


Gli Antidepressivi nella depressione maggiore

Trieste, 26 Febbraio 2009

PRINCIPI GENERALI (I)

- ❑ Gli antidepressivi dovrebbero essere prescritti nei soggetti con depressione maggiore di intensità media-grave
- ❑ Tutti gli antidepressivi hanno simile efficacia 
- ❑ La scelta del trattamento deve essere discussa con il paziente
- ❑ Il dosaggio deve essere "terapeutico"
- ❑ La prescrizione di due antidepressivi contemporaneamente dovrebbe essere evitata
- ❑ Il trattamento deve essere proseguito per almeno 6-8 mesi dopo la risoluzione della fase acuta
- ❑ Gli antidepressivi non devono essere interrotti bruscamente (almeno 4 settimane, a seconda del dosaggio)

The choice of antidepressants

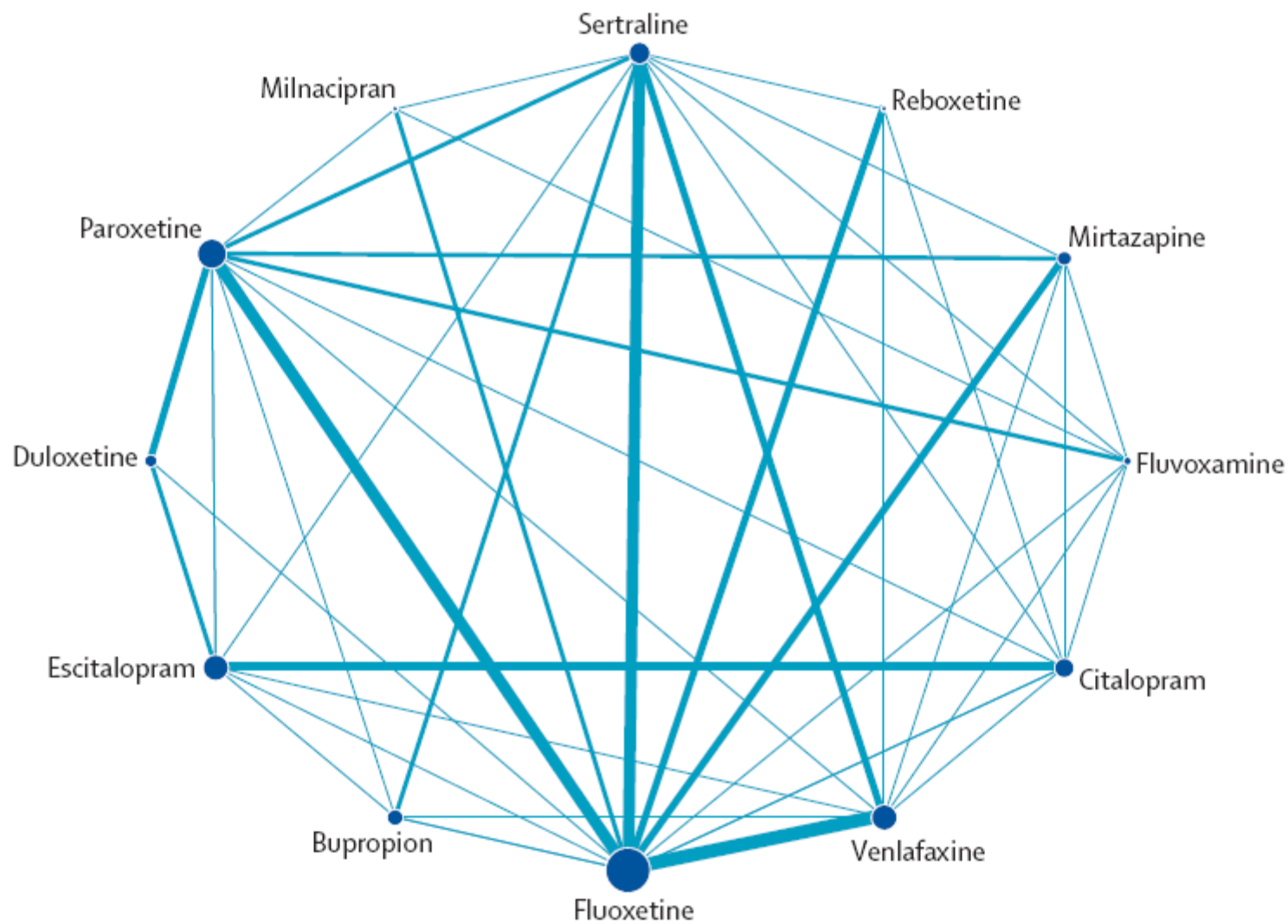
- 1.5.2.13 When an antidepressant is to be prescribed in routine care, it should be a selective serotonin reuptake inhibitor (SSRI), because SSRIs are as effective as tricyclic antidepressants and are less likely to be discontinued because of side effects. **A**
- 1.5.2.14 When prescribing an SSRI, consideration should be given to using a product in a generic form. Fluoxetine and citalopram, for example, would be reasonable choices because they are generally associated with fewer discontinuation/withdrawal symptoms. **C**



Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis

Andrea Cipriani, Toshiaki A Furukawa, Georgia Salanti, John R Geddes, Julian P T Higgins, Rachel Churchill, Norio Watanabe, Atsuo Nakagawa, Ichiro M Omori, Hugh McGuire, Michele Tansella, Corrado Barbui

	Number of trials	Year of publication			Country				
		Earliest	Median	Latest	Europe	North America	Africa	Asia	Multiple countries
Bupropion	14	1991	2003	2007	1	10	0	0	2
Citalopram	16	1993	2002	2007	4	4	0	1	4
Duloxetine	8	2002	2006	2007	2	5	0	0	1
Escitalopram	19	2000	2005	2007	5	11	0	0	2
Fluoxetine	54	1991	2000	2007	15	13	1	3	6
Fluvoxamine	11	1993	1998	2006	3	2	0	1	2
Milnacipran	6	1994	2000	2003	2	1	0	2	0
Mirtazapine	13	1997	2002	2005	3	3	1	1	5
Paroxetine	32	1993	2001	2007	12	13	1	1	2
Reboxetine	8	1997	2003	2006	2	2	0	0	1
Sertraline	27	1993	2000	2007	10	9	0	2	1
Venlafaxine	28	1994	2002	2007	7	5	0	1	6



