



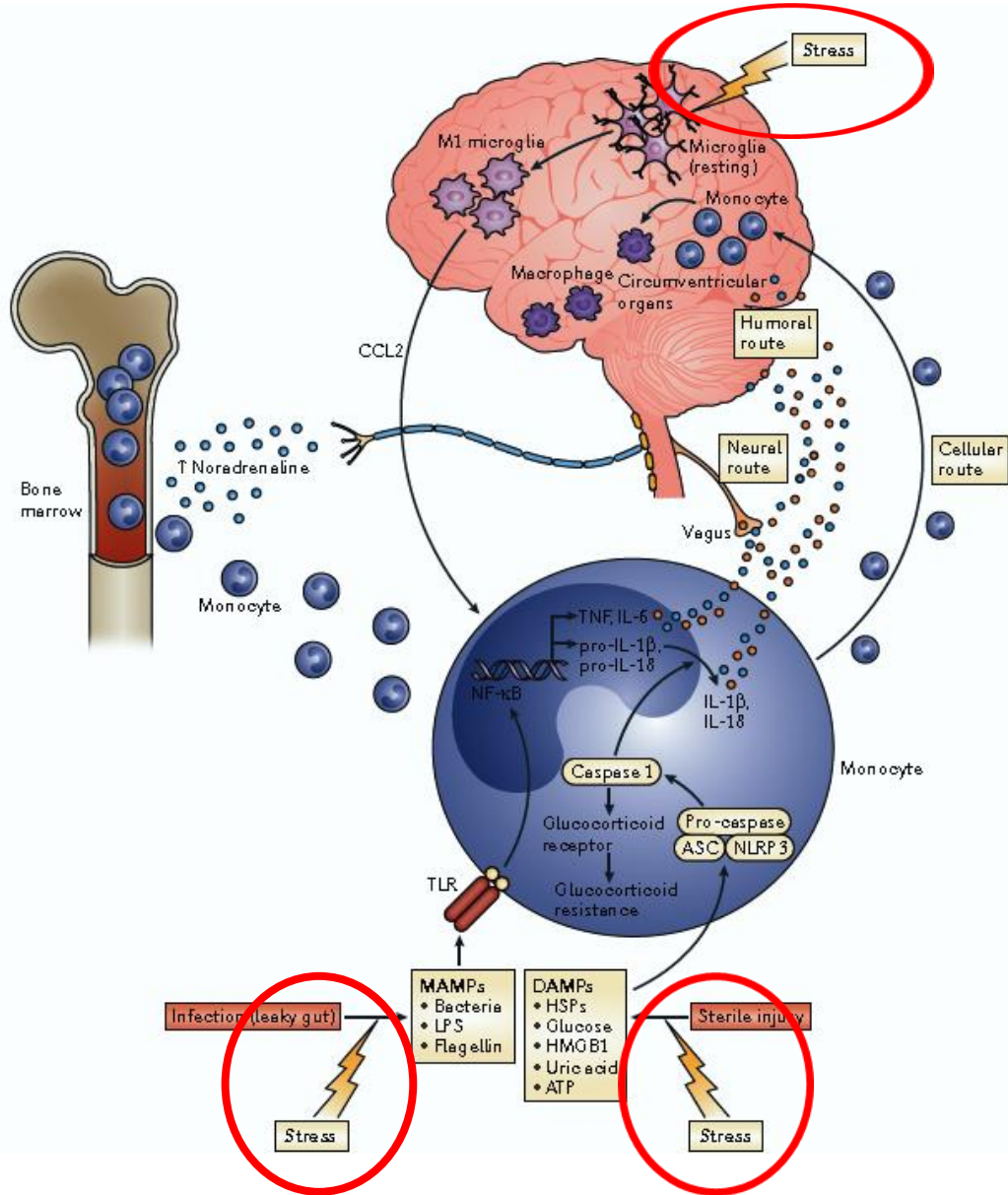
Università di Trieste



University of London

Infelicità, tristezza e depressione: un'epidemia di disturbi mentali?

Tullio Giraldi



Lo «stress»
causa
la «depressione»

Stress

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HANS SELYE
M.D.

STRESS WITHOUT DISTRESS

HOW TO USE STRESS AS
A POSITIVE FORCE TO ACHIEVE
A REWARDING LIFE STYLE.

“DR. HANS SELYE KNOWS MORE
ABOUT STRESS THAN ANY
OTHER SCIENTIST ALIVE!”

— Alvin Toffler, author of Future Shock

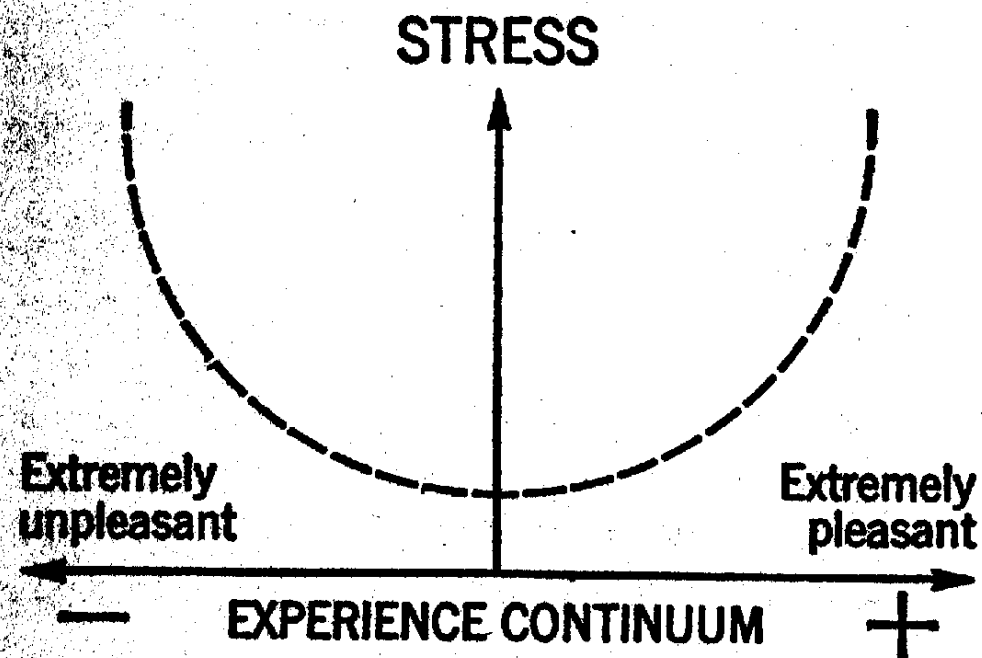


Figure 1. Theoretical model showing the relation between stress and various types of life experiences. (Courtesy L. Levi.)

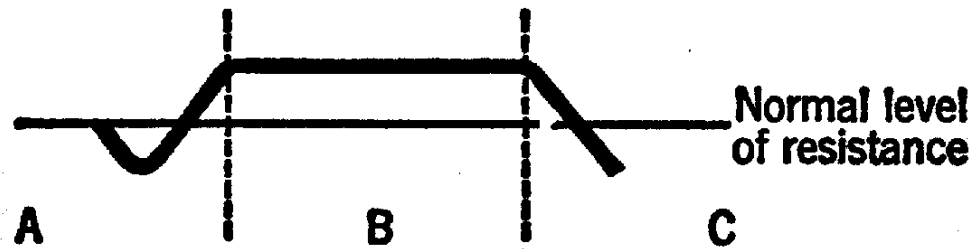


Figure 2. The three phases of the general adaptation syndrome (G.A.S.).

A. Alarm reaction. The body shows the changes characteristic of the first exposure to a stressor. At the same time, its resistance is diminished and, if the stressor is sufficiently strong (severe burns, extremes of temperature), death may result.

B. Stage of resistance. Resistance ensues if continued exposure to the stressor is compatible with adaptation. The bodily signs characteristic of the alarm reaction have virtually disappeared, and resistance rises above normal.

C. Stage of exhaustion. Following long-continued exposure to the same stressor, to which the body had become adjusted, eventually adaptation energy is exhausted. The signs of the alarm reaction reappear, but now they are irreversible, and the individual dies.

