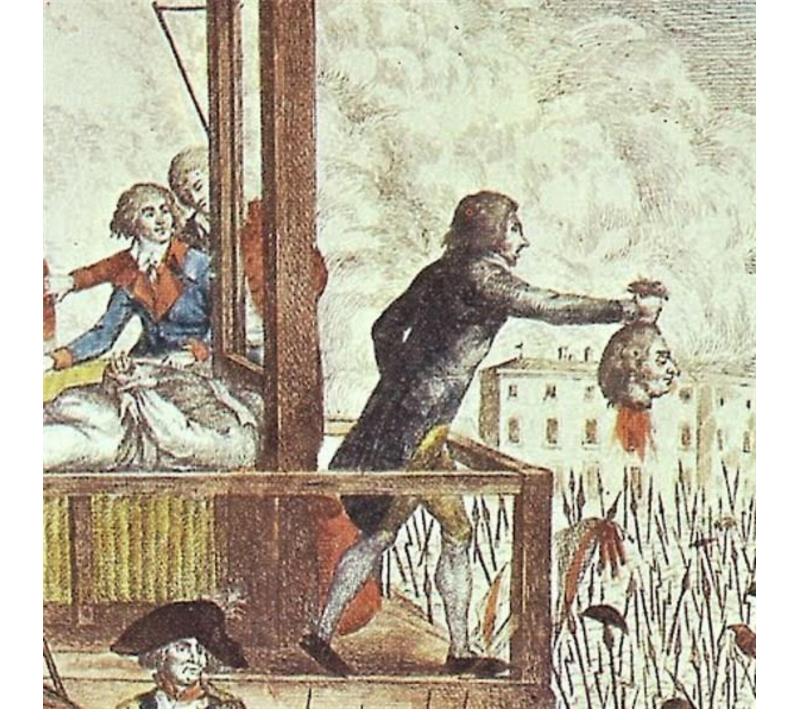
1649 William Petty

Political Medicine

GDP

EBM

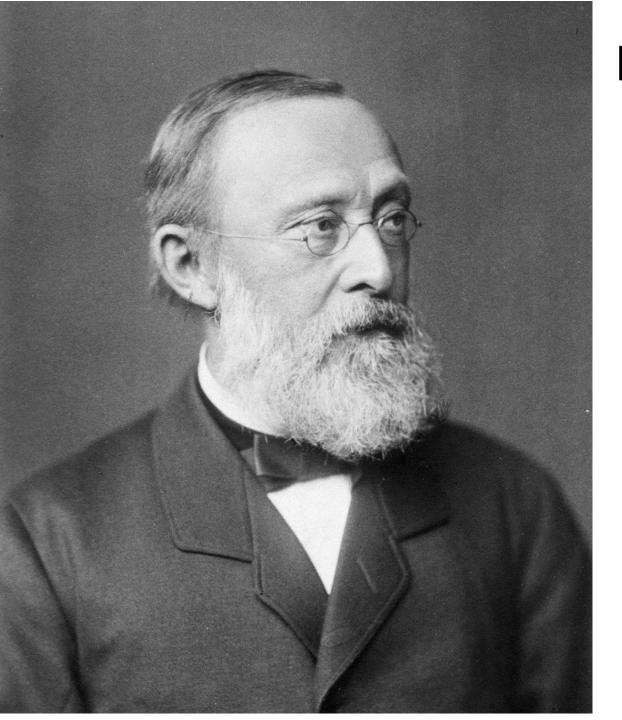
Brain



Economics

Medical Model Pinel

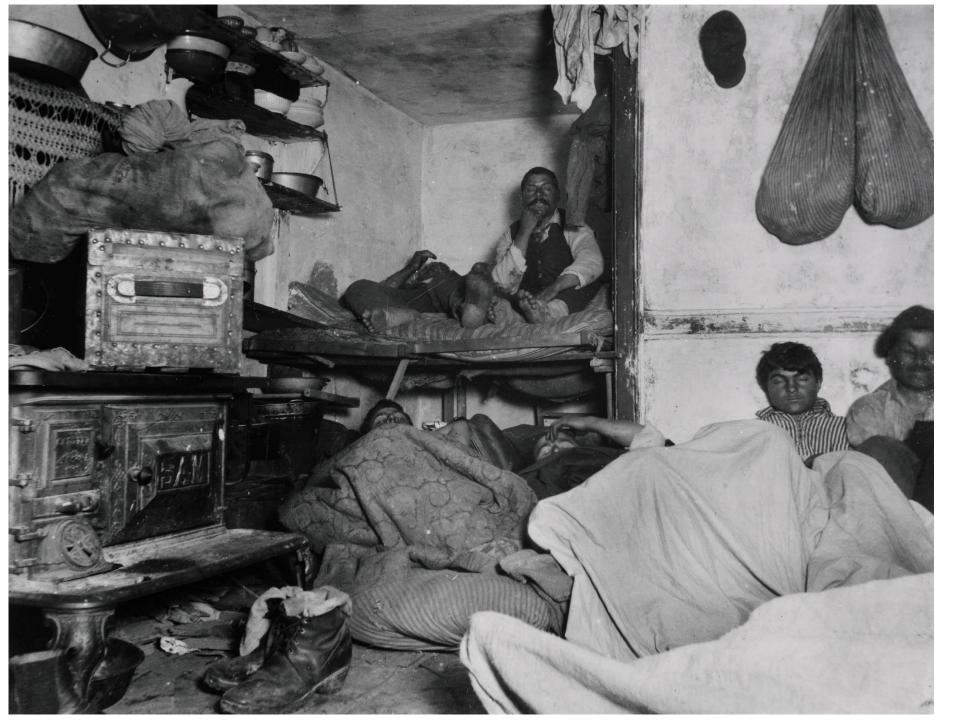
Technique



Medicine is a social science & politics is nothing more than medicine on a grand scale

Virchow 1848

Rosen – Bio Social



The Condition of the Working Class

Friedrich Engels

1848

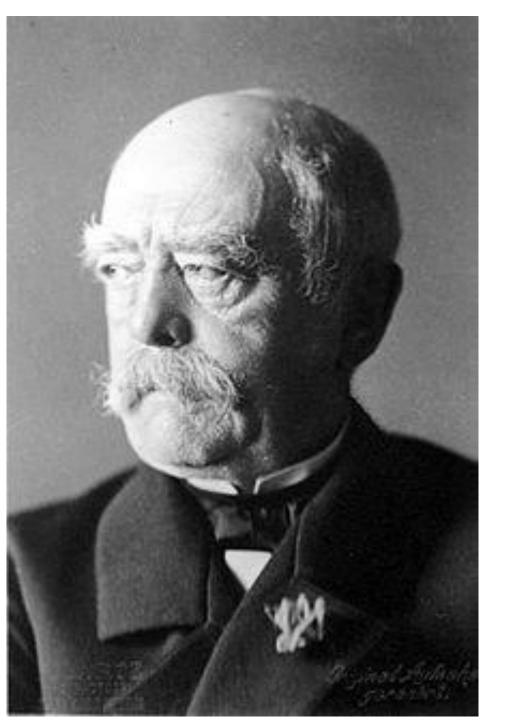


1848

Communism Liberalism

- vote
- education
- no state

Medicine



Politics is not an exact science...