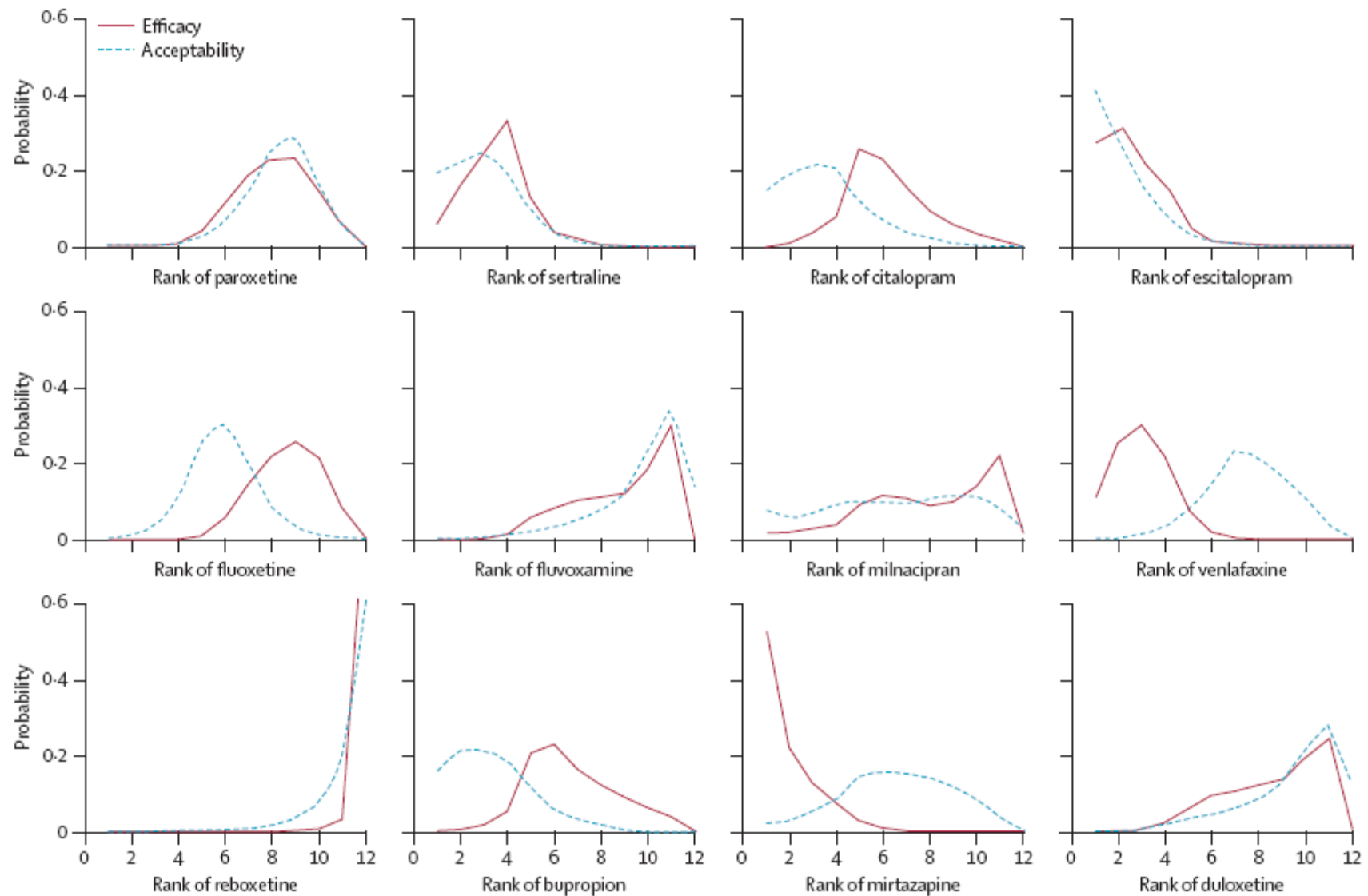
Efficacy (response rate) (95% CI)
 Comparison
 Acceptability (dropout rate) (95% CI)

BUP	1.00 (0.78-1.28)	0.75 (0.55-1.01)	1.06 (0.86-1.32)	0.89 (0.74-1.08)	0.73 (0.53-1.00)	0.87 (0.58-1.24)	0.87 (0.66-1.14)	0.81 (0.65-1.00)	0.62 (0.45-0.86)	1.01 (0.82-1.27)	0.84 (0.68-1.02)
0.98 (0.78-1.23)	CIT	0.75 (0.55-1.02)	1.07 (0.86-1.31)	0.90 (0.73-1.09)	<u>0.73</u> (0.54-0.99)	0.87 (0.60-1.24)	0.87 (0.66-1.15)	0.81 (0.65-1.01)	<u>0.62</u> (0.45-0.84)	1.02 (0.81-1.28)	0.84 (0.67-1.06)
1.09 (0.83-1.43)	1.12 (0.87-1.44)	DUL	<u>1.43</u> (1.09-1.85)	1.19 (0.91-1.57)	0.98 (0.67-1.41)	1.16 (0.77-1.73)	1.16 (0.83-1.61)	1.08 (0.84-1.40)	0.83 (0.57-1.22)	<u>1.36</u> (1.01-1.83)	1.12 (0.84-1.50)
0.82 (0.67-1.01)	0.84 (0.70-1.01)	0.75 (0.60-0.93)	ESC	0.84 (0.70-1.01)	0.69 (0.50-0.94)	0.81 (0.55-1.15)	0.81 (0.62-1.07)	0.76 (0.62-0.93)	0.58 (0.43-0.81)	0.95 (0.77-1.19)	0.78 (0.64-0.97)
1.08 (0.90-1.29)	1.10 (0.93-1.31)	0.99 (0.79-1.24)	<u>1.32</u> (1.12-1.55)	FLU	0.82 (0.62-1.07)	0.97 (0.69-1.32)	0.97 (0.77-1.21)	0.91 (0.79-1.05)	<u>0.70</u> (0.53-0.92)	1.14 (0.96-1.36)	0.94 (0.81-1.09)
1.10 (0.83-1.47)	1.13 (0.86-1.47)	1.01 (0.74-1.38)	<u>1.35</u> (1.02-1.76)	1.02 (0.81-1.30)	FVX	1.18 (0.76-1.75)	1.18 (0.87-1.61)	1.10 (0.84-1.47)	0.85 (0.57-1.26)	<u>1.38</u> (1.03-1.89)	1.14 (0.86-1.54)
1.07 (0.77-1.48)	1.09 (0.78-1.50)	0.97 (0.69-1.38)	1.30 (0.95-1.78)	0.99 (0.74-1.31)	0.97 (0.68-1.37)	MIL	0.99 (0.69-1.53)	0.94 (0.68-1.31)	0.72 (0.48-1.10)	1.17 (0.84-1.72)	0.97 (0.69-1.40)
0.79 (0.72-1.00)	0.80 (0.63-1.01)	<u>0.72</u> (0.54-0.94)	0.96 (0.76-1.19)	<u>0.73</u> (0.60-0.88)	<u>0.71</u> (0.55-0.92)	0.74 (0.53-1.01)	MIR	0.93 (0.75-1.17)	0.72 (0.51-1.03)	1.17 (0.91-1.51)	0.97 (0.76-1.23)
1.06 (0.87-1.30)	1.08 (0.90-1.30)	0.97 (0.78-1.20)	<u>1.30</u> (1.10-1.53)	0.98 (0.86-1.12)	0.96 (0.76-1.23)	1.00 (0.74-1.33)	<u>1.35</u> (1.11-1.64)	PAR	0.77 (0.56-1.05)	<u>1.25</u> (1.04-1.52)	1.03 (0.86-1.24)
<u>1.60</u> (1.20-2.16)	<u>1.63</u> (1.25-2.14)	<u>1.46</u> (1.05-2.02)	<u>1.95</u> (1.47-2.59)	<u>1.48</u> (1.16-1.90)	<u>1.45</u> (1.03-2.02)	<u>1.50</u> (1.03-2.18)	<u>2.03</u> (1.52-2.78)	<u>1.50</u> (1.16-1.98)	REB	<u>1.63</u> (1.19-2.24)	1.34 (0.99-1.83)
0.87 (0.72-1.05)	0.88 (0.72-1.07)	0.79 (0.62-1.01)	1.06 (0.88-1.27)	<u>0.80</u> (0.69-0.93)	0.79 (0.61-1.01)	0.81 (0.60-1.11)	1.10 (0.90-1.36)	<u>0.82</u> (0.69-0.96)	<u>0.54</u> (0.41-0.71)	SER	0.82 (0.67-1.00)
0.85 (0.70-1.01)	0.86 (0.71-1.05)	<u>0.77</u> (0.60-0.99)	1.03 (0.86-1.24)	<u>0.78</u> (0.68-0.90)	<u>0.77</u> (0.59-0.99)	0.79 (0.58-1.08)	1.08 (0.87-1.33)	<u>0.79</u> (0.67-0.94)	<u>0.53</u> (0.40-0.69)	0.98 (0.82-1.16)	VEN