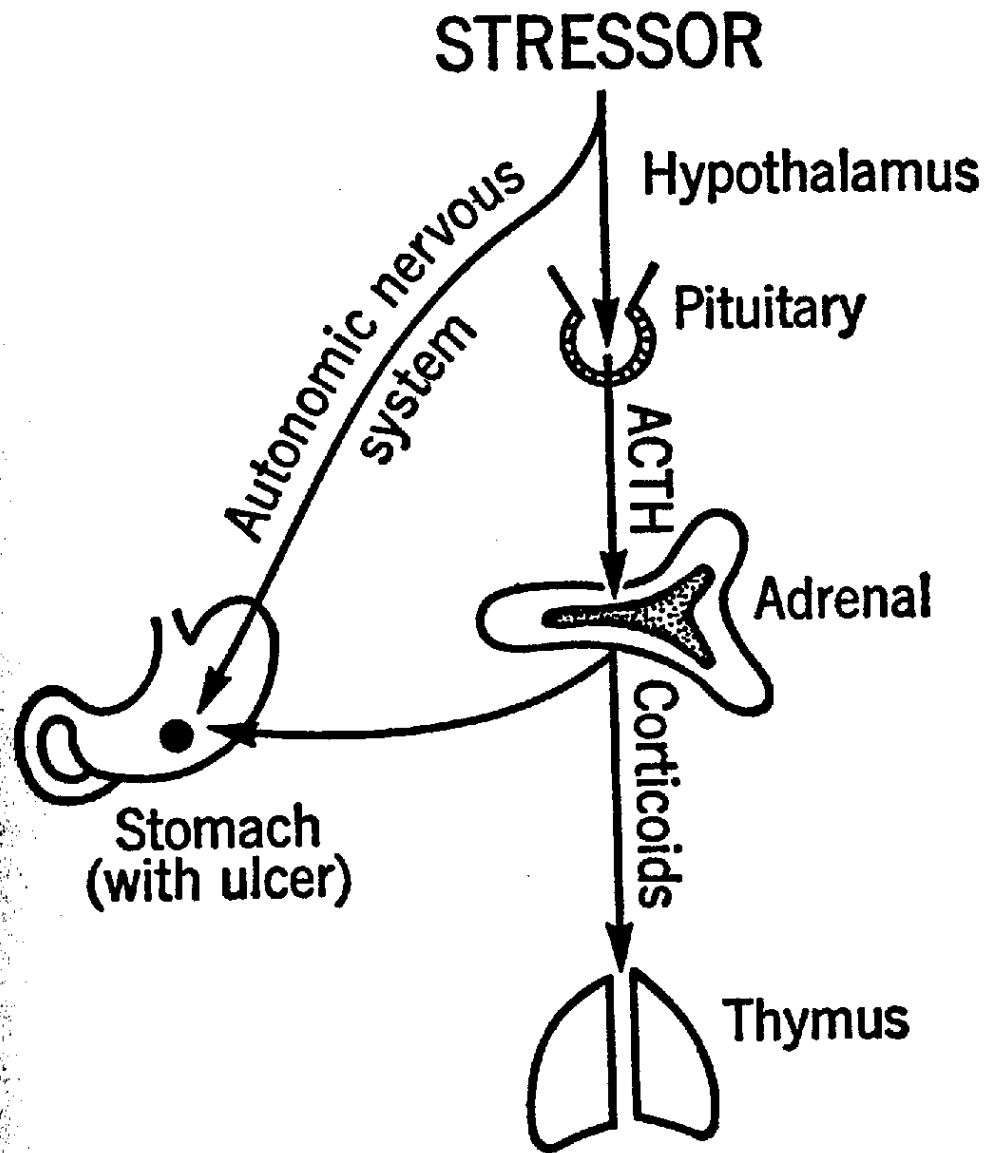


Figure 3. Principal pathways mediating the response to a stressor

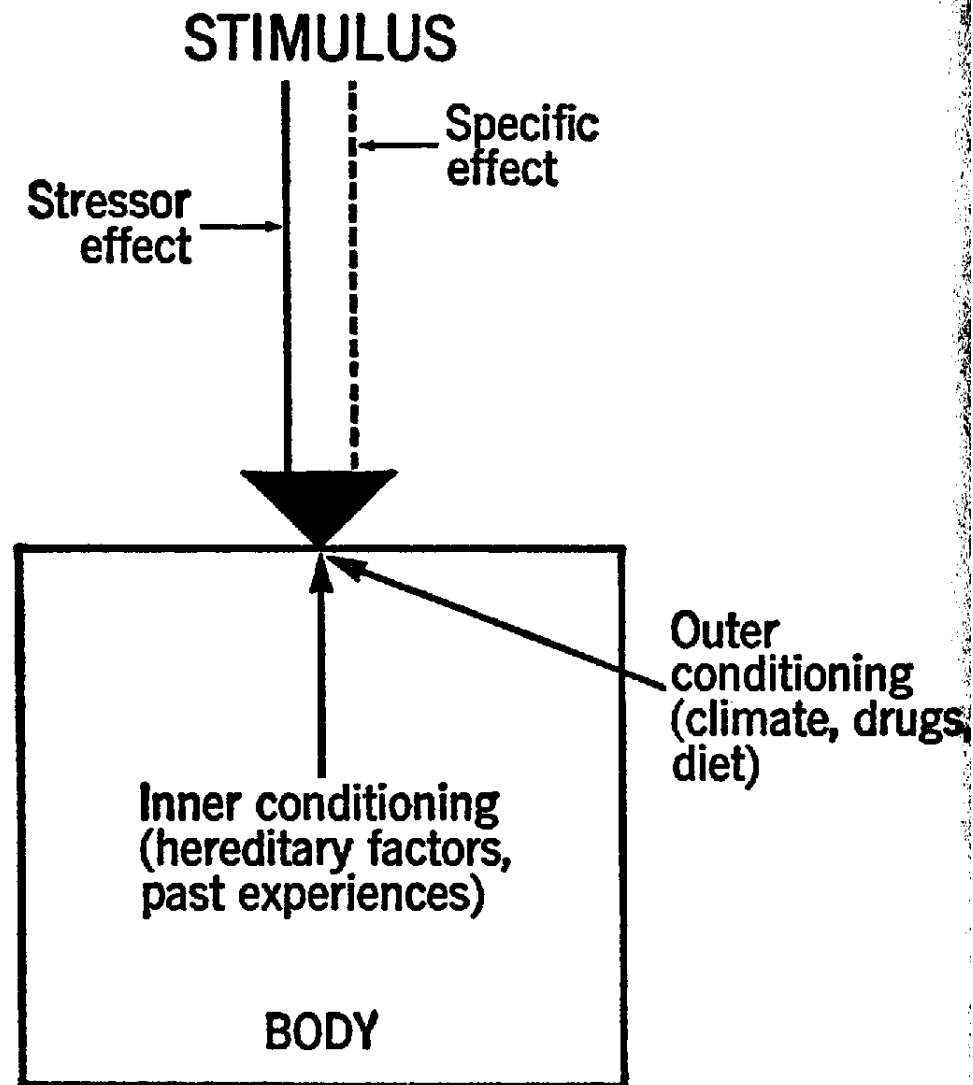
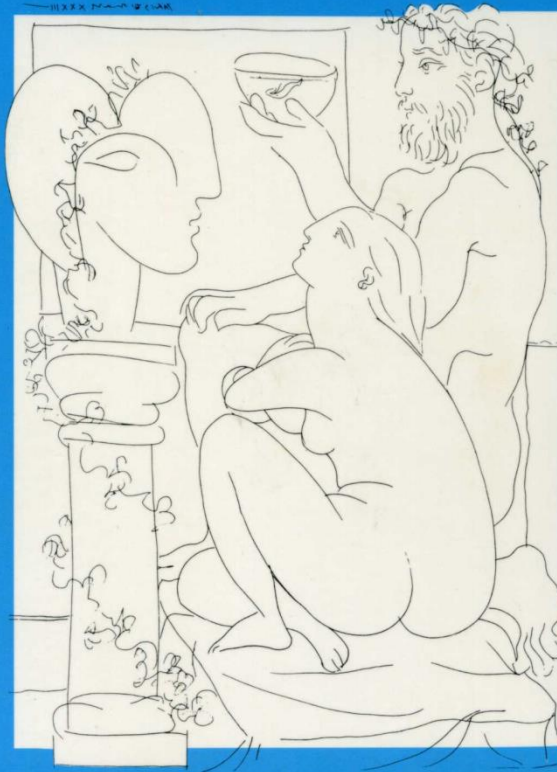


Figure 4. Factors influencing the response to stressors

THE PSYCHOBIOLOGY OF
MIND-BODY HEALING

NEW CONCEPTS OF THERAPEUTIC HYPNOSIS



ERNEST LAWRENCE ROSSI

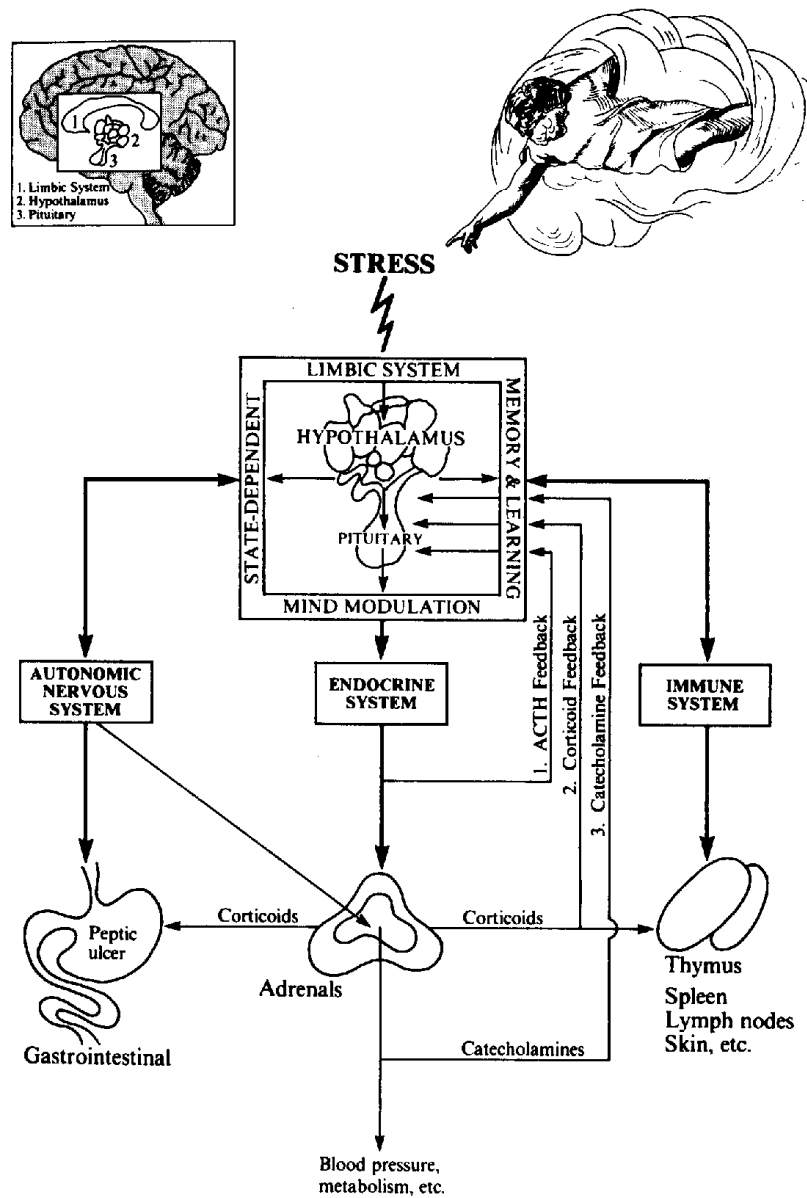


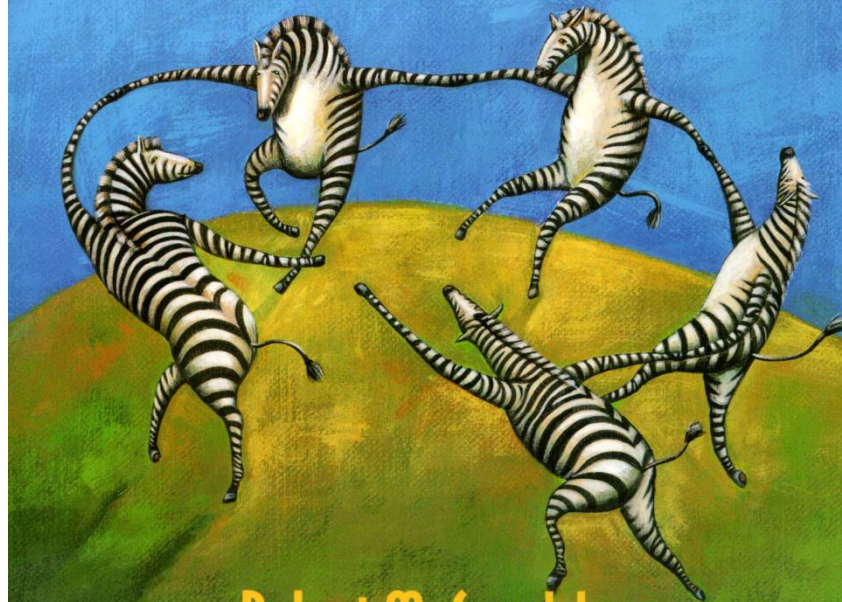
FIGURE 1 Selye's General Adaptation Syndrome updated to emphasize the mind-modulating role of the limbic-hypothalamic system on the autonomic, endocrine, and immune systems. The state-dependent memory and learning theory of therapeutic hypnosis is illustrated by the limbic system "filter" (square box) surrounding the hypothalamus.

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—KIRKUS REVIEWS

WHY ZEBRAS DON'T GET ULCERS

An Updated Guide to Stress,
Stress-Related Diseases, and Coping



Robert M. Sapolsky

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Stress: eventi di vita e depressione



"Oh, that's Edward and his fight or flight mechanism."

THE SOCIAL READJUSTMENT RATING SCALE*†

THOMAS H. HOLMES and RICHARD H. RAHE‡

Journal of Psychosomatic Research, Vol. 11, pp. 213 to 218. Pergamon Press, 1967.

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THOMAS H. HOLMES and RICHARD H. RAHE

TABLE 3. SOCIAL READJUSTMENT RATING SCALE

Rank	Life event	Mean value
1	Death of spouse	100
2	Divorce	73
3	Marital separation	65
4	Jail term	63
5	Death of close family member	63
6	Personal injury or illness	53
7	Marriage	50
8	Fired at work	47
9	Marital reconciliation	45
10	Retirement	45
11	Change in health of family member	44
12	Pregnancy	40
13	Sex difficulties	39
14	Gain of new family member	39
15	Business readjustment	39
16	Change in financial state	38
17	Death of close friend	37
18	Change to different line of work	36
19	Change in number of arguments with spouse	35
20	Mortgage over \$10,000	31
21	Foreclosure of mortgage or loan	30
22	Change in responsibilities at work	29
23	Son or daughter leaving home	29
24	Trouble with in-laws	29
25	Outstanding personal achievement	28
26	Wife begin or stop work	26
27	Begin or end school	26
28	Change in living conditions	25
29	Revision of personal habits	24
30	Trouble with boss	23
31	Change in work hours or conditions	20
32	Change in residence	20
33	Change in schools	20
34	Change in recreation	19
35	Change in church activities	19
36	Change in social activities	18
37	Mortgage or loan less than \$10,000	17
38	Change in sleeping habits	16
39	Change in number of family get-togethers	15
40	Change in eating habits	15
41	Vacation	13
42	Christmas	12
43	Minor violations of the law	11

Scaling of Life Events

Eugene S. Paykel, MD, MRCP, DPM; Brigitte A. Prusoff, MPH, New Haven, Conn; and E. H. Uhlenhuth, MD, Chicago

Varied subjects were asked to judge, on a 0 to 20 scale, the degree to which 61 life events were upsetting. Mean event scores covered almost the entire scale range and ranked in a meaningful way. At the top end of the scale were catastrophic and highly distressing events such as deaths of child or spouse. At the bottom of the scale were events which were either trivial, or important but desirable and not distressing. Consistency of the scaling indicated acceptable interrater reliability. Individual variability reflected in standard deviations was moderate. Agreement across groups was high, although there were small differences due to sociodemographic group, item order, and recent experience of the event. Consensus scaling of events may facilitate use of a quantified methodology in empirical studies of life stress.

