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: Universiteitsingel 50 (UN650), 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
Anesthesia

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

Medicine - Poison Mutilate

Surgery – Analgesia
Hygiene
Emergency Medicine

1848
WHAT DRIVES HISTORY?
Providence
Individual Genius
Or
Technique?
The Virus of Central Planning
1944
Never doubt that a small group of thoughtful committed citizens can change the world – it’s the only thing that ever has.

Margaret Mead
Closed Systems
Open Systems
Responsibility

Full Artificial Intelligence
Full Technique
The New Industrial State
John Kenneth Galbraith

THE AFFLUENT SOCIETY

Distribution Channels

THE INVISIBLE HAND OF THE CORPORATION
Enha...
Operational Thinking

Prescribing by Numbers

Pecunia non Olet

DSM non Olet

1976
Thalidomide

Randomized Controlled Trials

Efficacy & Safety

A New Technique
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.

“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”
RANDOMIZED CONTROLLED DISEASE TRIALS

Severe Depression Imipramine Suicidal Acts:

screening

Run-in/wash out

randomization

Start treatment

drug

pbo

Stop treatment

follow-up
RANDOMIZED CONTROLLED DISEASE TRIALS

Mild-Mod Depression SSRI Suicidal Acts:

- **Screening**
- **Randomization**
- **Drug** (left) and **pbo** (right)
- **Run-in/wash out**
- **Start treatment**
- **Stop treatment**
- **Follow-up**
RANDOMIZED CONTROLLED DISEASE TRIALS

Mild-Mod Depression Imipramine Suicidal Acts:

- Screening
- Run-in/wash out
- Randomization
- Drug → pbo
- Start treatment
- Stop treatment
- Follow-up
Table 1. Summary of Events of Suicidal Behavior by Study Population, Treatment Group, and Age Band* (5)

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<th>Group</th>
<th>18-24 year olds</th>
<th>25-64 year olds</th>
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<tr>
<td>All Indications</td>
<td>17/776 (2.19%)</td>
<td>5/542 (0.92%)</td>
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<tr>
<td>Major Depressive Disorder†</td>
<td>3/230 (1.30%)</td>
<td>0/104 (0.00%)</td>
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Paroxetine Suicidal Acts 11 v 0 Placebo Suicidal Acts
N = 2943        N = 1671
RR > 6.0
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<tr>
<td>Intermittent Brief Depression</td>
<td>10/35 (28.57%)</td>
<td>5/38 (13.61%)</td>
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Paroxetine Suicidal Acts 11 v 0 Placebo Suicidal Acts
N = 2943         N = 1671
RR > 6.0
Paroxetine Suicidal Acts 32 v 35 Placebo Suicidal Acts
N = 147         N = 147
Table 1. Summary of Events of Suicidal Behavior by Study Population, Treatment Group, and Age Band

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<td>5/38</td>
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Paroxetine Suicidal Acts 43 v 35 Placebo Suicidal Acts

N = 3090          N = 1818

RR < 0.80
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 analeptic.
Operational thinking drives Risk
Risk Societies

Prescribing by Numbers
Numero non Olet
Neo-Medicalism
Neo-Liberalism
The Bell-Curve Shift in Populations

Shifting the whole population into a lower risk category benefits more individuals than shifting high risk individuals into a lower risk category.

Population approach: encourage everyone to change, shifting the entire distribution.

Risk reduction approach: Move high risk individuals into normal range.

Asthma – Peak Flow
Lipid Levels
Blood Glucose
Blood Pressure
Eating Disorders
The Measurement is the Illness
Anorexia
“A FILM TO PROVOKE FURY - ★★★★”
EMPIRE

“INDISPENSABLE...EXTREMELY MOVING... A POWERFUL DOCUMENTARY THAT DEMANDS TO BE SEEN”
THE HOLLYWOOD REPORTER

MEDICINE MONOPOLY MALICE

fire in the blood

CERT 15

WWW.FIREINTHEBLOOD.COM
Helping people live the lives they chose to live

Havel 2010
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.

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

Operational thinking drives Risk Societies

Risk
The Assembly Line

Assembling

What?
## ANXIETY
### POST-TRAUMATIC STRESS DISORDER

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<td>Paladin</td>
<td>Poster presented at ECNP, 1997. Paper is completed, but revisions are needed.</td>
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<tr>
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<td>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 <em>New England Journal of Medicine</em> and the other to <em>JAMA</em>.</td>
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If X
Then Y
If the figures for X are low or high

Then give Brand Y

Avoid Adverse Events &
The pain started the day my daughter left home.

Have you ever had blood in your urine?

PERSONAL CONTACT

JUDGMENT - DISCRETION

GP uses clinical judgement atrocity.
THE LOGIC of CARE
From Health Care To Health Services
1960 Service Industries
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
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

Division of Clinical Neurosciences, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Indiana 46285, USA

Charles M Beasley Jr, MD, clinical resource physician
Bruce E Dornseif, PhD, research scientist
Janet C Bosomworth, BS, statistician
Mary E Sayler, MS, statistician
Alvin H Rampey Jr, PhD, senior statistician
John H Heiligenstein, MD, clinical research physician
Vicki L Thompson, MSN, clinical research administrator
David J Murphy, BBA, senior information analyst
Daniel N Masica, MD, international research adviser

Correspondence to: Dr Charles M Beasley Jr, Lilly Research Laboratories, Eli Lilly and Company, Lilly Corporate Center 2128, Indianapolis, Indiana 46285, USA.

BMJ 1991;303:885-92

Abstract
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.

Multiple data sources 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) or 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 χ2) 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).

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 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 54-9%, 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).

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 suicide, there is a need to study the effects of
The plural of anecdote is not data

Journals Changed
Drugs Bulletins Vanished
Guidelines - Benefits

Invisible.

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

SUICIDAL AND SELF-INJURIOUS BEHAVIOR
PAXIL STUDY 329

RIAT

- PAROXETINE
- IMIPRAMINE
- PLACEBO

SKB

- PAROXETINE
- IMIPRAMINE
- PLACEBO

KELLER

- PAROXETINE
- IMIPRAMINE
- PLACEBO

WEEK

- ON MEDS
- ON TAPER

- DEFINITE
- POSSIBLE
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 BMJ published Restoring Study 329, 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 ... more

See news coverage
70
OPEN LABEL STUDIES
ALL POSITIVE
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Figure 4. Trends in antidepressant use among persons aged 12 and over, by sex: United States, 1999–2014

- **Females**:
  - 1999–2002: 10.0%
  - 2003–2006: 13.8%
  - 2007–2010: 14.2%
  - 2011–2014: 16.5%

- **Both sexes**:
  - 1999–2002: 7.7%
  - 2003–2006: 10.2%
  - 2007–2010: 10.3%
  - 2011–2014: 12.7%

- **Males**:
  - 1999–2002: 5.1%
  - 2003–2006: 6.3%
  - 2007–2010: 6.3%
  - 2011–2014: 8.6%
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.
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.

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
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