	Efficacy (response rate) OR (95% CI)	Acceptability (dropout rate) OR (95% CI)
Bupropion	0.93 (0.77–1.11)	1.12 (0.92–1.36)
Citalopram	0.91 (0.76–1.08)	1.11 (0.91–1.37)
Duloxetine	1.01 (0.81–1.27)	0.84 (0.64–1.10)
Escitalopram	0.76 (0.65–0.89)*	1.19 (0.99–1.44)
Fluvoxamine	1.02 (0.81–1.30)	0.82 (0.62–1.07)
Milnacipran	0.99 (0.74–1.31)	0.97 (0.69–1.32)
Mirtazapine	0.73 (0.60–0.88)*	0.97 (0.77–1.21)
Paroxetine	0.98 (0.86–1.12)	0.91 (0.79–1.05)
Reboxetine	1.48 (1.16–1.90)*	0.70 (0.53–0.92)*
Sertraline	0.80 (0.69–0.93)*	1.14 (0.96–1.36)
Venlafaxine	0.78 (0.68–0.90)*	0.94 (0.81–1.09)

OR=odds ratio. CI=credibility interval. *p<0.05. For efficacy, OR higher than 1 favours fluoxetine. For acceptability, OR lower than 1 favours fluoxetine.

Table 4: Efficacy and acceptability using fluoxetine as reference compound



Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis

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Interpretation Clinically important differences exist between commonly prescribed antidepressants for both efficacy and acceptability in favour of escitalopram and sertraline. Sertraline might be the best choice when starting treatment for moderate to severe major depression in adults because it has the most favourable balance between benefits, acceptability, and acquisition cost.

- 1.5.2.18 When a patient's depression fails to respond to the first antidepressant prescribed, the prescriber should check that the drug has been taken regularly and in the prescribed dose. **GPP**
- 1.5.2.19 If the response to a standard dose of an antidepressant is inadequate, and there are no significant side effects, a gradual increase in dose should be considered in line with the schedule suggested by the Summary of Product Characteristics. **C**
- 1.5.2.20 Prescribers should consider switching to another antidepressant if there has been no response at all after 1 month, but if there has been a partial response, a decision to switch can be postponed until 6 weeks. **C**
- 1.5.2.21 If an antidepressant has not been effective or is poorly tolerated and – after consideration of a range of other treatment options – the decision is made to offer a further course of antidepressants, then another single antidepressant should be prescribed. **C**

- 1.5.2.22 Reasonable choices for a second antidepressant include a different SSRI or mirtazapine, but consideration may also be given to other alternatives, including moclobemide, reboxetine *and lofepramine*. *Other tricyclic antidepressants (except dosulepin) and venlafaxine may be considered, especially for more severe depression.* **B**
- 1.5.2.23 When switching from one antidepressant to another, prescribers should be aware of the need for gradual and modest incremental increases of dose, of interactions between antidepressants and the risk of serotonin syndrome when combinations of serotonergic antidepressants are prescribed. Features include confusion, delirium, shivering, sweating, changes in blood pressure and myoclonus. **C**