Table 2.—Scaling Scores for Life Events

Rank	Event	Mean	SD
1	Death of child	19.33	2.22
2	Death of spouse	18.76	3.21
3	Jail sentence	17.60	3.56
4	Death of close family member (parent, sibling)	17.21	3.69
5	Spouse unfaithful	16.78	4.14
6	Major financial difficulties (very heavy debts, bankruptcy)	16.57	3.83
7	Business failure	16.46	3.71
8	Fired	16.45	4.20
9	Miscarriage or stillbirth	16.34	4.59
10	Divorce	16.18	4.95
11	Marital separation due to argument	15.93	4.55
12	Court appearance for serious legal violation	15.79	4.26
13	Unwanted pregnancy	15.57	5.18
14	Hospitalization of family member (serious illness)	15.30	4.15
15	Unemployed for one month	15.26	4.38
16	Death of close friend	15.18	4.55
17	Demotion	15.05	4.57
18	Major personal physical illness (hospitalization or one month off work)	14.61	4.44
19	Begin extramarital affair	14.09	5.40
20	Loss of personally valuable object	14.07	4.90
21	Law suit	13.78	5.02
22	Academic failure (important exam or course)	13.52	5.07
23	Child married against respondent's wishes	13.24	5.36
24	Break engagement	13.23	5.31
25	Increased arguments with spouse	13.02	4.91
26	Increased arguments with resident family member	12.83	5.15
27	Increased arguments with fiancé or steady date	12.66	4.96
28	Take a large loan (more than one-half of a year's earnings)	12.64	5.43
29	Son drafted	12.32	5.75
30	Arguments with boss or co-worker	12.21	5.06
31	Argument with nonresident family member (in-laws, relatives)	12.11	5.09
32	Move to another country	11.37	6.05

Table 2 (continued)

Rank	Event	Mean	SD
33	Menopause	11.02	5.78
34	Moderate financial difficulties (bothersome but not serious, ie, increased expenses, trouble from bill collectors)	10.96	4.98
35	Separation from significant person (close friend or relative)	10.68	5.18
36	Take important exam	10.44	5.09
37	Marital separation not due to argument	10.33	5.68
38	Change in work hours (much overtime, second job, much less than usual)	9.96	5.49
39	New person in household	9.71	5.45
40	Retirement	9.33	6.02
41	Change in work conditions (new department, new boss, big reorganization)	9.23	5.12
42	Change in line of work	8.84	5.38
43	Cease steady dating (of at least three months)	8.80	5.34
44	Move to another city	8.52	5.59
45	Change in schools	8.15	5.39
46	Cease full-time education (graduate or drop out)	7.65	5.73
47	Child leaves home (eg, college)	7.20	4.96
48	Marital reconciliation (after one partner left home)	6.95	5.91
49	Minor legal violation	6.05	4.78
50	Birth of live child (for mother)	5.91	5.70
51	Wife becomes pregnant	5.67	5.23
52	Marriage	5.61	5.67
53	Promotion	5.39	4.90
54	Minor personal physical illness (one that requires physician's attention)	5.20	4.29
55	Move in same city	5.14	4.49
56	Birth of a child (father) or adoption	5.13	5.45
57	Begin education (full time or half-time)	5.09	4.48
58	Child becomes engaged	4.53	4.57
59	Become engaged	3.70	4.64
60	Wanted pregnancy	3.56	5.39
61	Child married with respondent's approval	2.94	3.75

Life Events and Depression

A Controlled Study

Table 1.—Individual Events*

Event	Depressed		Significance†
	Patients	Controls	
1. Increase in arguments with spouse	39	1	<0.01
2. Marital separation	23	2	<0.01
3. Start new type of work	17	1	<0.01
4. Change in work conditions	27	11	<0.05
5. Serious personal illness	21	7	<0.05
6. Death of immediate family member	16	4	<0.05
7. Serious illness of family member	23	9	<0.05
8. Family member leaves home	6	0	<0.05
9. Move	36	25	NS
10. New person in home	11	6	NS
11. Major financial problems	8	3	NS
12. Pregnancy	7	4	NS
13. Unemployed	7	5	NS
14. Court appearance	6	2	NS
15. Childbirth	6	2	NS
16. Lawsuit	6	3	NS
17. Engagement	0	4	NS
18. Demotion	3	0	NS
19. Change schools	3	0	NS
20. Child engaged	4	3	NS
21. Promotion	3	4	NS
22. Fired	3	1	NS
23. Leave school	1	3	NS
24. Marriage	3	2	NS
25. Child married	3	2	NS
26. Jail	2	0	NS
27. Son drafted	2	1	NS
28. Birth of child (for father)	1	2	NS
29. Divorce	1	0	NS
30. Business failure	1	1	NS
31. Stillbirth	1	1	NS
32. Pregnancy of wife	0	0	NS
33. Retirement	0	0	NS

* Number of depressed patients and controls reporting event at least once.

† χ^2 (With Yates Correction).

Table 2.—Entrances and Exits From Social Field*

Category	Depressed Patients	Controls	Significance†	Events Included in Category
Entrance	21	18	NS	Engagement Marriage Birth of child New person in home
Exit	46	9	<0.01	Death of close family member Separation Divorce Family member leaves home Child married Son drafted

* Number of individuals reporting at least one event in category.

† χ^2 (With Yates correction).

Table 3.—Desirable and Undesirable Events*

Category	Depressed Patients	Controls	Significance†	Events Included in Category
Desirable	6	10	NS	Engagement Marriage Promotion
Undesirable	82	31	<0.01	Death of family member Separation Demotion Serious illness of family member Jail Major financial problems Unemployment Court appearance Son drafted Divorce Business failure Fired Stillbirth

* Number of individuals reporting at least one event in category.

† χ^2 (With Yates correction).

Table 4.—Events Grouped by Area of Activity*


Category	Depressed Patients	Controls	Significance†	Events Included in Category
Employment	46	20	<0.01	Begin new job Changes at work Demotion Fired Unemployment Promotion Retirement Business failure
Health	53	24	<0.01	Serious personal illness Serious illness of family member Pregnancy Childbirth Stillbirth
Family	22	11	NS (<i>P</i> =0.07)	Child engaged Child married Son drafted Family member leaves home New person in home
Marital	63	5	<0.01	Marriage Separation Divorce Increase in arguments with spouse
Legal	14	5	NS (<i>P</i> =0.06)	Court appearance Lawsuit Jail

* Number of individuals reporting at least one event in category.

† χ^2 (With Yates correction).

L'epidemia di depressione

SPECIAL

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THE GREAT DEPRESSION

DEPRESSION

Depression causes a greater burden of disability than any other condition, yet it is widely undiagnosed and untreated. In this special collection of articles, *Nature* asks why that burden is so great, how science is helping and where research is running aground.

Image credit: Carl De Torres

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A world of depression

Depression is a major human blight. Globally, it is responsible for more 'years lost' to disability than any other condition. This is largely because so many people suffer from it – some 230 million, according to the World Health Organization – and the fact that it lasts for many years. (When ranked by disability and death combined, depression comes ninth behind prolific killers such as heart disease, stroke and HIV.) Yet depression is widely undiagnosed and untreated because of stigma, lack of effective therapies and inadequate mental health resources. Almost half of the world's population lives in a country with only two psychiatrists per 100,000 people.

● Prevalence of depression ● Psychiatrists per 100,000 people

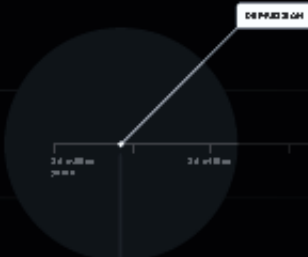
PREVALENCE OF DEPRESSION

230 million people live with depression (5.0%)
230 million people live with depression (5.0%)

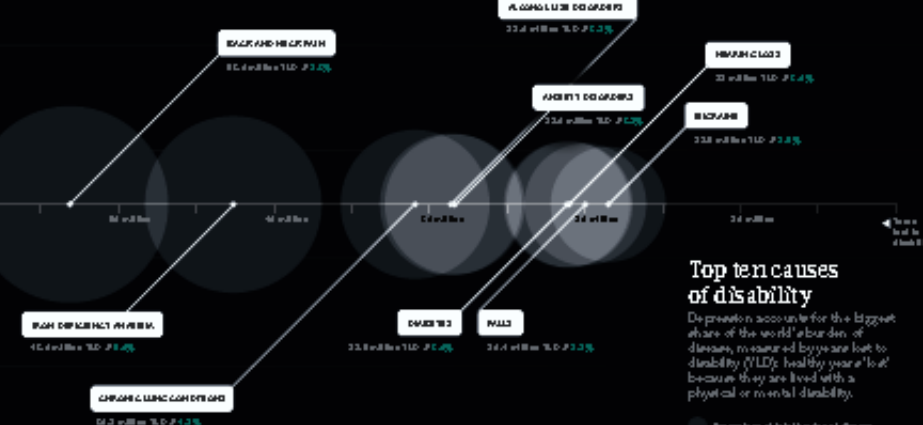
230 million people live with depression (5.0%)

Switzerland ● 6.16% ● 41.42
This western country reports the world's highest prevalence of depression, and yet little among the best equipped to deal with it. Conflict is a well-established risk factor for depression, as are child sexual abuse and domestic violence.

Source: World Health Organization, Global Burden of Disease Study 2019. Prevalence of depression (5.0%) and number of psychiatrists per 100,000 people (41.42) in Switzerland. Data for other countries are available on request.



230 million people live with depression (5.0%)
230 million people live with depression (5.0%)



Top ten causes of disability
Depression accounts for the largest share of the world's burden of disease, measured by years lost to disability (YLDs). Healthy years are lost because they are lived with a physical or mental disability.

● Percentage of total disability

PSYCHIATRISTS PER 100,000 PEOPLE

230 million people live with depression (5.0%)

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Source: World Health Organization, Global Burden of Disease Study 2019. Prevalence of depression (5.0%) and number of psychiatrists per 100,000 people (41.42) in Switzerland. Data for other countries are available on request.

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This western country reports the world's highest prevalence of depression, and yet little among the best equipped to deal with it. Conflict is a well-established risk factor for depression, as are child sexual abuse and domestic violence.

United States ● 4.45% ● 7.79

Depression receives significantly less research funding from the US National Institutes of Health than do cancer or heart disease. This is partly because of a lack of patient advocacy and the stigma that surrounds the condition.



China ● 3.02% ● 1.53

The relatively low prevalence of depression in China could be the result of the way in which it is diagnosed, rather than lower actual rates. People with depression here often report symptoms such as stomach pain or headache, and so may be missed by the standard diagnostic criteria used to calculate prevalence, which focus on mood and lack of motivation and fatigue.

BYRON SMITH | INFOGRAPHIC BY CYRIL DE TORRES

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DEPRESSION: *A Global Crisis*

World Mental Health Day, October 10 2012

World Federation for Mental Health



DEPRESSION

A Global Public Health Concern

*Developed by Marina Marcus, Taghi Yasamy, Mark van Ommeren, and Dan Chisholm, Shekhar Saxena
WHO Department of Mental Health and Substance Abuse*

Depression is a significant contributor to the global burden of disease and affects people in all communities across the world. Depression is one of the leading causes of disability worldwide. Today, depression is estimated to affect 350 million people. The World Mental Health Survey conducted in 17 countries found that on average about 1 in 20 people reported having an episode of depression in the previous year. Depressive disorders often start at a young age; they reduce people's functioning and often are recurring. For these reasons, depression is currently near the top of the global list of disabling conditions in global burden of disease studies. The demand for curbing depression and other mental health conditions is on the rise globally. A recent World Health Assembly called on the World Health Organization and its member states to take action in this direction (WHO, 2012).