I fully recognize the prominence of the speaker [Virchow] in his field of expertise

[but] since [he] has amateurishly stepped out of his field into mine,

I must say that his politics strike me as lightweight.

Bismarck 1882

A CALCULUS and Anesthesia in Nineteenth-Century OF SUFFERING America



MARTIN S. PERNICK

Anesthesia

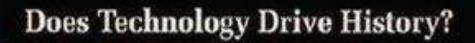
Ends and Means Is it right to do wrong Even though good may result?

Medicine - Poison Mutilate

Surgery – Analgesia Hygiene Emergency Medicine

1848





The Dilemma of Technological Determinism



edhed by Merritt Roe Smith and Leo Marx

WHAT DRIVES HISTORY?

Providence

Individual Genius

Or

Technique?

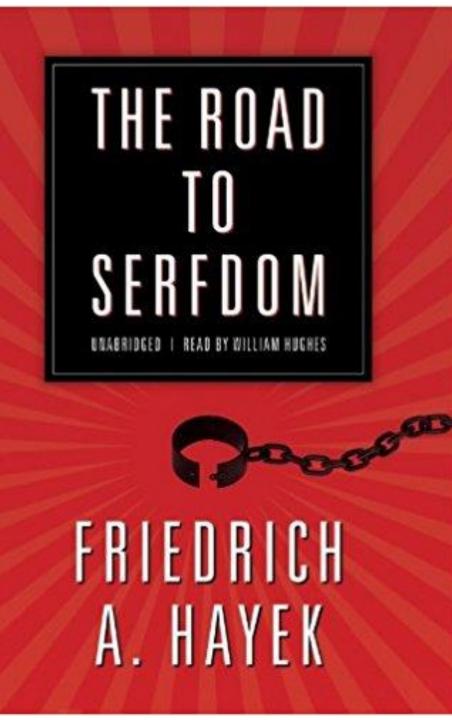


Max Weber 1919

Franz Kafka 1925

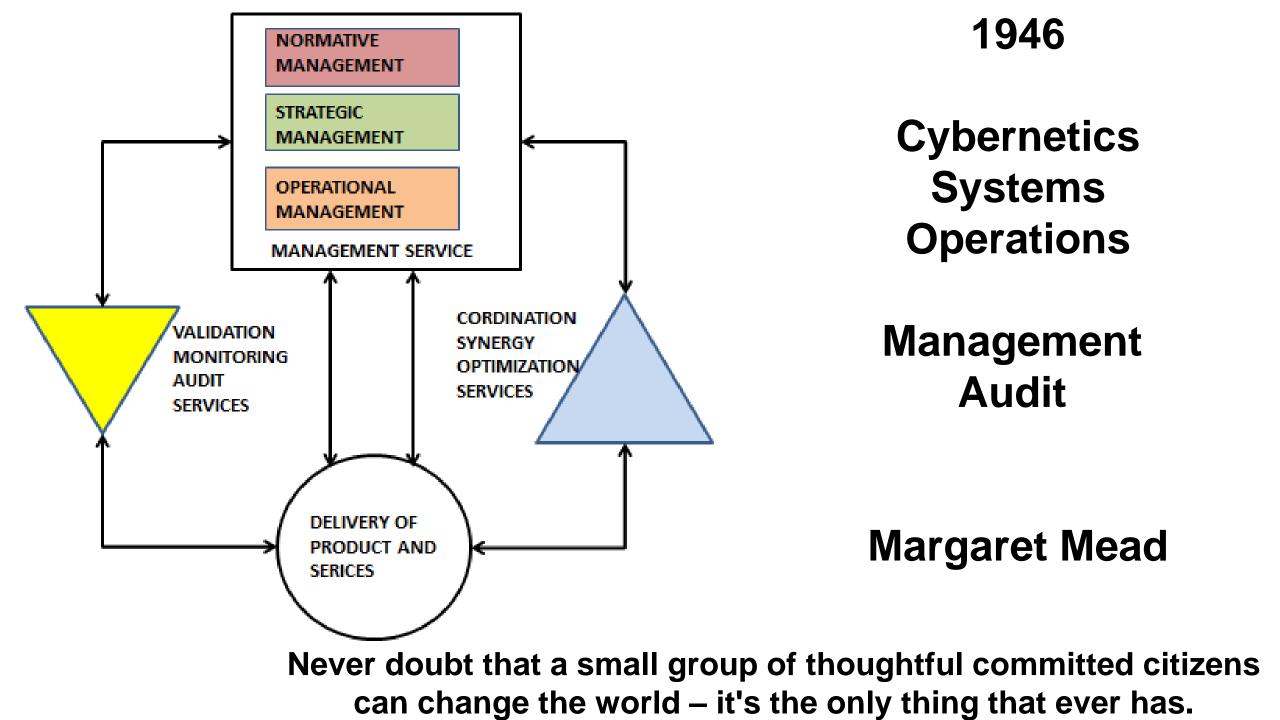
Politician

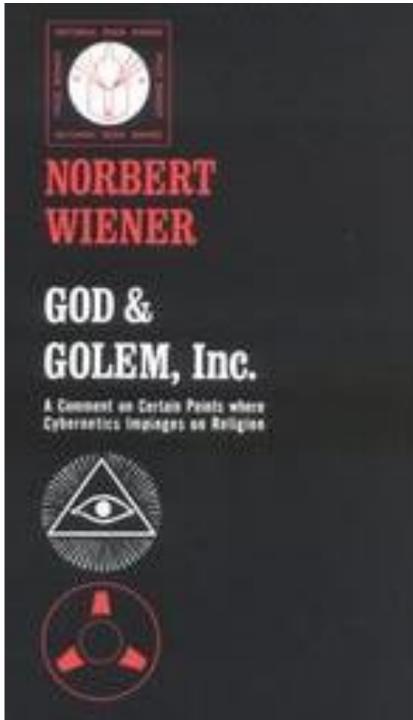
Bureaucratic Technique



The Virus of Central Planning

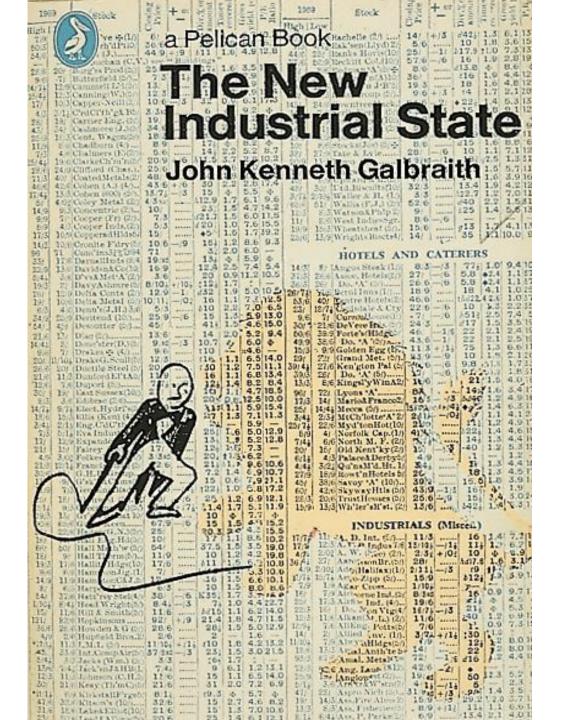