The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

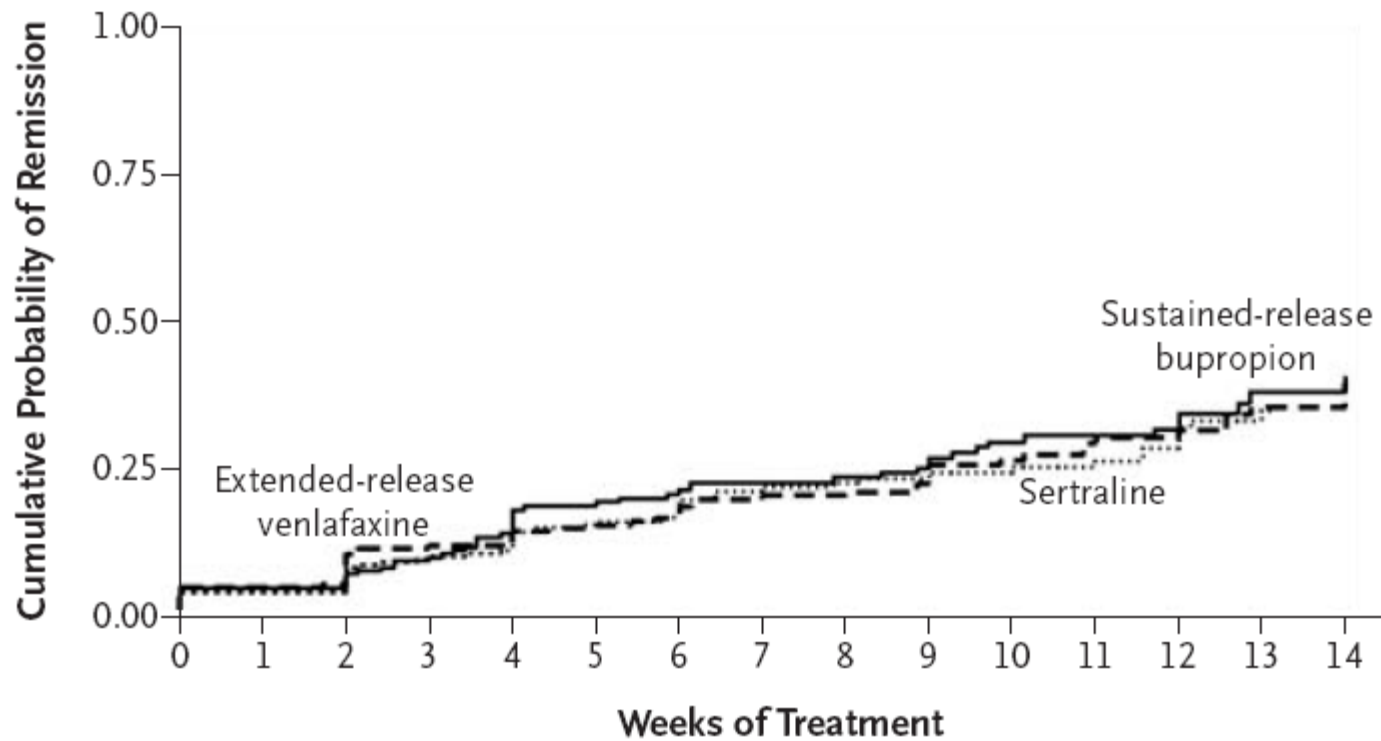
MARCH 23, 2006

VOL. 354 NO. 12

Bupropion-SR, Sertraline, or Venlafaxine-XR after Failure
of SSRIs for Depression

A. John Rush, M.D., Madhukar H. Trivedi, M.D., Stephen R. Wisniewski, Ph.D., Jonathan W. Stewart, M.D.,
Andrew A. Nierenberg, M.D., Michael E. Thase, M.D., Louise Ritz, M.B.A., Melanie M. Biggs, Ph.D.,
Diane Warden, Ph.D., M.B.A., James F. Luther, M.A., Kathy Shores-Wilson, Ph.D., George Niederehe, Ph.D.,
and Maurizio Fava, M.D., for the STAR*D Study Team*

- ❑ 727 adult outpatients with a nonpsychotic major depressive disorder who had no remission of symptoms or could not tolerate the SSRI citalopram
- ❑ Sustained-release bupropion (239 patients) at a maximal daily dose of 400 mg, sertraline (238 patients) at a maximal daily dose of 200 mg, or extended-release venlafaxine (250 patients) at a maximal daily dose of 375 mg
- ❑ 18 primary and 23 psychiatric care settings
- ❑ The primary outcome was symptom remission at week 14, defined by a total score of 7 or less on the 17-item Hamilton Rating Scale for Depression (HRSD-17) at the end of the study.



“ After unsuccessful treatment with an SSRI, approximately one in four patients had a remission of symptoms after switching to another antidepressant. Any one of the medications in the study provided a reasonable second-step choice for patients with depression.”

N Engl J Med 2006;354:1231-42.

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Treatment of SSRI-Resistant Depression: A Meta-Analysis Comparing Within- Versus Across-Class Switches

George I. Papakostas, Maurizio Fava, and Michael E. Thase

- ❑ Several sources were searched for randomized clinical trials comparing these two switch strategies.
- ❑ Data from four clinical trials ($n = 1496$) were combined using a random-effects model.

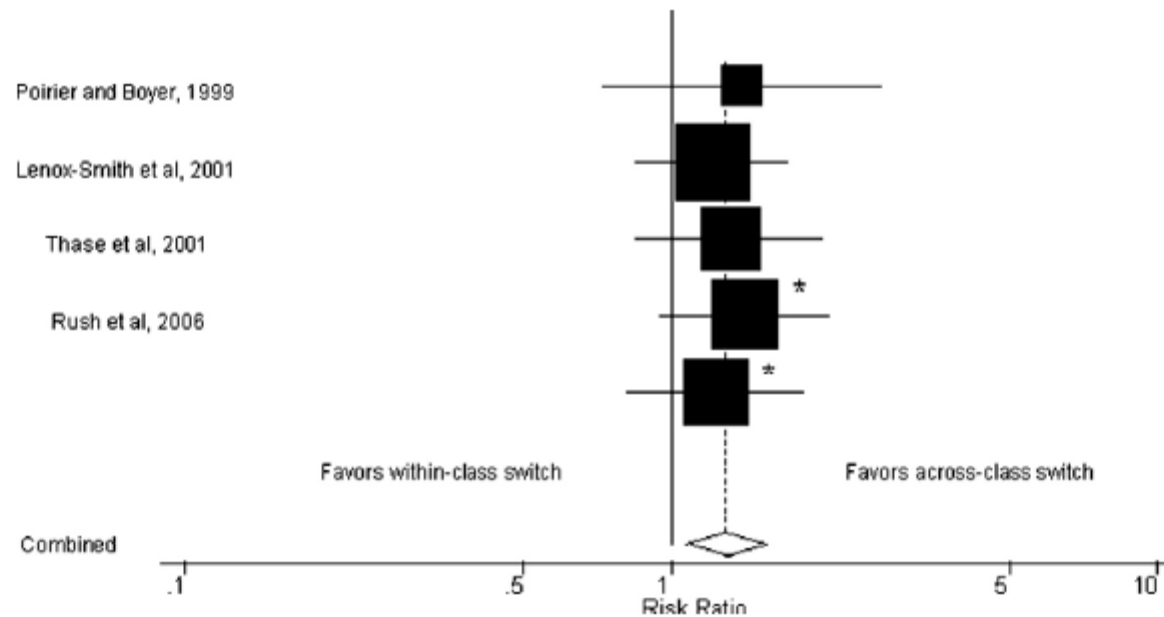


Figure 1. Primary meta-analytic findings: remission. Boxes represent the individual study risk ratios. The size of a box is proportional to the study sample size; horizontal lines represent the 95% confidence interval for the risk ratio; and the diamond represents the pooled risk ratio. x-axis: risk ratio; y-axis: risk ratio = 1. *The top box represents the sertraline-venlafaxine pairwise comparison and the bottom box the sertraline-bupropion pairwise comparison.