What is depression?

Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, decreased energy, feelings of guilt or low self-worth, disturbed sleep or appetite, and poor concentration. Moreover, depression often comes with symptoms of anxiety. These problems can become chronic or recurrent and lead to substantial impairments in an individual's ability to take care of his or her everyday responsibilities. At its worst, depression can lead to suicide. Almost 1 million lives are lost yearly due to suicide, which translates to 3000 suicide deaths every day. For every person who completes a suicide, 20 or more may attempt to end his or her life (WHO, 2012).

There are multiple variations of depression that a person can suffer from, with the most general dis-

tinction being depression in people who have or do not have a history of manic episodes.

- *Depressive episode* involves symptoms such as depressed mood, loss of interest and enjoyment, and increased fatigability. Depending on the number and severity of symptoms, a depressive episode can be categorized as mild, moderate, or severe. An individual with a mild depressive episode will have some difficulty in continuing with ordinary work and social activities, but will probably not cease to function completely. During a severe depressive episode, on the other hand, it is very unlikely that the sufferer will be able to continue with social, work, or domestic activities, except to a very limited extent.
- *Bipolar affective disorder* typically consists of both manic and depressive episodes separated by periods of normal mood. Manic episodes involve elevated mood and increased energy, resulting in over-activity, pressure of speech and decreased need for sleep.

While depression is the leading cause of disability for both males and females, the burden of depression is 50% higher for females than males (WHO, 2008). In fact, depression is the leading cause of disease burden for women in both high-income and low- and middle-income countries (WHO, 2008). Research in developing countries suggests that maternal depression may be a risk factor for poor growth in young children (Rahman et al, 2008). This risk factor could mean that maternal mental health in low-income countries may have a substantial influence on growth during childhood, with the effects of depression affecting not only this generation but also the next.

Secondo l'OMS, la depressione è la principale causa di disabilità in termini di YLD (anni vissuti con disabilità), e la quarta causa del carico di malattia globale in termini di DALY (attesa di vita corretta per disabilità) nel 2000. La proiezione per il 2020 è che essa raggiunga il secondo posto per il carico di malattia globale (DALY) calcolato per i due sessi e per tutte le età.

Depression as a consequence of the **ECONOMIC CRISIS**

Normal sadness and depression

It is important to differentiate between normal sadness and depression. Under adverse conditions like death of a relative, personal humiliation (especially in certain cultures), disappointment, loss of social status, even financial loss, a psychological response is expected and is, of course, normal. Under these circumstances, it is lack of response that would be abnormal, as is the case with the absence of response (apathy) often encountered in patients with schizophrenia and some patients with personality disorders (Christodoulou et al 2000).

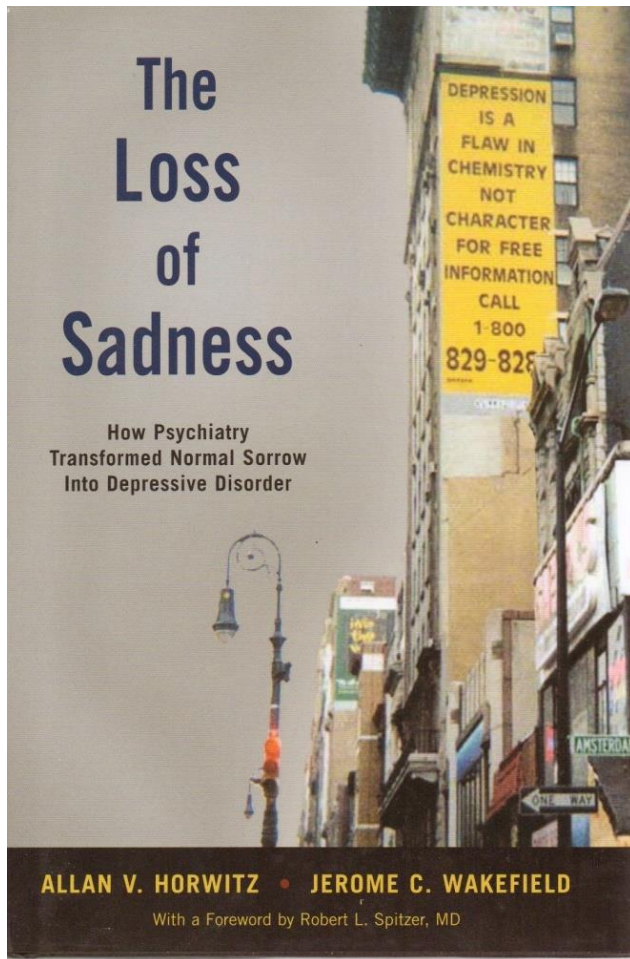
It is, therefore, important to differentiate between sadness and depression, i.e. between an “adaptive” and a “dysfunctional” response to an adverse life event, even though this distinction is sometimes difficult (Maj, 2011).

university requires clinical skills and experience on the part of the clinician.

La diagnosi

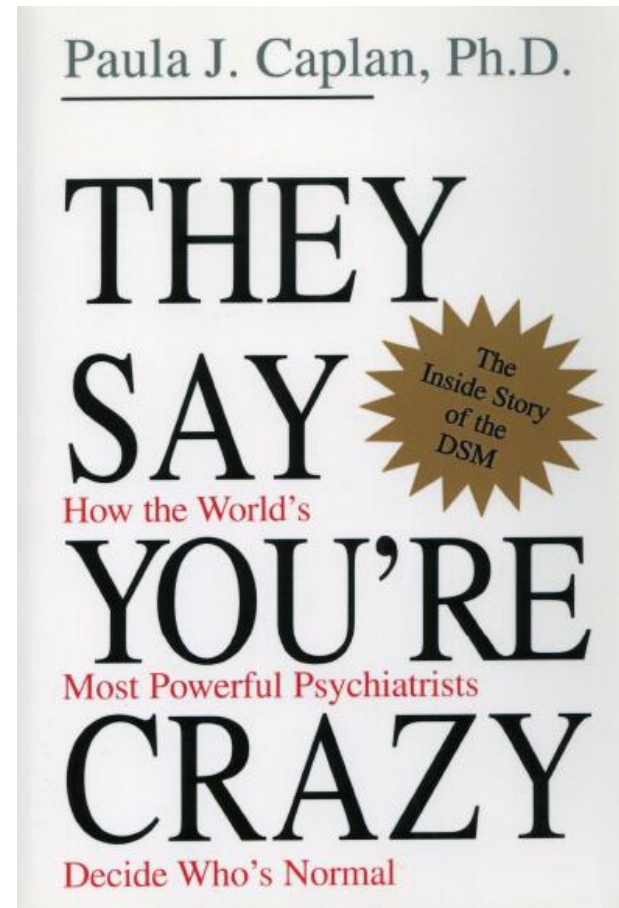
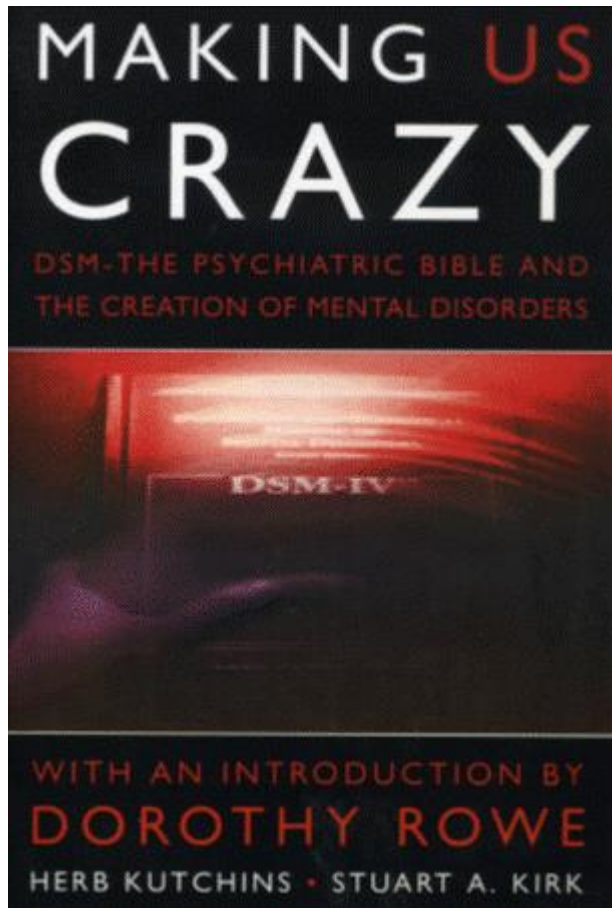
La «depressione» è divenuta sinonimo del «disturbo depressivo maggiore», i cui criteri diagnostici sono quelli del *Diagnostic and Statistic Manual* (DSM) dell'*American Psychiatric Association*.

Per la diagnosi e per la valutazione della severità della depressione vengono inoltre comunemente impiegate, oltre ai criteri del DSM, varie scale psicometriche.



L'approccio neo-Kraepeliniano del DSM rende l'adattamento (fisiologico) ad eventi di vita stressanti un *disturbo mentale* (patologico, richiedente trattamento), senza distinzione tra situazioni reattive e la ben più rara (e grave) *depressione endogena o vitale*

La *tristezza* (emozione *normale*) diventa *depressione*, (*patologica*), richiedente trattamento



DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS

FIFTH EDITION

DSM-5™

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Washington, DC
London, England

Major Depressive Disorder

Diagnostic Criteria

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

Note: Do not include symptoms that are clearly attributable to another medical condition.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). (**Note:** In children and adolescents, can be irritable mood.)
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).

Major Depressive Disorder

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3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (**Note:** In children, consider failure to make expected weight gain.)
 4. Insomnia or hypersomnia nearly every day.
 5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
 6. Fatigue or loss of energy nearly every day.
 7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
 8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
 9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.
- B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- C. The episode is not attributable to the physiological effects of a substance or to another medical condition.

Note: Criteria A–C represent a major depressive episode.

Note: Responses to a significant loss (e.g., bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgment based on the individual's history and the cultural norms for the expression of distress in the context of loss.¹

- D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.

- E. There has never been a manic episode or a hypomanic episode.

Note: This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition.

La Scala di Hamilton

HDRS

HDRS

saving

nor•mal (nôr'mal)

1. an insider's revolt against out-of-control psychiatric diagnosis, *DSM-5*, big pharma, and the medicalization of ordinary life

Allen Frances, M.D.¹

¹Chair of the DSM-IV Task Force

Nel 2016 US Preventive Services Task Force ha proposto per ogni adulto negli Stati Uniti lo screening per la depressione, seguito per coloro che ne risultano affetti dal trattamento e dal follow up.

I criteri diagnostici sono ancora più inclusivi di quelli del DSM, e sono basati sull'uso di comuni scale psicometriche quali *Patient Health Questionnaire*, *Hospital Anxiety and Depression Scales*, *Geriatric Depression Scale* e *Edinburgh Postnatal Depression Scale*.

JAMA[®]

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Research

Original Investigation

353 Effect of Vitamin D₃ Supplementation During Pregnancy on Risk of Persistent Wheeze in the Offspring: A Randomized Clinical Trial

BL Chawes and Coauthors

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In merito allo screening proposto dalla US Preventive Services Task Force, Allen Frances ha dichiarato :

«A good intention, a very bad idea, which will create an army of pseudo-patients while the really sick are shamefully neglected.»

**Il trattamento:
la farmacoterapia e
l'aumento della prescrizione
di antidepressivi**

Negli Stati Uniti, i dati del National Center for Health Statistics indicano che nel periodo 2005-8 gli antidepressivi (AD):

- costituiscono la terza prescrizione per tutte le fasce di età**
- sono i farmaci più comunemente assunti dalle persone di 18-44 anni**
- il loro uso è salito dal 1988-94 al 2005-8 del 400 % per tutte le fasce di età**
- il 10% degli americani di più di 12 anni è in trattamento con AD**
- il 23 % delle donne di 40-59 anni di età è in trattamento**

In Gran Bretagna, l'analisi effettuata da *Quality Watch of the Health Foundation of the Nuffield Trust* indica un aumento della prescrizione da parte dei GP nel periodo 1998-2012 del 165 %.