1944





Closed Systems Open Systems Responsibility

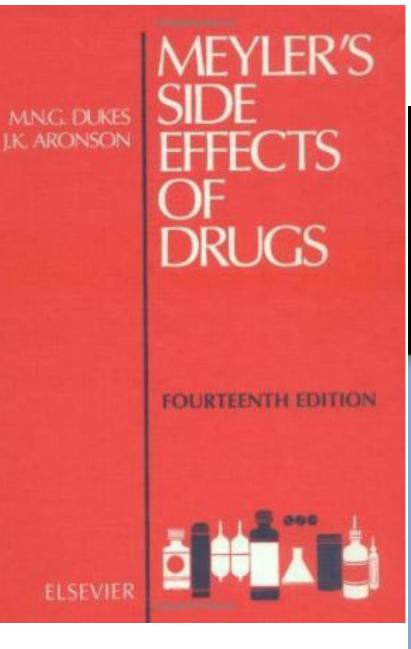
Full Artificial Intelligence Full Technique



THE AFFLUENT SOCIETY

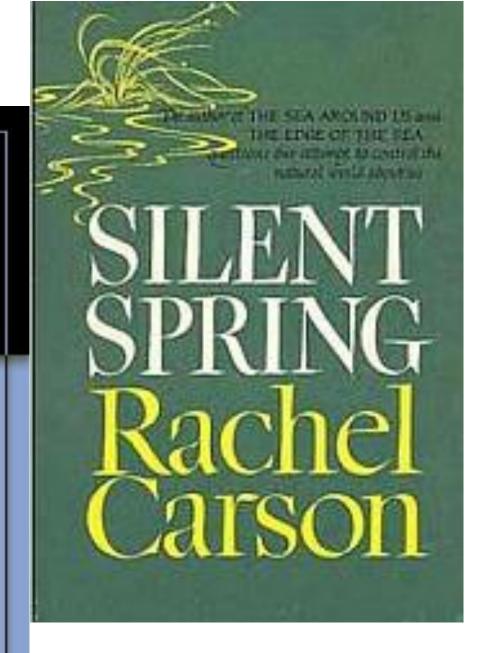
Distribution Channels

THE INVISIBLE HAND OF THE CORPORATION



Hunter's Diseases of Occupations

Hunter, Donald

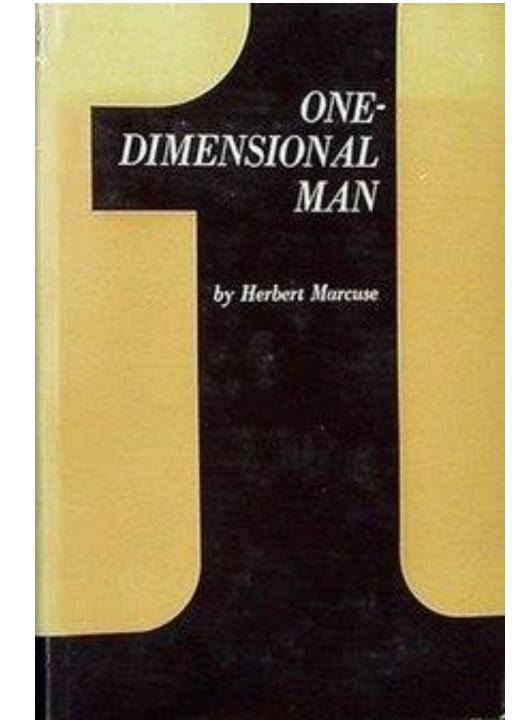


Note: This is not the actual book cover



Enhance or Diminish

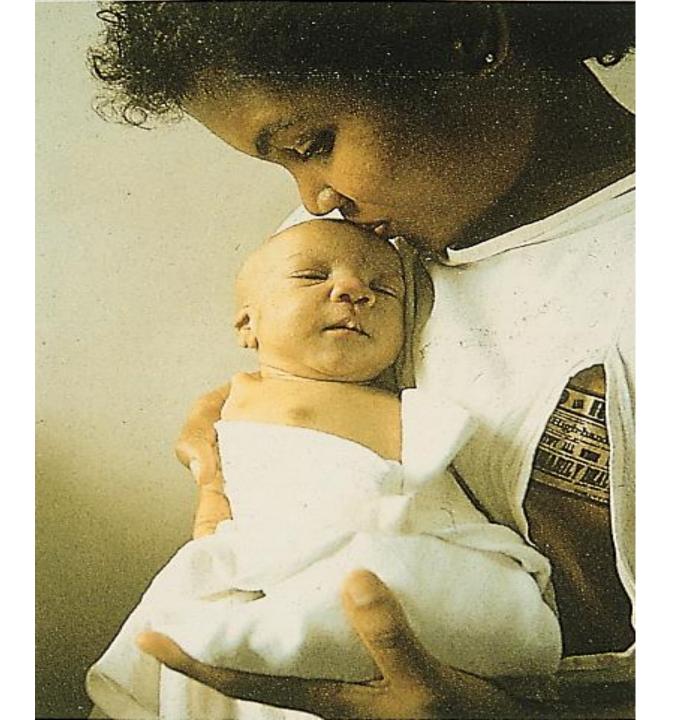
PARIS 1968



Operational Thinking

Prescribing by Numbers

Pecunia non Olet DSM non Olet 1976



Thalidomide

Randomized Controlled Trials

Efficacy & Safety

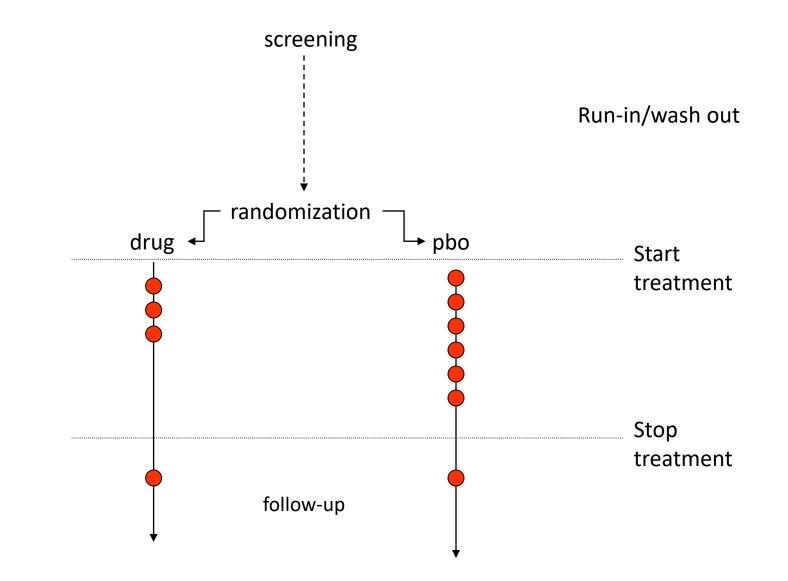
A New Technique

"If one came to the conclusion that the only way to find out the truth about a medication was to use a controlled clinical trial, it would mean not that the pendulum had swung too far but that it had come completely off its hook"