- ❑ Pooled remission rates were 28% (for non-SSRIs) and 23.5% (for SSRIs)
- ❑ Nearly 22 SSRI nonresponders would need to be switched to a non-SSRI rather than a second SSRI antidepressant to obtain one additional remitter.

- 1.5.2.31 *Before prescribing venlafaxine, practitioners should take into account the increased likelihood of patients stopping treatment because of side effects, and its higher cost, compared with equally effective SSRIs. **B***
- 1.5.2.32 *Before prescribing venlafaxine, practitioners should ensure pre-existing hypertension is controlled in line with the current NICE guideline on hypertension (see www.nice.org.uk/CG034).*
- 1.5.2.33 *For patients prescribed venlafaxine, blood pressure should be checked on initiation and regularly during treatment, particularly during dosage titration. For patients who experience a sustained increase in blood pressure, the dose should be reduced or discontinuation considered. **C***
- 1.5.2.34 *Practitioners should monitor patients prescribed venlafaxine for the signs and symptoms of cardiac dysfunction, particularly in those with known cardiovascular disease, and take appropriate action as necessary. **C***

Age

- 1.5.2.40 For older adults with depression, antidepressant treatment should be given at an age-appropriate dose for a minimum of 6 weeks before treatment is considered to be ineffective. If there has been a partial response within this period, treatment should be continued for a further 6 weeks. **C**
- 1.5.2.41 When prescribing antidepressants – in particular tricyclics – for older adults with depression, careful monitoring for side effects should be undertaken. **C**
- 1.5.2.42 Healthcare professionals should be aware of the increased frequency of drug interactions when prescribing an antidepressant to older adults who are taking other medications. **GPP**

Antidepressant-induced hyponatraemia

Most antidepressants have been associated with hyponatraemia. The mechanism of this adverse effect is probably the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). Hyponatraemia is a rare but potentially serious adverse effect of antidepressants that demands careful monitoring, particularly in those patients at greatest risk (see table below).

Table Risk factors¹⁻⁴

Old age

Female sex

Low body weight

Some drug treatments (e.g. diuretics, NSAIDs, carbamazepine, cancer chemotherapy)

Reduced renal function (especially acute and chronic renal failure)

Medical co-morbidity (e.g. hypothyroidism, diabetes, COPD, hypertension, head injury, CVA, various cancers)

Warm weather (summer)

Antidepressants

No antidepressant has been shown *not* to be associated with hyponatraemia and most have a reported association⁵. It has been suggested that serotonergic drugs are relatively more likely to cause hyponatraemia^{6,7}, although this is disputed⁸. There are certainly literature reports of hyponatraemia occurring with noradrenergic drugs^{9,10}.

Monitoring

All patients taking antidepressants should be observed for signs of hyponatraemia (dizziness, nausea, lethargy, confusion, cramps, seizures). Serum sodium should be determined (at baseline and 2 and 4 weeks, and then 3-monthly¹¹) for those at high risk of drug-induced hyponatraemia. The high-risk factors are as follows:

- extreme old age (>80 years)
- history of hyponatraemia
- co-therapy with other drugs known to be associated with hyponatraemia (as above)
- reduced renal function (GFR < 50 ml/min)
- medical co-morbidity (as above).

Note that hyponatraemia is common in elderly patients so monitoring is essential^{12,13}.

Treatment¹⁴

Withdraw antidepressant immediately (note risk of discontinuation effects which may complicate clinical picture):

- If serum sodium is >125 mmol/l – monitor sodium daily until normal.
- If serum sodium is <125 mmol/l – refer to specialist medical care.

Patients with dementia

- 1.5.2.43 Depression in patients with dementia should be treated in the same way as depression in other older adults. **C**
- 1.5.2.44 Healthcare professionals should be aware that depression responds to antidepressants even in the presence of dementia. **C**

Patients with cardiovascular disease

- 1.5.2.45 When initiating treatment in a patient with a recent myocardial infarction or unstable angina, sertraline is the treatment of choice as it has the most evidence for safe use in this situation. **B**
- 1.5.2.46 An ECG should be carried out *and blood pressure measurement taken* before prescribing a tricyclic antidepressant for a depressed patient at significant risk of cardiovascular disease. **GPP**
- 1.5.2.47 *Venlafaxine and tricyclic antidepressants (with the exception of lofepramine) should not be prescribed for patients with a:*
- *high risk of serious cardiac arrhythmias*
 - *recent myocardial infarction.* **C**

Sertraline Treatment of Major Depression in Patients With Acute MI or Unstable Angina

Alexander H. Glassman, MD

Christopher M. O'Connor, MD

Robert M. Califf, MD

Karl Swedberg, MD

Peter Schwartz, MD

J. Thomas Bigger, Jr, MD

K. Ranga Rama Krishnan, MD

Louis T. van Zyl, MD

J. Robert Swenson, MD

Mitchell S. Finkel, MD

Charles Landau, MD

Peter A. Shapiro, MD

Carl J. Pepine, MD

Jack Mardekian, PhD

Wilma M. Harrison, MD

for the Sertraline Antidepressant
Heart Attack Randomized Trial
(SADHART) Group

Context Major depressive disorder (MDD) occurs in 15% to 23% of patients with acute coronary syndromes and constitutes an independent risk factor for morbidity and mortality. However, no published evidence exists that antidepressant drugs are safe or efficacious in patients with unstable ischemic heart disease.

Objective To evaluate the safety and efficacy of sertraline treatment of MDD in patients hospitalized for acute myocardial infarction (MI) or unstable angina and free of other life-threatening medical conditions.

Design and Setting Randomized, double-blind, placebo-controlled trial conducted in 40 outpatient cardiology centers and psychiatry clinics in the United States, Europe, Canada, and Australia. Enrollment began in April 1997 and follow-up ended in April 2001.

Patients A total of 369 patients with MDD (64% male; mean age, 57.1 years; mean 17-item Hamilton Depression [HAM-D] score, 19.6; MI, 74%; unstable angina, 26%).

Intervention After a 2-week single-blind placebo run-in, patients were randomly assigned to receive sertraline in flexible dosages of 50 to 200 mg/d (n=186) or placebo (n=183) for 24 weeks.

Main Outcome Measures The primary (safety) outcome measure was change from baseline in left ventricular ejection fraction (LVEF); secondary measures included surrogate cardiac measures and cardiovascular adverse events, as well as scores on the HAM-D scale and Clinical Global Impression Improvement scale (CGI-I) in the total randomized sample, in a group with any prior history of MDD, and in a more severe MDD subgroup defined a priori by a HAM-D score of at least 18 and history of 2 or more prior episodes of MDD.