In Italia, il *Rapporto OSMED* dell'AIFA indica che nel 2015 una diagnosi di depressione è stata ricevuta dal 18,6 % delle donne e dal 9,0 % degli uomini (media 12,6 %).

Nel 29,0% dei casi hanno ricevuto una prescrizione di farmaci antidepressivi (per il 55,7% SSRI).

Riguardo la prescrizione degli SSRI nei giovani, a partire dal 2004, FDA ed altri Enti Regolatori nazionali hanno reso obbligatorio l'avvertenza che questi AD aumentano il rischio suicidario nei bambini ed adolescenti.

Ciononostante, l'uso di AD nei soggetti di età 0-19 anni nel periodo 2005 al 2012 è cresciuto del 26,1% negli USA, del 54,4% in UK, del 60,5 in Danimarca, del 17,6% in Olanda e del 49,2% in Germania.

Bachmann C.J. et al. (2016) Eur Neuropsychopharmacol. 2016 Mar;26: 411-9

Il trattamento: con antidepressivi

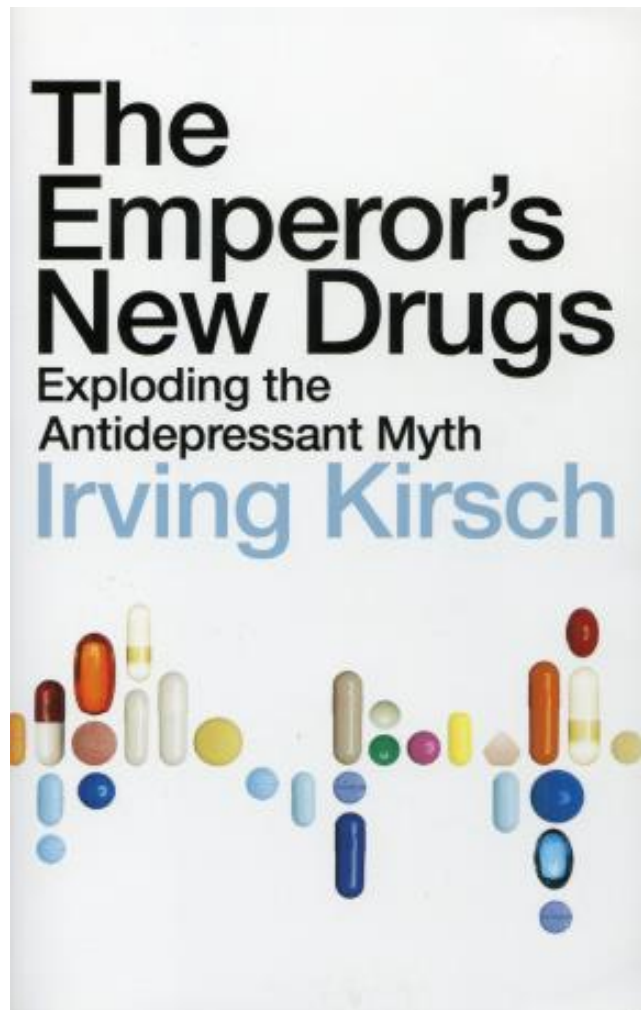
In Italia i farmaci antidepressivi SSRI sono prescritti nel 55,7% dei casi, ed hanno largamente soppiantato i TCA (6,1%); la prescrizione di SNRI è del 13,8% e degli atipici del 13,5%.

L'aderenza al trattamento è del 31,6%.

E' comunemente ritenuto che la risposta avviene in circa 2/3 dei casi trattati.

La prevalente prescrizione degli SSRI è ascritta alla loro efficacia accompagnata da una tollerabilità migliore di quella degli altri gruppi di antidepressivi.

**Gli antidepressivi
sono sempre efficaci ?**



Per le forme lievi e moderate di disturbo depressivo maggiore, l'effetto degli AD SSRI è uguale a quello del placebo

Initial Severity and Antidepressant Benefits: A Meta-Analysis of Data Submitted to the Food and Drug Administration

Irving Kirsch^{1*}, Brett J. Deacon², Tania B. Huedo-Medina³, Alan Scoboria⁴, Thomas J. Moore⁵, Blair T. Johnson³

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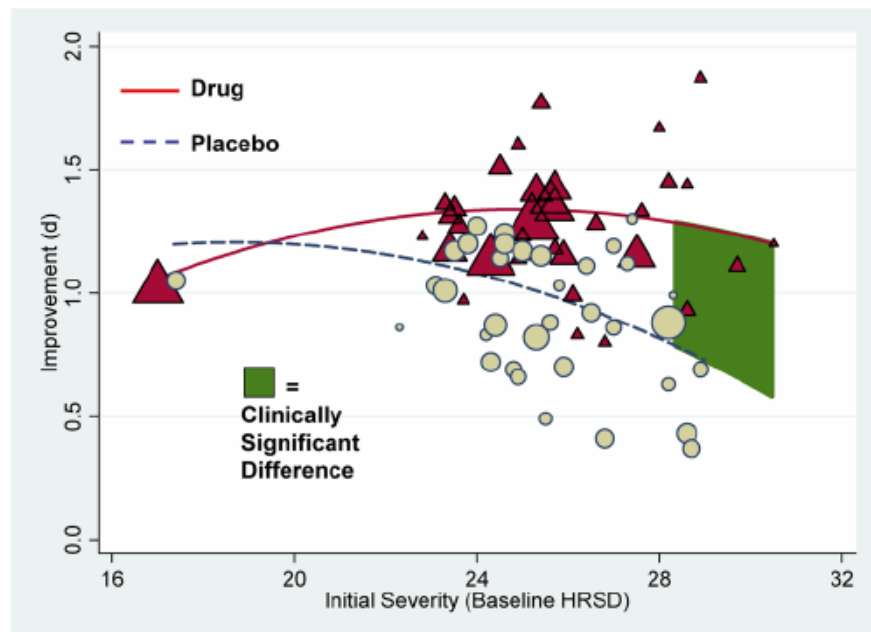


Figure 2. Mean Standardized Improvement as a Function of Initial Severity and Treatment Group

Drug improvement is portrayed as red triangles around their solid red regression line and placebo improvement as blue circles around their dashed blue regression line; the green shaded area indicates the point at which comparisons of drug versus placebo reach the NICE clinical significance criterion of $d = 0.50$. Plotted values are sized according to their weight in analyses.

doi:10.1371/journal.pmed.0050045.g002

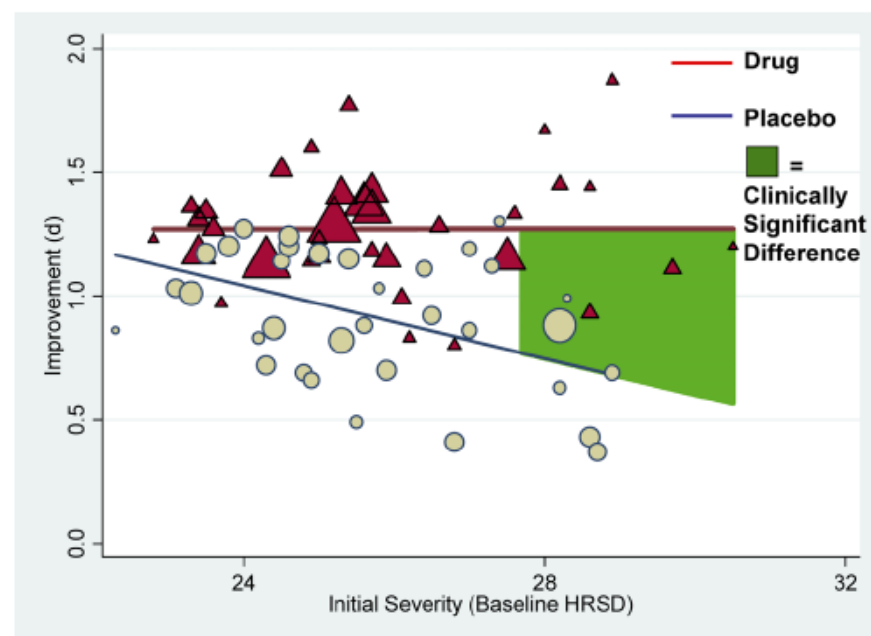
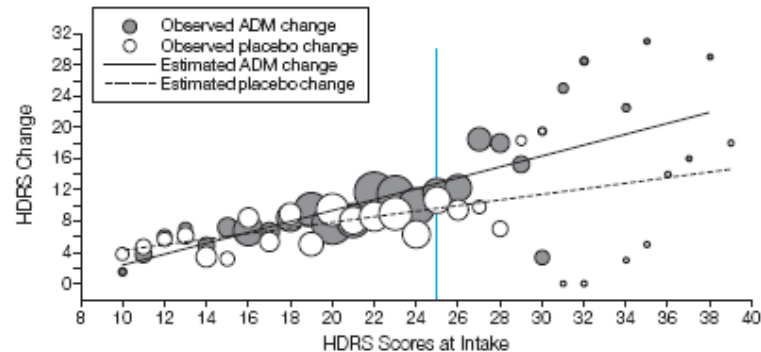


Figure 3. Mean Standardized Improvement as a Function of Initial Severity and Treatment Group, Including Only Trials Whose Samples Had High Initial Severity

Drug improvement is portrayed as red triangles around their solid red regression line and placebo improvement as blue circles around their dashed blue regression line; the green shaded area indicates the point at which comparisons of drug versus placebo reach the NICE clinical significance criterion of $d = 0.50$. Plotted values are sized according to their weight in analyses.

doi:10.1371/journal.pmed.0050045.g003

Figure 2. Observed and Estimated Change in HDRS Scores Following Treatment With ADM and Placebo



Circles represent observed (raw) mean change in depressive symptoms from intake to the end of treatment at each initial Hamilton Depression Rating Scale (HDRS) score for both the antidepressant medication (ADM) and placebo conditions. The size (area) of the circles is proportional to the number of data points that contributed to each mean. Regression lines represent estimates of change in depression symptoms from intake to end of treatment for ADM and placebo conditions as a function of baseline symptom severity. These regression lines were estimated from a model of the baseline severity \times treatment interaction, controlling for the effects of the study from which the data originated. The National Institute for Clinical Excellence threshold for clinical significance (an HDRS point difference ≥ 3) was met for intake HDRS scores of 25 or greater, indicated by the blue line.

Results Medication vs placebo differences varied substantially as a function of baseline severity. Among patients with HDRS scores below 23, Cohen d effect sizes for the difference between medication and placebo were estimated to be less than 0.20 (a standard definition of a small effect). Estimates of the magnitude of the superiority of medication over placebo increased with increases in baseline depression severity and crossed the threshold defined by the National Institute for Clinical Excellence for a clinically significant difference at a baseline HDRS score of 25.

Conclusions The magnitude of benefit of antidepressant medication compared with placebo increases with severity of depression symptoms and may be minimal or non-existent, on average, in patients with mild or moderate symptoms. For patients with very severe depression, the benefit of medications over placebo is substantial.

The National Institute of Mental Health, Thomas Insel e lo studio *Sequenced Treatment Alternatives to Relieve Depression* (STAR*D).

Iniziato nel 2000, della durata di 6 anni con un costo 35 milioni di dollari, è stato definito il più grande trial pragmatico per esaminare il trattamento del *disturbo depressivo maggiore* con la farmacoterapia e con la psicoterapia cognitivo comportamentale, e per accertare se alcuni trattamenti siano efficaci per i pazienti per i quali il trattamento iniziale non sia stato efficace.

I soggetti arruolati dovevano aver ricevuto la diagnosi di *disturbo depressivo maggiore* secondo i criteri del DSM, ed avere un punteggio alla scala di Hamilton di almeno 14 punti.

Hanno inizialmente ricevuto un trattamento standard con *citalopram*. Se la risposta al *citalopram* era insufficiente, i pazienti venivano randomizzati a successivi *trials* con altri trattamenti (*switching*), incrementi di dose (*augmentation therapy*), ed all'associazione di più di un farmaco (*combination therapy*), o con la psicoterapia.