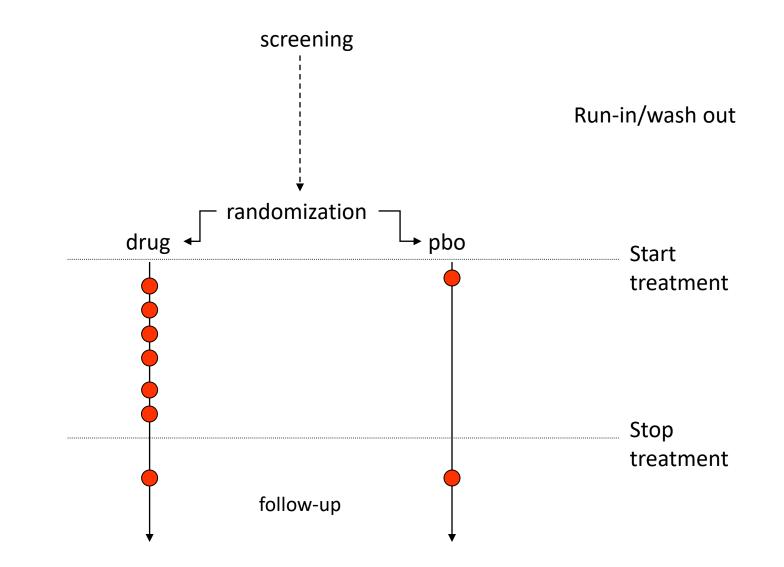


Evidence Based Medicine has become synonymous with RCTs even though such trials invariably fail to tell the physician what he or she wants to know which is which drug is best for Mr Jones or Ms Smith – not what happens to a non-existent average person

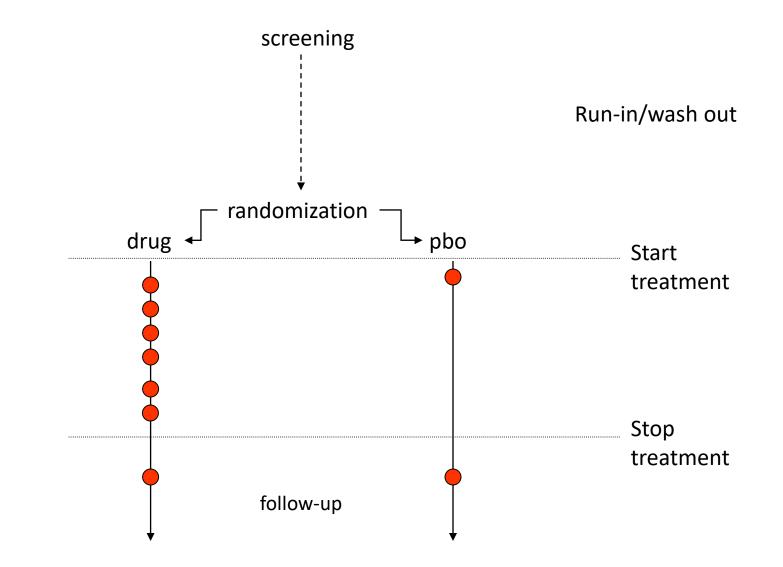
RANDOMIZED CONTROLLED **DISEASE** TRIALS Severe Depression Imipramine Suicidal Acts:



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



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



GlaxoSmithKline - 2006

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

Group	18-24 year olds			25-64 year olds		
	PAR	РВО	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 O Placebo Suicidal Acts N = 2943 N = 1671 RR > 6.0

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 ActsN = 2943N = 1671RR > 6.0Paroxetine Suicidal Acts 32 v 35 Placebo Suicidal ActsN = 147N = 147

GSK - 2006

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Paroxetine Suicidal Acts 43 v 35 Placebo Suicidal Acts N = 3090 N = 1818 RR < 0.80 Reprinted from JOURNAL OF CHRONIC DISEASES, St. Louis Vol. 11, No. 6, Pages 627-631, June, 1960 (Printed in the U. S. (Copyright © 1960 by The C. V. Mosby Company)



THALIDOMIDE—A NEW NONBARBITURA 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 analeptic.

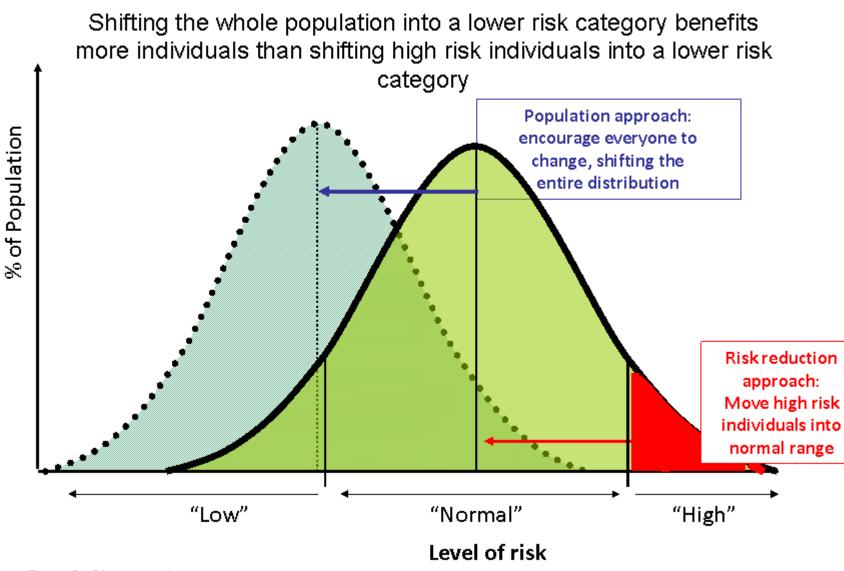


Advert Security and advertised of the second of the secon

RISK

Prescribing by Numbers Numero non Olet Neo-Medicalism Neo-Liberalism

The Bell-Curve Shift in Populations



Source: Rose G. Sick Individuals and sick populations. *Int J Epidemiol.* 1985; 12:32-38.



Asthma – Peak Flow

Lipid Levels

Blood Glucose

Blood Pressure

Eating Disorders

The Measurement is the Illness

Anorexia





Helping people live the lives They chose to live

Havel 2010

A Specter is haunting Europe... the Specter of Dissent

You do not become a 'dissident' just because you decide one day to take up this most unusual career. You are thrown into it by your personal sense of responsibility... You are cast out of the existing structures and placed in a position of conflict with them. It begins as an attempt to do your work well and ends with being branded an enemy of society. ... The dissident is not seeking power. He has no desire for office and does not gather votes. He does not attempt to charm the public. He offers nothing and promises nothing. He can offer, if anything, only his own skin-He offers it solely because he has no other way of affirming the truth he stands for.