Results Sertraline had no significant effect on mean (SD) LVEF (sertraline: baseline, 54% [10%]; week 16, 54% [11%]; placebo: baseline, 52% [13%]; week 16, 53% [13%]), treatment-emergent increase in ventricular premature complex (VPC) runs (sertraline: 13.1%; placebo: 12.9%), QTc interval greater than 450 milliseconds at end point (sertraline: 12%; placebo: 13%), or other cardiac measures. All comparisons were statistically nonsignificant ($P \geq .05$). The incidence of severe cardiovascular adverse events was 14.5% with sertraline and 22.4% with placebo. In the total randomized sample, the CGI-I ($P = .049$), but not the HAM-D ($P = .14$), favored sertraline. The CGI-I responder rates for sertraline were significantly higher than for placebo in the total sample (67% vs 53%; $P = .01$), in the group with at least 1 prior episode of depression (72% vs 51%; $P = .003$), and in the more severe MDD group (78% vs 45%; $P = .001$). In the latter 2 groups, both CGI-I and HAM-D measures were significantly better in those assigned to sertraline.

Conclusion Our results suggest that sertraline is a safe and effective treatment for recurrent depression in patients with recent MI or unstable angina and without other life-threatening medical conditions.

Effects of Citalopram and Interpersonal Psychotherapy on Depression in Patients With Coronary Artery Disease

The Canadian Cardiac Randomized Evaluation of Antidepressant and Psychotherapy Efficacy (CREATE) Trial

- ❑ A randomized, controlled, 12-week, parallel-group trial
- ❑ 284 patients with CAD from 9 Canadian academic centers. All patients met
- ❑ *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria for diagnosis of major depression
- ❑ Mean HAM-D response (52.8% vs 40.1%; $P=.03$) and remission rates (35.9% vs 22.5%; $P=.01$) favored citalopram.

Tabella 3. - *Effetti indesiderati degli antidepressivi.*

Triciclici	Bocca secca, stipsi, difficoltà a urinare, ipotensione ortostatica, disturbi della sfera sessuale, aumento di peso, tremore alle mani, disturbi della memoria e dell'attenzione (nell'anziano)
Inibitori selettivi della ricaptazione di serotonina	Nausea, insonnia, cefalea, vertigini, disturbi della sfera sessuale, diminuzione del desiderio sessuale, eiaculazione ritardata, difficoltà a raggiungere l'orgasmo, tremori
Duloxetina	Nausea, stipsi, sonnolenza, insonnia
Venlafaxina	Vertigini, bocca secca, insonnia, nervosismo, sonnolenza, stipsi, nausea, sudorazione, occasionali rialzi della pressione arteriosa, disturbi della sfera sessuale
Reboxetina	Aumento della frequenza cardiaca, insonnia, irrequietezza, bocca secca, stipsi, sudorazione, vertigini
Mirtazapina	Bocca secca, sedazione, sonnolenza, aumento dell'appetito e incremento di peso, alterazione della performance cognitiva e psicomotoria
Bupropione	Bocca secca, nausea e vomito, stipsi, insonnia, tremore, disturbi della concentrazione, cefalea, vertigini, rash cutanei, prurito, sudorazione

Table Antidepressants: relative adverse effects – a rough guide

<i>Drug</i>	<i>Sedation</i>	<i>Hypotension</i>	<i>Anticholinergic effects</i>	<i>Forms available</i>
Tricyclics				
Amitriptyline	+++	+++	+++	tabs/caps, liq, inj
Clomipramine	++	+++	++	tabs/caps, liq
Desipramine	+	++	+	tabs
Dothiepin	+++	+++	++	tabs, caps
Doxepin	+++	++	++	caps
Imipramine	++	+++	+++	tabs, liq
Lofepramine	+	+	+	tabs
Nortriptyline	+	++	+	tabs
Trimipramine	+++	+++	++	tabs, caps

Table Antidepressants: relative adverse effects – a rough guide

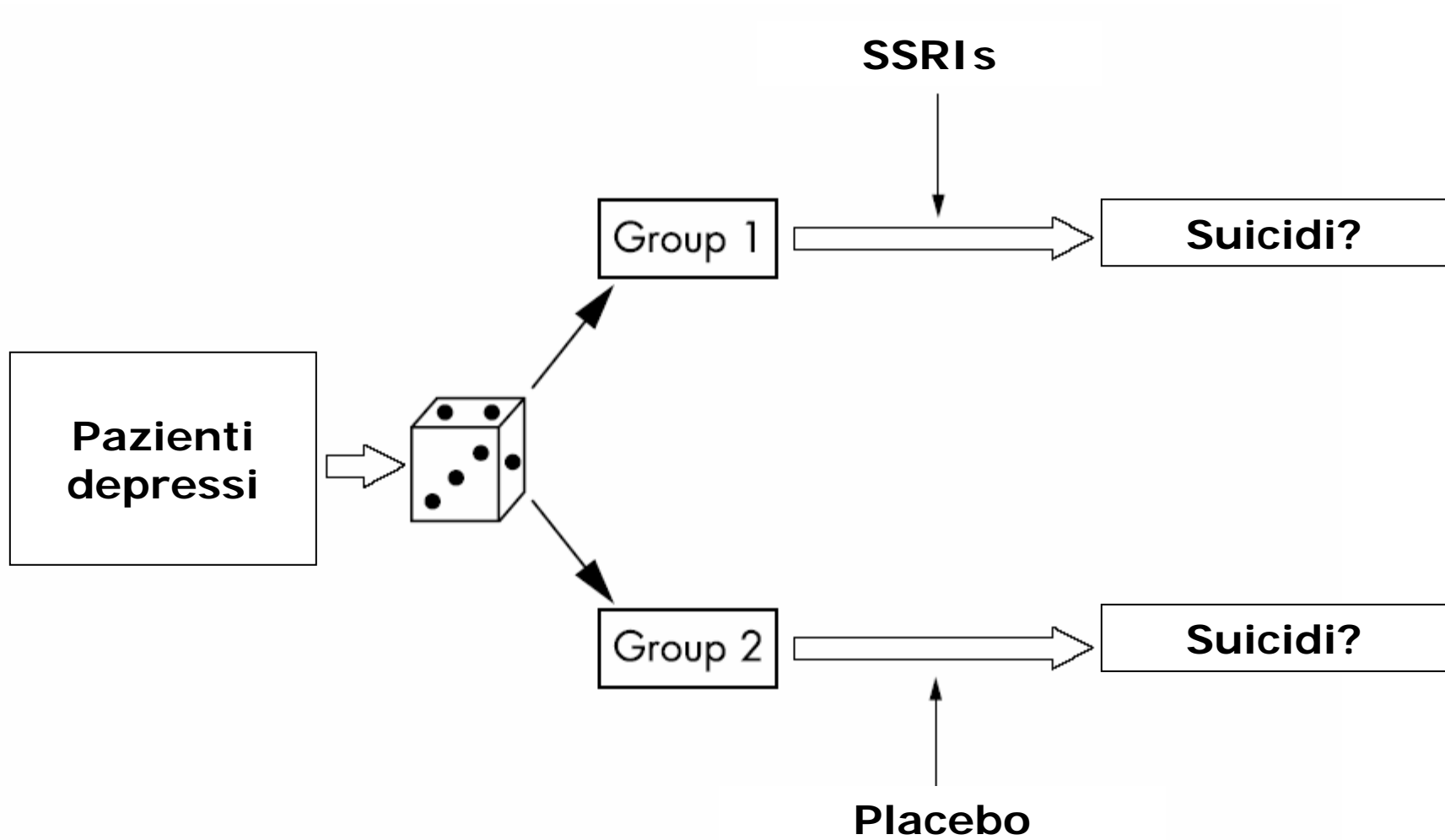
Drug	Sedation	Hypotension	Anticholinergic effects	Forms available
Other antidepressants				
Duloxetine	+/-	-	-	caps
Mianserin	++	-	-	tabs
Mirtazapine	+++	-	+	tabs
Reboxetine	+	-	+	tabs
Trazodone	+++	++	-	caps, liq
Venlafaxine	+/-	-	+	tabs
Selective serotonin reuptake inhibitors (SSRIs)				
Citalopram	+/-	-	-	tabs, liq
Escitalopram	+/-	-	-	tabs
Fluoxetine	-	-	-	caps, liq
Fluvoxamine	+	-	-	tabs
Paroxetine	+	-	+	tabs, liq
Sertraline	-	-	-	tabs