Il criterio di valutazione principale (*primary outcome*) alla fine del trattamento era la scomparsa dei sintomi o la risposta in termini di riduzione del punteggio alla scala di Hamilton: il protocollo dello studio è privo di gruppi di controllo con placebo.

I soggetti arruolati nello studio erano istituzionalizzati ed ambulatoriali provenienti dalla medicina generale, privi di sintomi psicotici.

Lo studio si è concluso nel 2006, ed i risultati ottenuti sono disponibili dal 2008. I risultati dello studio sono stati tanto deludenti da far intitolare una rassegna pubblicata:

*«STAR*D. Revising conventional wisdom».*

*Rush A.J. et al. STAR*D: revising conventional wisdom. CNS Drugs. (2009) 23(8):627-47.*

						Remissioni %	Lost %
Level 1		Citalopram				30	21
Level 2	Switch to	Sertralina Bupropione Velafaxina	Add on	Bupropione Buspirone	Psicoterapia	25	30
Level 3	Switch to	Mirtazapina Nortriptilina	Add on	Litio T3		12-20	42
Level 4	Switch to	Tranilcipromina				10	
		Venlafaxina Mirtazapina				10	
Totale						70 (of 32 %)	68 *

**Gli antidepressivi
sono sempre sicuri ?**

Gli SSRI sono ben tollerati, ed in generale causano effetti avversi (anticolinergici, antiadrenergici ed antistaminergici) meno pronunciati di quelli dei TCA.

Causano però specifici effetti avversi che sono largamente sottovalutati:

- aumento del rischio suicidario nei bambini ed adolescenti**
- malformazioni dopo trattamento di donne gravide**
- disfunzioni sessuali nei soggetti di sesso maschile**
- sindrome da sospensione del trattamento**
- sanguinamento**

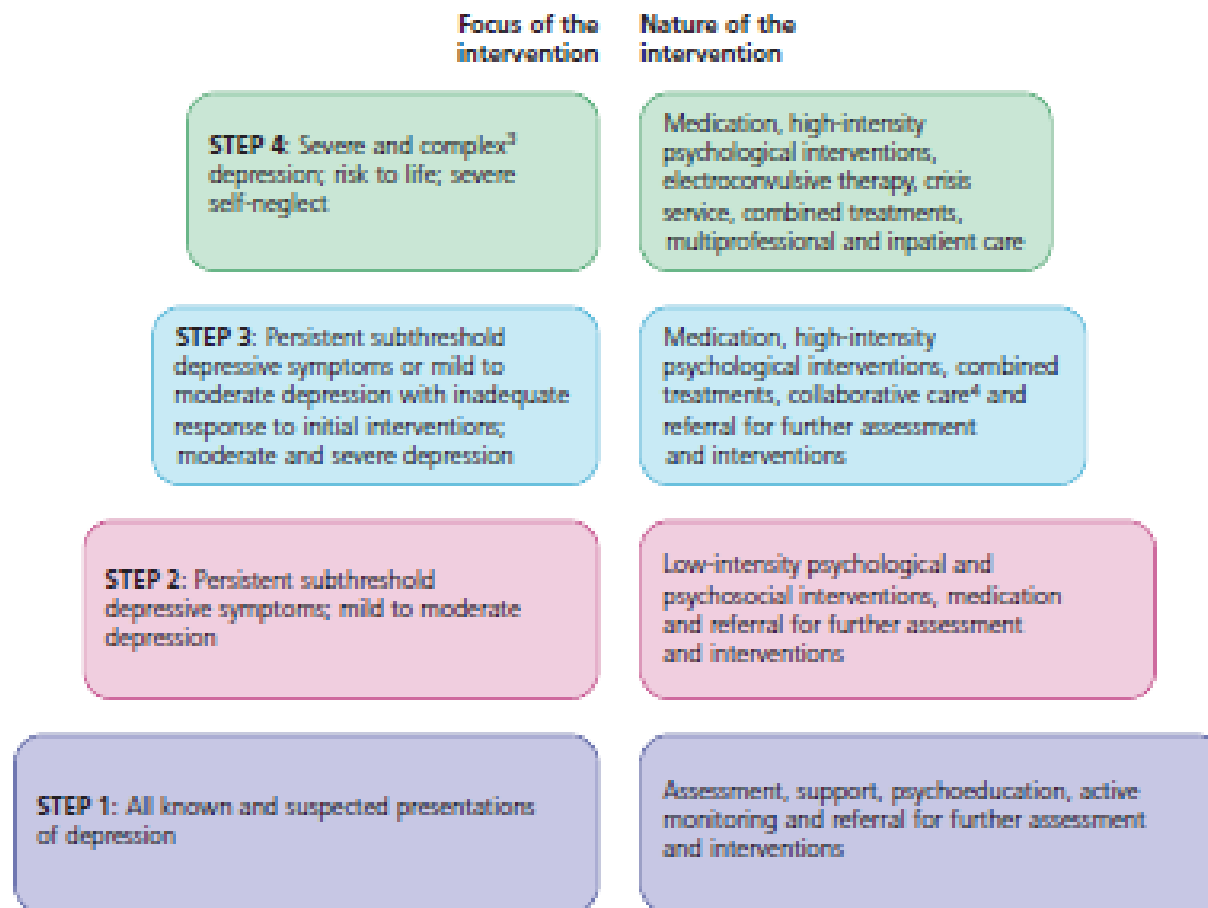
Per gli SSRI l'efficacia è stata enfatizzata, e gli effetti avversi sono stati minimizzati, grazie a:

- risultati dei trials clinici non pubblicamente accessibili
- *biases* da selezione dei dati pubblicati ed impiegati per la registrazione
- *outcomes* nei trials clinicamente poco rilevanti
- efficacia dimostrata solo contro placebo
- conflitti di interesse
- dati pubblicati con l'impiego di *scrittori ombra*

La Gran Bretagna, E linee guida del NICE ed il programma IAPT (Improving Access to Psychotherapy)

The stepped-care model

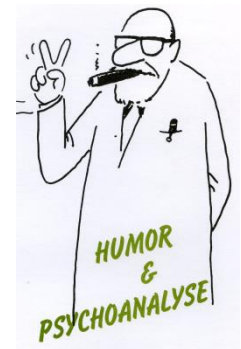
This model provides a framework for organising the provision of services, and helps patients, carers and practitioners to identify and access the most effective interventions. The least intrusive, most effective intervention is provided first. If a person does not benefit from that intervention, or declines an intervention, they should be offered an appropriate intervention from the next step.



Efficacia e *cost effectiveness* degli interventi

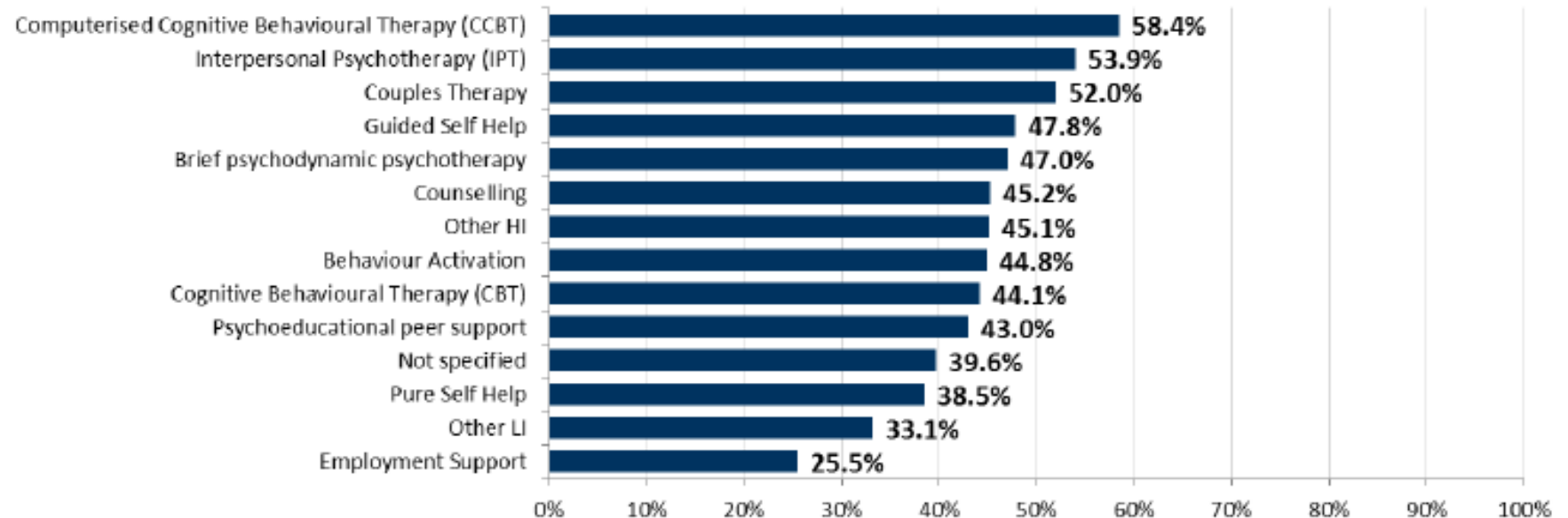
Quale approccio psicoterapeutico ?

JUNG ? ... ADLER ? ... FROMM ?

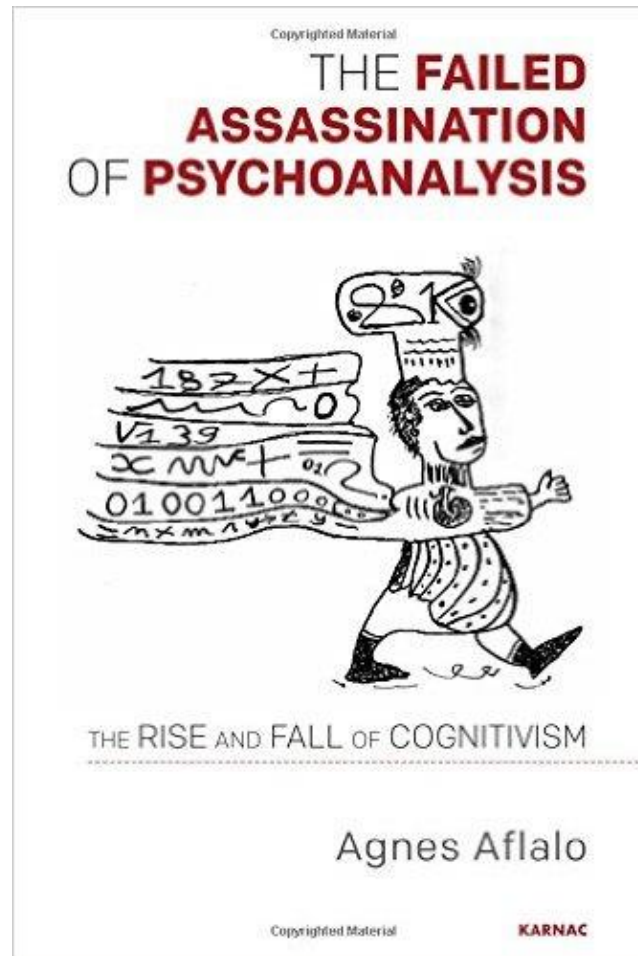


Vladimir Iranek

Figure 3: Recovery rates by therapy type for referrals with a problem descriptor of depression, 2014/15²³



Is everybody happy with cognitive therapies ?



The Efficacy of Psychodynamic Psychotherapy

Jonathan Shedler *University of Colorado Denver School of Medicine*

Empirical evidence supports the efficacy of psychodynamic therapy. Effect sizes for psychodynamic therapy are as large as those reported for other therapies that have been actively promoted as “empirically supported” and “evidence based.” In addition, patients who receive psychodynamic therapy maintain therapeutic gains and appear to continue to improve after treatment ends. Finally, nonpsychodynamic therapies may be effective in part because the more skilled practitioners utilize techniques that have long been central to psychodynamic theory and practice. The perception that psychodynamic approaches lack empirical support does not accord with available scientific evidence and may reflect selective dissemination of research findings.