Vaclav Havel, The Power of the Powerless, 1978



Advert Security and advertised of the second of the secon

RISK

Prescribing by Numbers Numero non Olet Neo-Medicalism Neo-Liberalism



The Assembly Line

Assembling What ?

Page 12 of 25

Prepared by Current Medical Directions. 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 New England Journal of Medicine and the other to JAMA.		

FAKE NEWS



If X Then Y

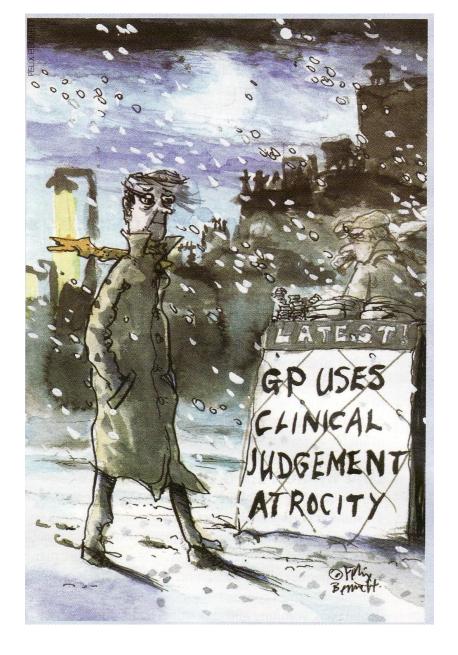


If the figures for X are low or high

Then give Brand Y

Avoid Adverse Events &





JUDGMENT - DISCRETION

PERSONAL CONTACT



THE LOGIC of CARE

From Health Care To Health Services

1960 Service Industries

National Institute for Health and Clinical Excellence

Issue date: January 2011

Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults

Management in primary, secondary and community care

This updates and replaces NICE clinical guideline 22

NICE: climical guidaline 113 Developed by the National Collaborating Centre for Mental Health and the National Collaborating Centre for Primary Care













1848

Communism Liberalism Why no Revolution?

Evidence Based Medicine Why no Revolution?

Fluoxetine and suicide: a meta-analysis of controlled trials of treatment for depression

Charles M Beasley Jr, Bruce E Dornseif, Janet C Bosomworth, Mary E Sayler, Alvin H Rampey Jr, John H Heiligenstein, Vicki L Thompson, David J Murphy, Daniel N Masica

Abstract

Division of Clinical

Neurosciences, Lilly

Lilly and Company,

46285, USA

research scientist

Mary E Sayler, MS.

statistician

statistician

Indianapolis, Indiana

Charles M Beasley Jr, MD,

clinical resource physician

Bruce E Dornseif, PHD,

Janet C Bosomworth, BS,

Alvin H Rampey Jr, PHD, senior statistician

John H Heiligenstein, MD,

clinical research physician

Vicki L Thompson, MSN,

David J Murphy, BBA,

Daniel N Masica, MD,

Correspondence to: Dr

senior information analyst

international research adviser

Charles M Beasley Jr, Lilly

Research Laboratories, Eli

Lilly and Company, Lilly

Indianapolis, Indiana 46285,

Corporate Center 2128.

BMY 1991;303:685-92

USA.

clinical research administrator

Research Laboratories, Eli

Objective-A comprehensive meta-analysis of clinical trial data was performed to assess the possible association of fluoxetine and suicidality (suicidal acts and ideation).

Design-Retrospective analysis of pooled data from 17 double blind clinical trials in patients with major depressive disorder comparing fluoxetine (n= 1765) with a tricyclic antidepressant (n=731) or placebo (n=569), or both.

were searched to identify patients with suicidal acts. Suicidal ideation was assessed with item 3 of the Hamilton depression rating scale, which systematically rates suicidality. Emergence of substantial suicidal ideation was defined as a change in the rating of this item from 0 or 1 at baseline to 3 or 4 during double blind treatment; worsening was defined as any increase from baseline; improvement was defined as a decrease from baseline at the last visit during the treatment.

Results-Suicidal acts did not differ significantly in comparisons of fluoxetine with placebo (0.2% v 0.2%, p=0.494, Mantel-Haenszel adjusted incidence difference) and with tricyclic antidepressants (0.7% v 0.4%, p=0.419). The pooled incidence of suicidal acts was 0.3% for fluoxetine, 0.2% for placebo, and 0.4% for tricyclic antidepressants, and fluoxetine did not differ significantly from either placebo (p=0.533, Pearson's γ^2) or tricyclic antidepressants (p=0.789). Suicidal ideation emerged marginally significantly less often with fluoxetine than with placebo (0.9% v 2.6%, p=0.094) and numerically less often than with tricyclic antidepressants (1.7% v 3.6%, p=0.102).

Main outcome measures-Multiple data sources

incidence was significantly lower with fluoxetine than with placebo (p=0.042) and tricyclic antidepressants (p=0.001). Any degree of worsening of suicidal ideation was similar with fluoxetine and placebo (15.4% v 17.9%, p=0.196) and with fluoxetine and tricyclic antidepressants (15.6% v 16.3%, p=0.793). The pooled incidence of worsening of suicidal ideation was 15.3% for fluoxetine, 17.9% for placebo, and 16.3% for tricyclic antidepressants. The incidence did not differ significantly with fluoxetine and placebo (p=0.141) or tricyclic antidepressants (p=0.542). Suicidal ideation improved significantly more with fluoxetine than with placebo (72.0% v 54.8%, p<0.001) and was similar to the improvement with tricyclic antidepressants (72-5% v 69-8%, p=0-294). The pooled incidence of improvement of suicidal ideation was 72.2% for fluoxetine, 54-8% for placebo, and 69-8% for tricyclic antidepressants. The incidence with fluoxetine was significantly greater than with placebo (p<0.001) and did not differ from that with tricyclic antidepressants (p=0.296).

The pooled incidence of emergence of substantial suicidal ideation was 1.2% for fluoxetine, 2.6% for

placebo, and 3.6% for tricyclic antidepressants. The

Conclusion-Data from these trials do not show that fluoxetine is associated with an increased risk of suicidal acts or emergence of substantial suicidal thoughts among depressed patients.

Introduction

Because depression is an important risk factor for suicide1-3 there is a need to study the effects of

September 20

1991





The plural of anecdote is not data

Journals Changed Drugs Bulletins Vanished Guidelines - Benefits

Harms Vanished Risk Benefit Ratio Up Against Science



Rossi et al state that spontaneous reporting is usually viewed as the least sophisticated and scientifically rigorous method of detecting new adverse drug reactions



This may be true in the Webster's dictionary sense of sophisticated meaning "adulterated" but I submit spontaneous reporting is more wordly wise, knowing, subtle and intellectually appealing than expensive RCTs [Phase IV schemes]".