Antidepressivi di nuova generazione

irritabilità, acatisia
miglioramento della inibizione
motoria



**IDEAZIONE
SUICIDARIA**



December 2006

Antidepressants and Suicidality in Adults: Data Overview



Trial Disposition

Disposition		Number of Trials
Included		372
Excluded	Exclusion Reason	26
	Fewer than 20 subjects per arm in test-drug or placebo arms	23
	Data not available for most subjects	3
Duplicate trials		6
Total		404



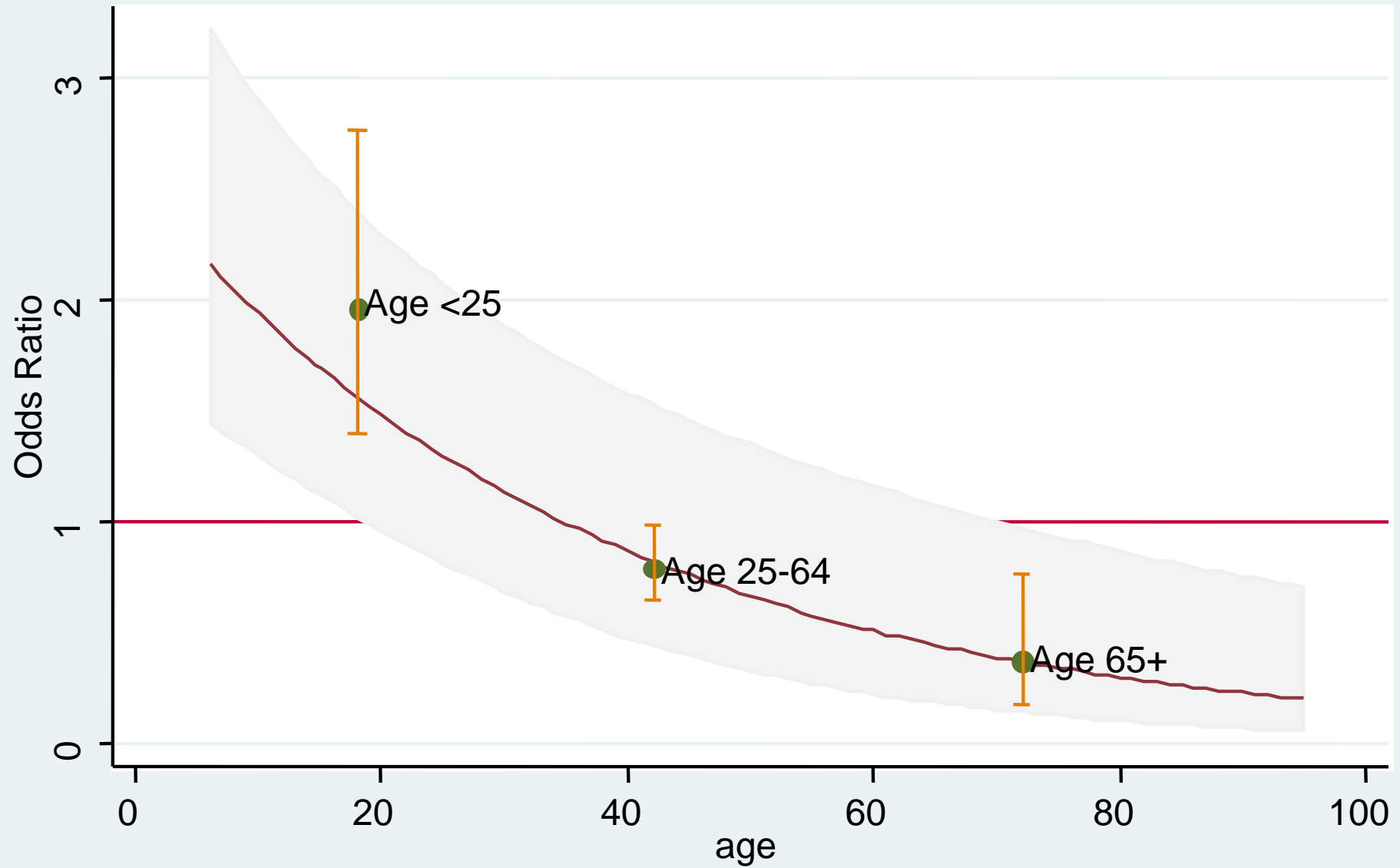
Number of Suicidality Events

Completed	Attempt	Preparation	Ideation	Indication
8	134	10	378	All
6	90	7	238	Major Depression
0	7	1	14	Other Depression
2	36	2	108	Other Psychiatric
0	1	0	8	Other Behavioral
0	0	0	10	Other



Suicidal Behavior or Ideation

Pediatric and Adult Studies



Expanding the Black Box — Depression, Antidepressants, and the Risk of Suicide

Richard A. Friedman, M.D., and Andrew C. Leon, Ph.D.