Table 1*Illustrative Effect Sizes From Meta-Analyses of Treatment Outcome Studies*

Treatment type and reference	Description	Effect size	N of studies or meta-analyses
General psychotherapy			
Smith et al. (1980)	Various therapies and disorders	0.85	475 studies
Lipsey & Wilson (1993)	Various therapies and disorders	0.75 ^a	18 meta-analyses
Robinson et al. (1990)	Various therapies for depression	0.73	37 studies
CBT and related therapies			
Lipsey & Wilson (1993)	CBT and behavior therapy, various disorders	0.62 ^b	23 meta-analyses
Haby et al. (2006)	CBT for depression, panic, and generalized anxiety	0.68	33 studies
Churchill et al. (2001)	CBT for depression	1.0	20 studies
Cuijpers et al. (2007)	Behavioral activation for depression	0.87	16 studies
Öst (2008)	Dialectical behavior therapy, primarily for borderline personality disorder	0.58	13 studies
Antidepressant medication			
Turner et al. (2008)	FDA-registered studies of antidepressants approved between 1987 and 2004	0.31	74 studies
Moncrieff et al. (2004)	Tricyclic antidepressants versus active placebo	0.17	9 studies
Psychodynamic therapy			
Abbass et al. (2006)	Various disorders, general symptom improvement	0.97	12 studies
Leichsenring et al. (2004)	Various disorders, change in target problems	1.17	7 studies
Anderson & Lambert (1995)	Various disorders and outcomes	0.85	9 studies
Abbass et al. (2009)	Somatic disorders, change in general psychiatric symptoms	0.69	8 studies
Messer & Abbass (in press)	Personality disorders, general symptom improvement	0.91	7 studies
Leichsenring & Leibing (2003)	Personality disorders, pretreatment to posttreatment	1.46 ^c	14 studies
Leichsenring & Rabung (2008)	Long-term psychodynamic therapy vs. shorter term therapies for complex mental disorders, overall outcome	1.8	7 studies
de Maat et al. (2009)	Long-term psychoanalytic therapy, pretreatment to posttreatment	0.78 ^c	10 studies

^a Median effects size across 18 meta-analyses (from Lipsey & Wilson, 1993, Table 1.1). ^b Median effects size across 23 meta-analyses (from Lipsey & Wilson, 1993, Table 1.2). ^c Pretreatment to posttreatment (within-group) comparison.

Comparative Effectiveness of Cognitive Therapy and Dynamic Psychotherapy for Major Depressive Disorder in a Community Mental Health Setting

A Randomized Clinical Noninferiority Trial

Mary Beth Connolly Gibbons, PhD; Robert Gallop, PhD; Donald Thompson, PhD; Debra Luther, PhD; Kathryn Crits-Christoph, PhD; Julie Jacobs, PhD; Seohyun Yin, BA; Paul Crits-Christoph, PhD

CONCLUSIONS AND RELEVANCE This study suggests that DT is not inferior to CT on change in depression for the treatment of MDD in a community mental health setting. The 95% CI suggests that the effects of DT are equivalent to those of CT.

JAMA Psychiatry. doi:10.1001/jamapsychiatry.2016.1720

Comparative Efficacy of Seven Psychotherapeutic Interventions for Patients with Depression: A Network Meta-Analysis

Jürgen Barth^{1☯*}, Thomas Munder^{1☯}, Heike Gerger¹, Eveline Nüesch^{1,2,3}, Sven Trelle^{1,2}, Hansjörg Znoj⁴, Peter Jüni^{1,2}, Pim Cuijpers⁵

Interpersonal psychotherapy (IPT)

Behavioural activation (ACT)

Cognitive behavioural therapy (CBT)

Problem solving therapy (PST)

Psychodynamic therapy (DYN)

Social skills training (SST)

Supportive counselling (SUP)

Conclusions: Overall our results are consistent with the notion that different psychotherapeutic interventions for depression have comparable benefits. However, the robustness of the evidence varies considerably between different psychotherapeutic treatments.



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Are all psychotherapies equally effective in the treatment of adult depression? The lack of statistical power of comparative outcome studies

Pim Cuijpers^{1,2}

¹Department of Clinical, Neuro and Developmental Psychology, VU University Amsterdam, Amsterdam, The Netherlands; ²EMGO Institute for Health and Care Research, VU University and VU University Medical Center Amsterdam, Amsterdam, The Netherlands

ABSTRACT

More than 100 comparative outcome trials, directly comparing 2 or more psychotherapies for adult depression, have been published. We first examined whether these comparative trials had sufficient statistical power to detect clinically relevant differences between therapies of $d=0.24$. In order to detect such an effect size, power calculations showed that a trial would need to include 548 patients. We selected 3 recent meta-analyses of psychotherapies for adult depression (cognitive behaviour therapy (CBT), interpersonal psychotherapy and non-directive counselling) and examined the number of patients included in the trials directly comparing other psychotherapies. The largest trial comparing CBT with another therapy included 178 patients, and had enough power to detect a differential effect size of only $d=0.42$. None of the trials in the 3 meta-analyses had enough power to detect effect sizes smaller than $d=0.34$, but some came close to the threshold for detecting a clinically relevant effect size of $d=0.24$. Meta-analyses may be able to solve the problem of the low power of individual trials. However, many of these studies have considerable risk of bias, and if we only focused on trials with low risk of bias, there would no longer be enough studies to detect clinically relevant effects. We conclude that individual trials are heavily underpowered and do not even come close to having sufficient power for detecting clinically relevant effect sizes. Despite this large number of trials, it is still not clear whether there are clinically relevant differences between these therapies.

Evid Based Mental Health May 2016 Vol 19 No 2



Lancet 2016;388:871–80
Published Online
July 22, 2016
[http://dx.doi.org/10.1016/S0140-6736\(16\)31140-0](http://dx.doi.org/10.1016/S0140-6736(16)31140-0)

Cost and Outcome of Behavioural Activation versus Cognitive Behavioural Therapy for Depression (COBRA): a randomised, controlled, non-inferiority trial

David A Richards, David Ekers, Dean McMillan, Rod S Taylor, Sarah Byford, Fiona C Warren, Barbara Barnett, Paul A Farrow, Simon Gilbody, Willem Kuyken, Heather O'Mahen, Ed R Watkins, Kim A Wight, Steven D Hollon, Nigel Reed, Shelley Rhodes, Emily Fletcher, Katie Finning

Summary

Background Depression is a common, debilitating, and costly disorder. Many patients request psychological therapy, but the best-evidenced therapy—cognitive behavioural therapy (CBT)—is complex and costly. A simpler therapy—behavioural activation (BA)—might be as effective and cheaper than is CBT. We aimed to establish the clinical efficacy and cost-effectiveness of BA compared with CBT for adults with depression.

Interpretation We found that BA, a simpler psychological treatment than CBT, can be delivered by junior mental health workers with less intensive and costly training, with no lesser effect than CBT. Effective psychological therapy for depression can be delivered without the need for costly and highly trained professionals.



**Cochrane
Library**

Cochrane Database of Systematic Reviews

'Third wave' cognitive and behavioural therapies versus other psychological therapies for depression (Review)

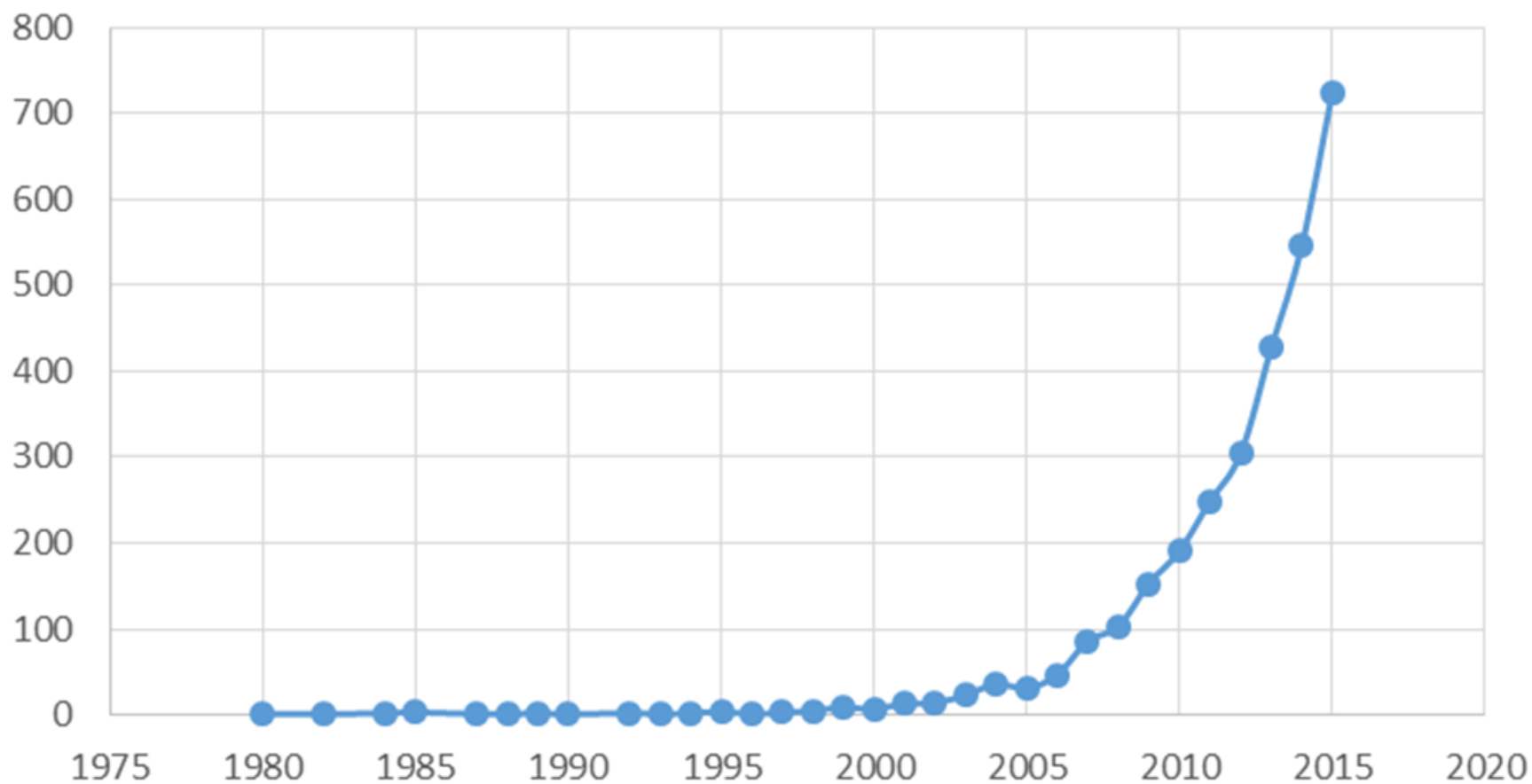
Hunot V, Moore THM, Caldwell DM, Furukawa TA, Davies P, Jones H, Honyashiki M, Chen P, Lewis G, Churchill R

Authors' conclusions

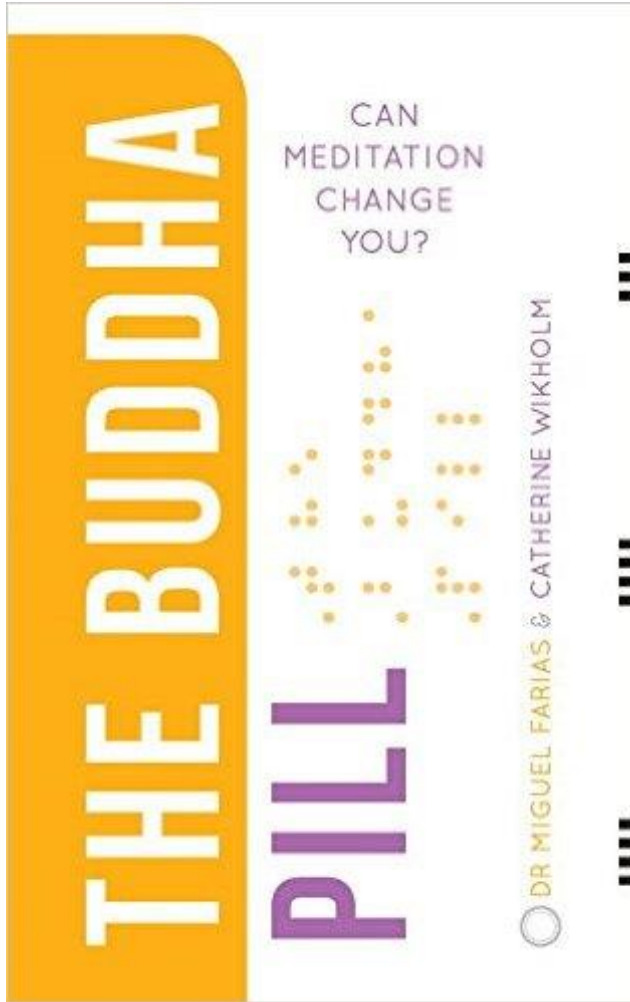
Very low quality evidence suggests that third wave CBT and CBT approaches are equally effective and acceptable in the treatment of acute depression. Evidence is limited in quantity, quality and breadth of available studies, precluding us from drawing any conclusions as to their short- or longer-term equivalence. The increasing popularity of third wave CBT approaches in clinical practice underscores the importance of completing further studies to compare various third wave CBT approaches with other psychological therapy approaches to inform clinicians and policymakers on the most effective forms of psychological therapy in treating depression.