WILLIAMS & WILKINS

Journal of the American Academy of

CADOLESCENT PSYCHIATRY

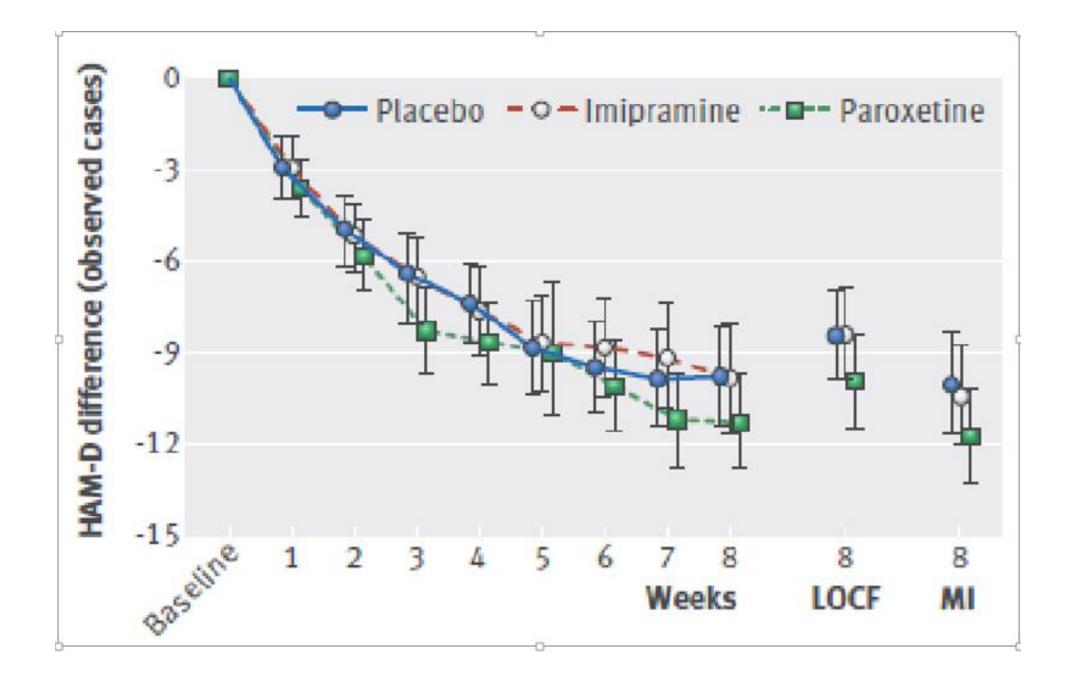
Copyright 2001 © American Academy of Child and Adolescent Psychiatry

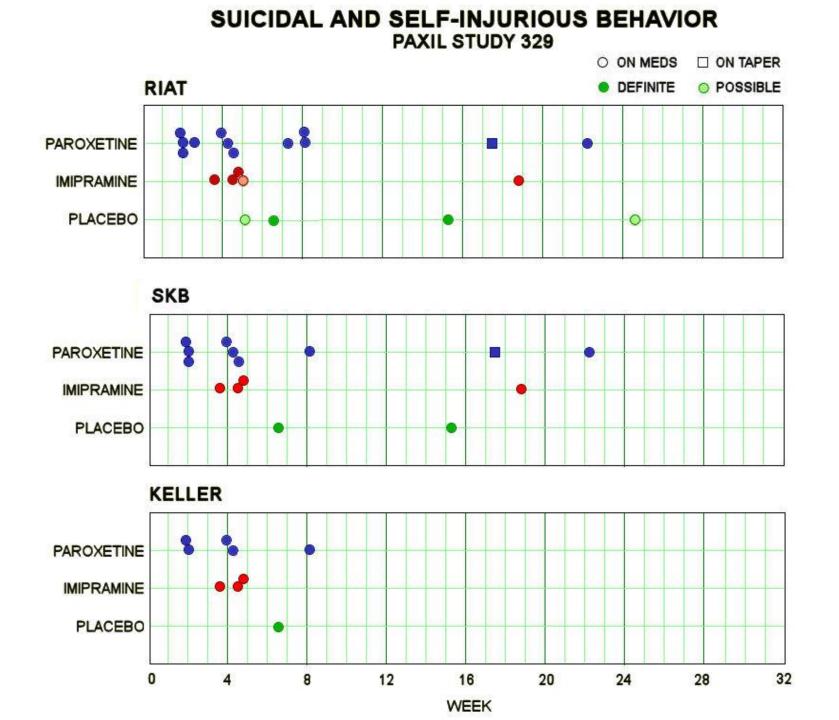
Volume 40(7) July 2001 pp 762-772

Efficacy of Paroxetine in the Treatment of Adolescent Major Depression: A Randomized, Controlled Trial

[Articles]

KELLER, MARTIN B. M.D.; RYAN, NEAL D. M.D.; STROBER, MICHAEL PH.D.;
KLEIN, RACHEL G. PH.D.; KUTCHER, STAN P. M.D.; BIRMAHER, BORIS M.D.;
HAGINO, OWEN R. M.D.; KOPLEWICZ, HAROLD M.D.; CARLSON, GABRIELLE A.
M.D.; CLARKE, GREGORY N. PH.D.; EMSLIE, GRAHAM J. M.D.; FEINBERG, DAVID
M.D.; GELLER, BARBARA M.D.; KUSUMAKAR, VIVEK M.D.; PAPATHEODOROU,
GEORGE M.D.; SACK, WILLIAM H. M.D.; SWEENEY, MICHAEL PH.D.; WAGNER,
KAREN DINEEN M.D., PH.D.; WELLER, ELIZABETH B. M.D.; WINTERS, NANCY C.
M.D.; OAKES, ROSEMARY M.S.; MCCAFFERTY, JAMES P. B.S.





Study329.org

Restoring Study 329

SCIENTIFIC INTEGRITY THROUGH DATA BASED MEDICINE

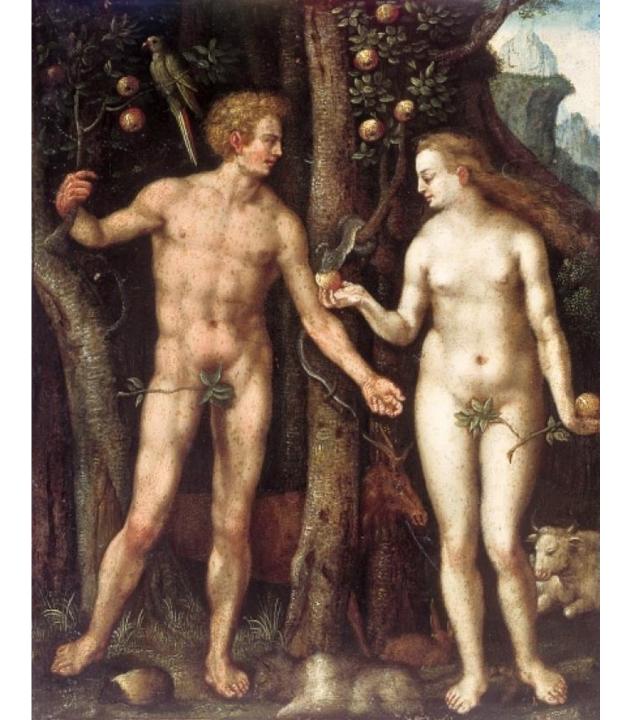
HOME BACKGROUND ▼ MEDIA ▼ TEAM ▼ WHAT CAN I DO?