Il nuovo boom: Mindfulness

N° of citations in PubMed for "mindfulness"



Not everybody is happy with meditation ...



Is meditation good for everybody ?

Can meditation be prescribed as a pill ?

A pill of which «medicine», and at which dosage ?

Effectiveness and cost-effectiveness of mindfulness-based cognitive therapy compared with maintenance antidepressant treatment in the prevention of depressive relapse or recurrence (PREVENT): a randomised controlled trial



Willem Kuyken, Rachel Hayes, Barbara Barrett, Richard Byng, Tim Dalgleish, David Kessler, Glyn Lewis, Edward Watkins, Claire Brejcha, Jessica Cardy, Aaron Causley, Suzanne Cowderoy, Alison Evans, Felix Gradinger, Surinder Kaur, Paul Lanham, Nicola Morant, Jonathan Richards, Pooja Shah, Harry Sutton, Rachael Vicary, Alice Weaver, Jenny Wilks, Matthew Williams, Rod S Taylor, Sarah Byford



Interpretation We found no evidence that MBCT-TS is superior to maintenance antidepressant treatment for the prevention of depressive relapse in individuals at risk for depressive relapse or recurrence. Both treatments were associated with enduring positive outcomes in terms of relapse or recurrence, residual depressive symptoms, and quality of life.

Lancet 2015; 386: 63-73



Contents lists available at ScienceDirect

Complementary Therapies in Clinical Practice

journal homepage: www.elsevier.com/locate/ctnm



Cultivating mindfulness in health care professionals: A review of empirical studies of mindfulness-based stress reduction (MBSR)

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A B S T R A C T

Keywords:

Mindfulness meditation
Health care professional's well-being
Clinician self-care
Mindfulness-based stress reduction

Demands faced by health care professionals include heavy caseloads, limited control over the work environment, long hours, as well as organizational structures and systems in transition. Such conditions have been directly linked to increased stress and symptoms of burnout, which in turn, have adverse consequences for clinicians and the quality of care that is provided to patients. Consequently, there exists an impetus for the development of curriculum aimed at fostering wellness and the necessary self-care skills for clinicians. This review will examine the potential benefits of mindfulness-based stress reduction (MBSR) programs aimed at enhancing well-being and coping with stress in this population. Empirical evidence indicates that participation in MBSR yields benefits for clinicians in the domains of physical and mental health. Conceptual and methodological limitations of the existing studies and suggestions for future research are discussed.

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Conclusioni

Per la depressione lieve e moderata:

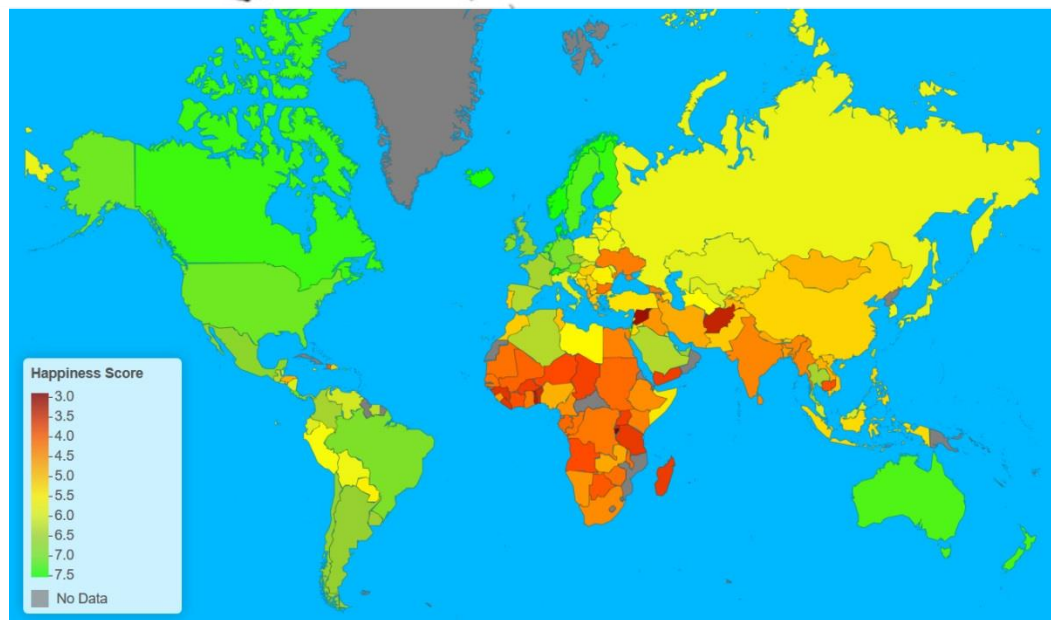
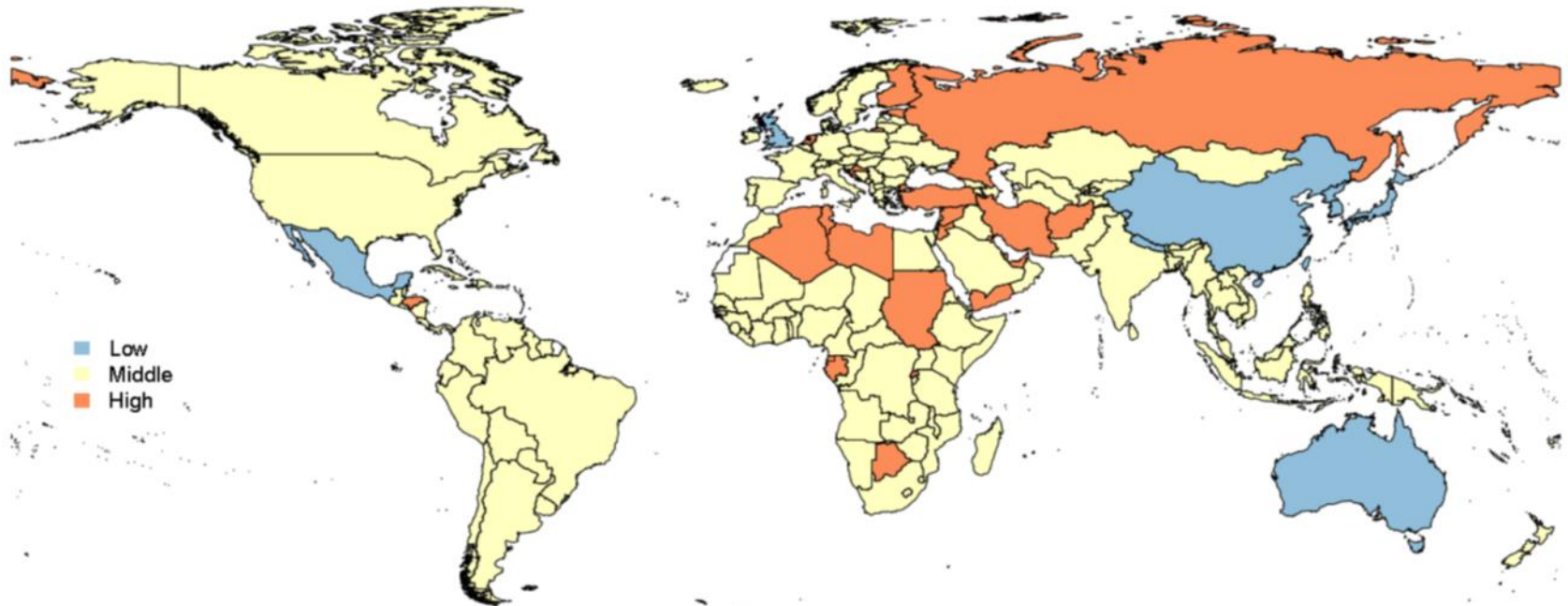
- La farmacoterapia con AD SSRI ha effetti uguali a quelli del placebo
- Gli SSRI causano effetti avversi largamente sottostimati, per di più non controbilanciati dall'azione terapeutica uguale al placebo
- La psicoterapia è altrettanto o più efficace della farmacoterapia, specie nel lungo termine e nell'evitare ricadute, ed è *cost effective*

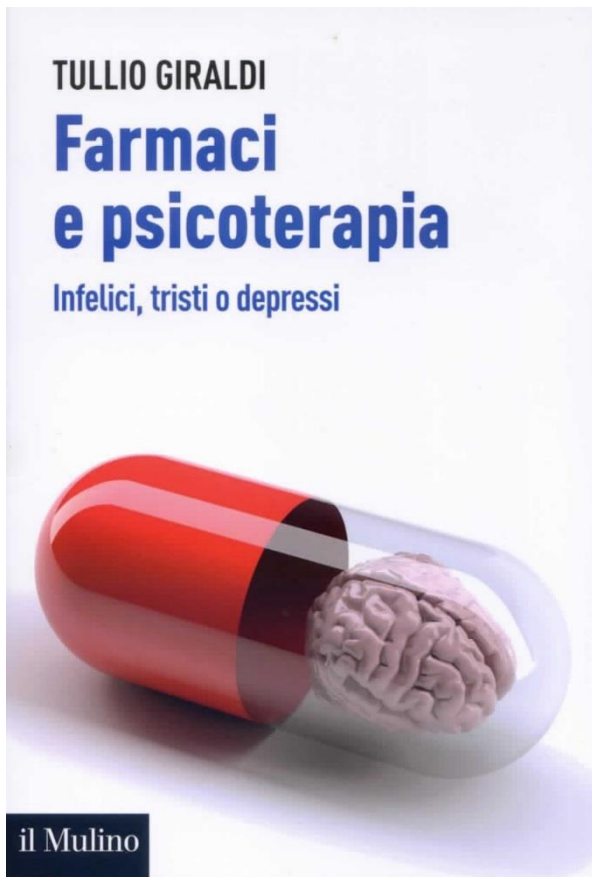
L'evidenza disponibile indica che considerazioni analoghe valgono per disturbi di ansia lievi o moderati

- L'intervento psico-sociale permette ai pazienti l'acquisizione di migliori modalità di adattamento agli eventi di vita stressanti alla base del disagio
- Gli effetti sono stabili, a differenza dell'attenuazione di sintomi causata dalla farmacoterapia, che può addirittura influenzare negativamente le risorse di adattamento dei soggetti ed il loro *empowerment*
- Ulteriori ricerche devono essere indirizzate per identificare, in alternativa ed in combinazione con la farmacoterapia, gli interventi più semplici e *cost effective*, in una prospettiva di rigorosa evidenza scientifica

- L'obiettivo complessivo dell'intervento deve essere quello di fornire in maniera individualizzata la risposta più appropriata al bisogno dei singoli soggetti
- evitando i presenti eccessi nella diagnosi di depressione e la conseguente obbligata prescrizione di farmaci antidepressivi,
- con la medicalizzazione delle persone che affrontano con emozioni *normali* situazioni di vita difficili e stressanti.

Plot 2: World map marking countries with statistically higher or lower YLD rates compared to the global mean





Grazie per l'attenzione