BMJ Publishes Study Revealing How Flawed Drug Research Fails a Trusting Public

Band of Intrepid Researchers "Sets the Record Straight" on Ghostwritten Study

Toronto (September 16, 2015) — Today the <u>BMJ published Restoring Study 329</u>, a decade-long effort by researchers to uncover the truth about the safety of an antidepressant approved for use by adolescents. Restoring Study 329 is a reanalysis and rebuttal of the original Study 329 ... <u>more</u>

See news coverage



70 Open label studies All positive

Т	Η	

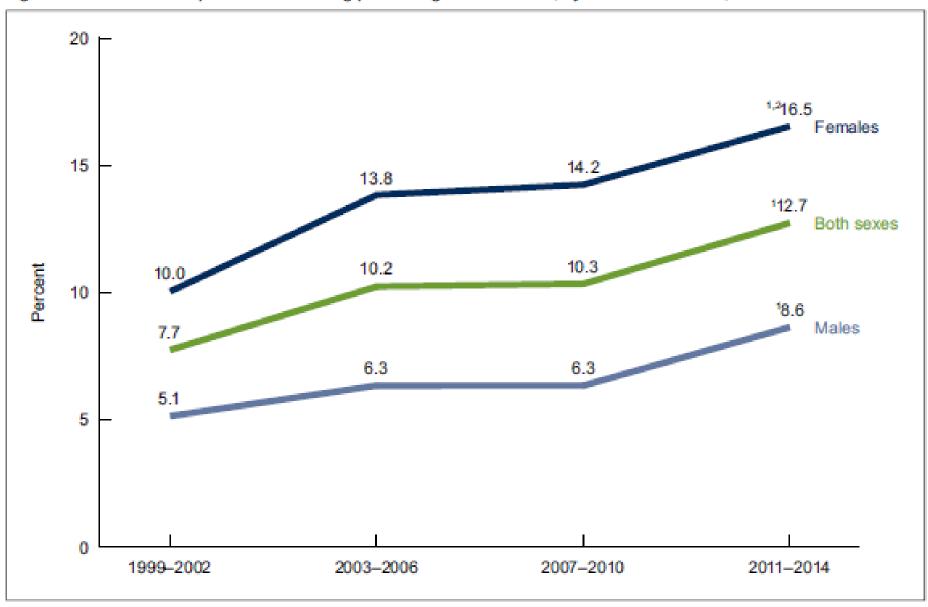
STUDY	Primary Outcome	Source	SUICIDAL	Numbers
PAROXETINE				
329	Ν	Le Noury et al	XS	275
377	Ν	Laughren	XS	276
701	Ν	Mosholder	XS	206
511	Ν	Braconnier et al	XS	125
SERTRALINE				
1001	Ν	Laughren	XS	373
1017	Ν	Laughren	XS	
FLUOXETINE				
1990	Ν	Simeon et al	XS	40
X065	Ν	Mosholder	XS	96
HJCE	Ν	Mosholder	XS	219
HCCJ	Ν	Mosholder	XS	40
TADS	Ν	March et al	XS (34v3)	439
VENLAFAXINE				
Mandoki	Ν	Mandoki et al	XS	40
382	Ν	Laughren	XS	165
394	Ν	Laughren	XS	196
CITALOPRAM				
94404	Ν	Laughren	XS	233
Cit 18	Ν	Jureidini et al	?	174
Sct 15	Ν	CSR	?	266
NEFAZODONE				
141	Ν	Laughren	XS	190
187	Ν	Laughren	XS	278
MIRTAZAPINE				
0045	Ν	Laughren	XS	258

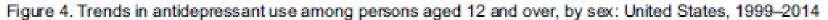
FALL

AFTER

STUDY	Primary Outcome	Source	SUICIDAL	Nos
PAROXETINE				
2487	Ν	ClinTrials.gov	?	56
FLUOXETINE				
F	Ν		?	34
0	NN		XSS	
VENLAFAXINE				
1012	Ν	ClinTrials.gov	XS	40
1014	Ν	ClinTrials.gov	XS	340
1032	Ν	ClinTrials.gov	XS	363
Tordia	Ν		XS	334
CITALOPRAM				
Sct 32	N?	CSR	XS	316
DULOXETINE				
6223	Ν	ClinTrials.gov	XS	337
7109	Ν	ClinTrials.gov	XS	463
L-MILNACIPRAN				
Lev-MD-11	Not Reported		660	660
VORTIOXETINE				
12712	OL		1068	1068
12709	Not Reported		750	750
12710	Not Reported		750	750
VILAZODONE				
	OL		250	250

THE FALL

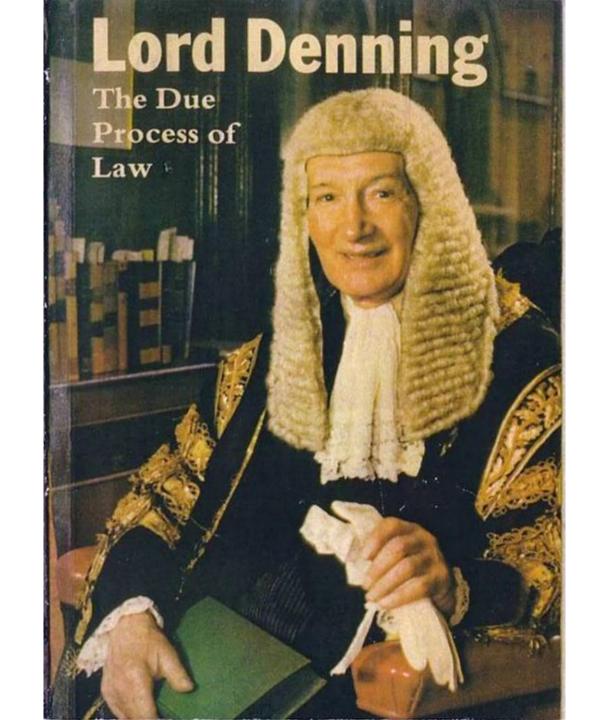




THE GUILDFORD FOUR

If their story is right it is such an appalling vista it cannot be

Wrongfully convicted prisoners should stay in jail rather than be freed and risk a loss of public confidence in the law.



JAMES HOLMES TRADE

Aurora 2012

Sertraline

A Specter is haunting Health Care... the Specter of Dissent

You do not become a 'dissident' just because you decide one day to take up this most unusual career. You are thrown into it by your personal sense of responsibility... You are cast out of the existing structures and placed in a position of conflict with them. It begins as an attempt to do your work well and ends with being branded an enemy of society. ... The dissident is not seeking power. She has no desire for office and does not gather votes. She does not attempt to charm the public. She offers nothing and promises nothing. She can offer, if anything, only her own skin— She offers it solely because she has no other way of affirming the truth she stands for.

Vaclav Havel, The Power of the Powerless, 1978

Technician

AERS v ASRS

JOB

© www.123rf.com



Even such is time that takes in trust Our youth our joys our all we have And pays us with but age and dust Who in the dark and silent grave When we have wandered all our ways Shuts up the story of our days But from this earth this grave this dust My God shall raise me up I trust

Walter Raleigh



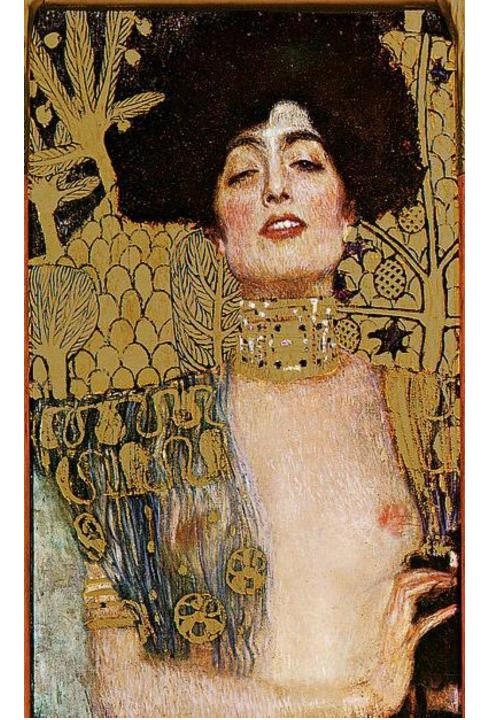
HEARSAY

BOYCOTT

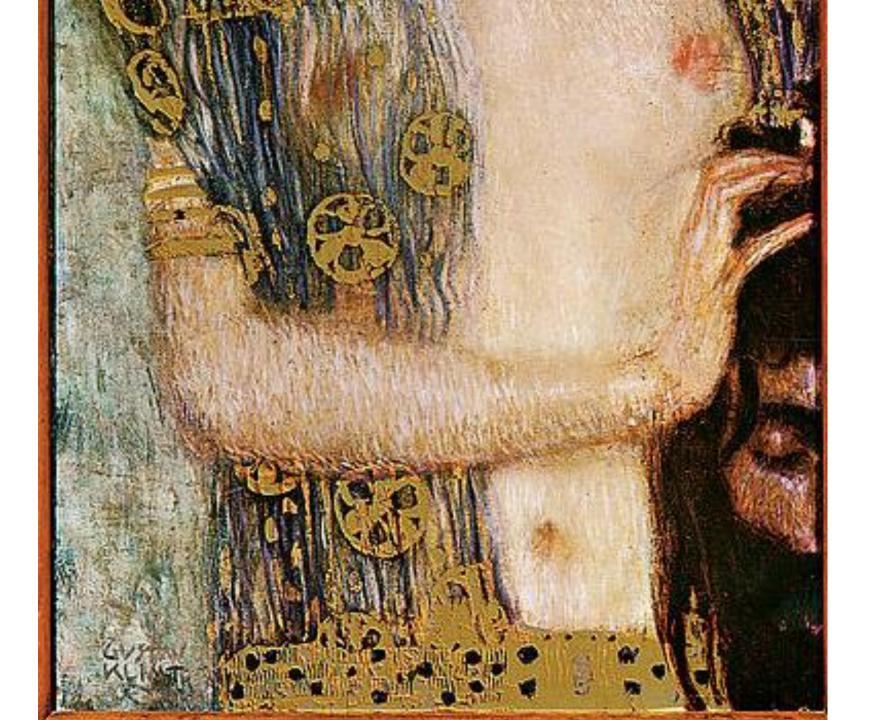
HUNGER STRIKE

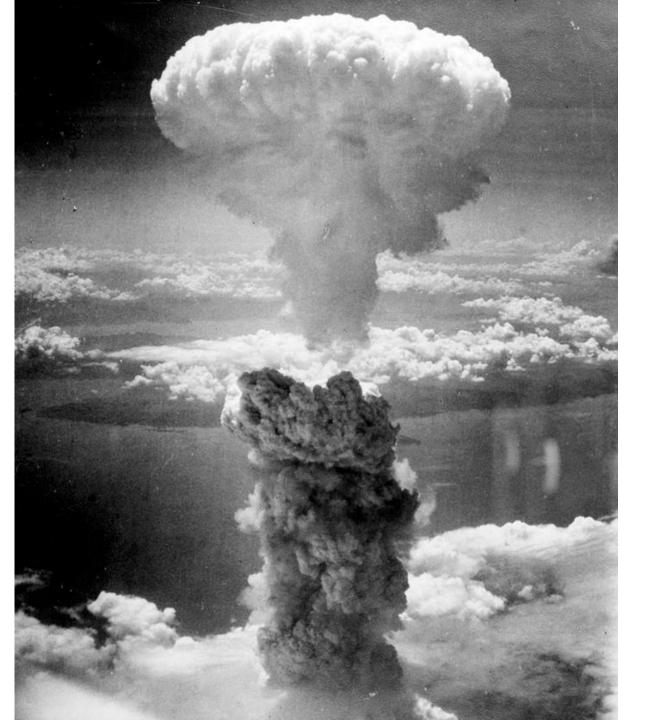
CLINICAL TRIALS

BACKSTOP



Die on your Feet Or Live on your Knees

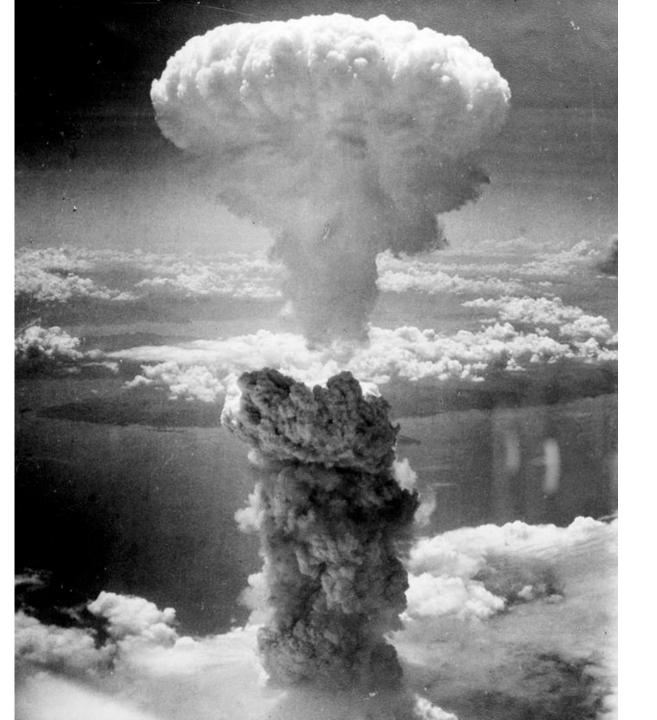




TECHNIQUE

Q FIX

Enhance or Diminish



Life Expectancy is Falling

40% of over 45s On 3 or more drugs

40% of over 65s On 5 or more drugs

De-prescribing Reduces hospitalisation & increases life expectancy



Economics Medical Model Pinel Technique

Money gave the owner, the capitalist, controlling power in the enterprise So it still does in small businesses.

But in large firms the decisive power now lies with a bureaucracy that controls, but does not own, the capital.

This bureaucracy is what business schools teach their graduates to navigate.

But bureaucratic motivation and power are outside

the central subject of economics.

We have corporate management,

but we do not study its internal dynamics

or explain why certain behaviors are rewarded with money and power.

Galbraith 1999