On May 2, 2007, the Food and Drug Administration (FDA) ordered that all antidepressant medications carry an expanded black-box warning incorporating information about an increased risk of suicidal symptoms in young adults 18 to 24 years of age.

Antidepressants and suicide

Corrado Barbui,¹ Andrea Cipriani,¹ John R Geddes²

Table Selected findings from the FDA analysis investigating suicide behaviour risk in adults with psychiatric disorders relative to placebo in adults with psychiatric disorders*

Antidepressant	Ideation or worse [†]	Preparation or worse [‡]
	OR§ (95% CI)	OR (95% CI)
SSRI¶		
Citalopram	2.11 (0.90 to 4.94)	1.97 (0.56 to 7.00)
Escitalopram	2.44 (0.90 to 6.63)	5.67 (0.94 to 34.2)
Fluoxetine	0.71 (0.52 to 0.99)§§	1.08 (0.52 to 2.23)
Fluvoxamine	1.25 (0.66 to 2.39)	1.31 (0.51 to 3.38)
Paroxetine	0.93 (0.62 to 1.42)	2.76 (1.16 to 6.60)¶¶
Sertraline	0.51 (0.29 to 0.91)§§	0.25 (0.07 to 0.90)§§
SNRI**		
Duloxetine	0.88 (0.47 to 1.63)	1.17 (0.18 to 7.53)
Venlafaxine	0.71 (0.44 to 1.16)	0.69 (0.25 to 1.89)
Other antidepressants††		
Bupropion	1.35 (0.45 to 4.06)	2.41 (0.48 to 12.1)
Mirtazapine	0.97 (0.34 to 2.78)	1.25 (0.34 to 4.62)
Nefazodone	0.65 (0.30 to 1.41)	0.53 (0.15 to 1.82)

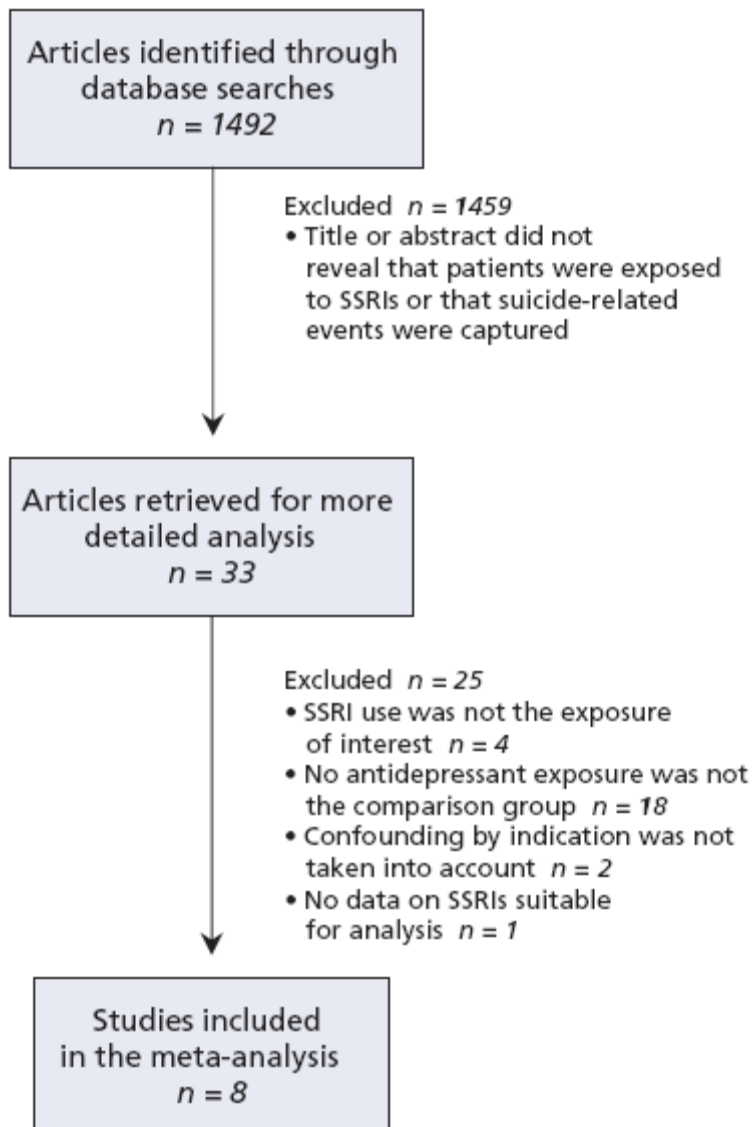
Non tutti gli antidepressivi sono uguali

Selective serotonin reuptake inhibitors and risk of suicide: a systematic review of observational studies

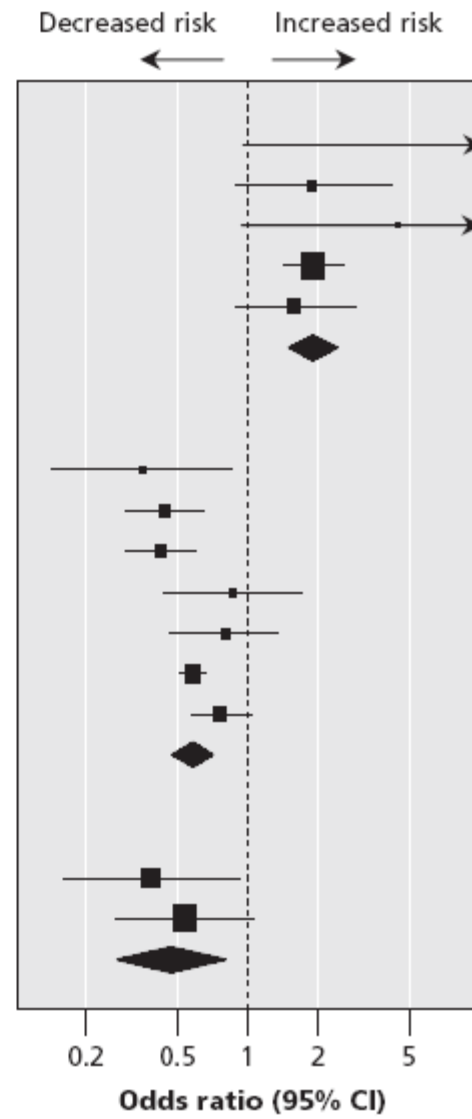
Corrado Barbui MD, Eleonora Esposito MD, Andrea Cipriani MD

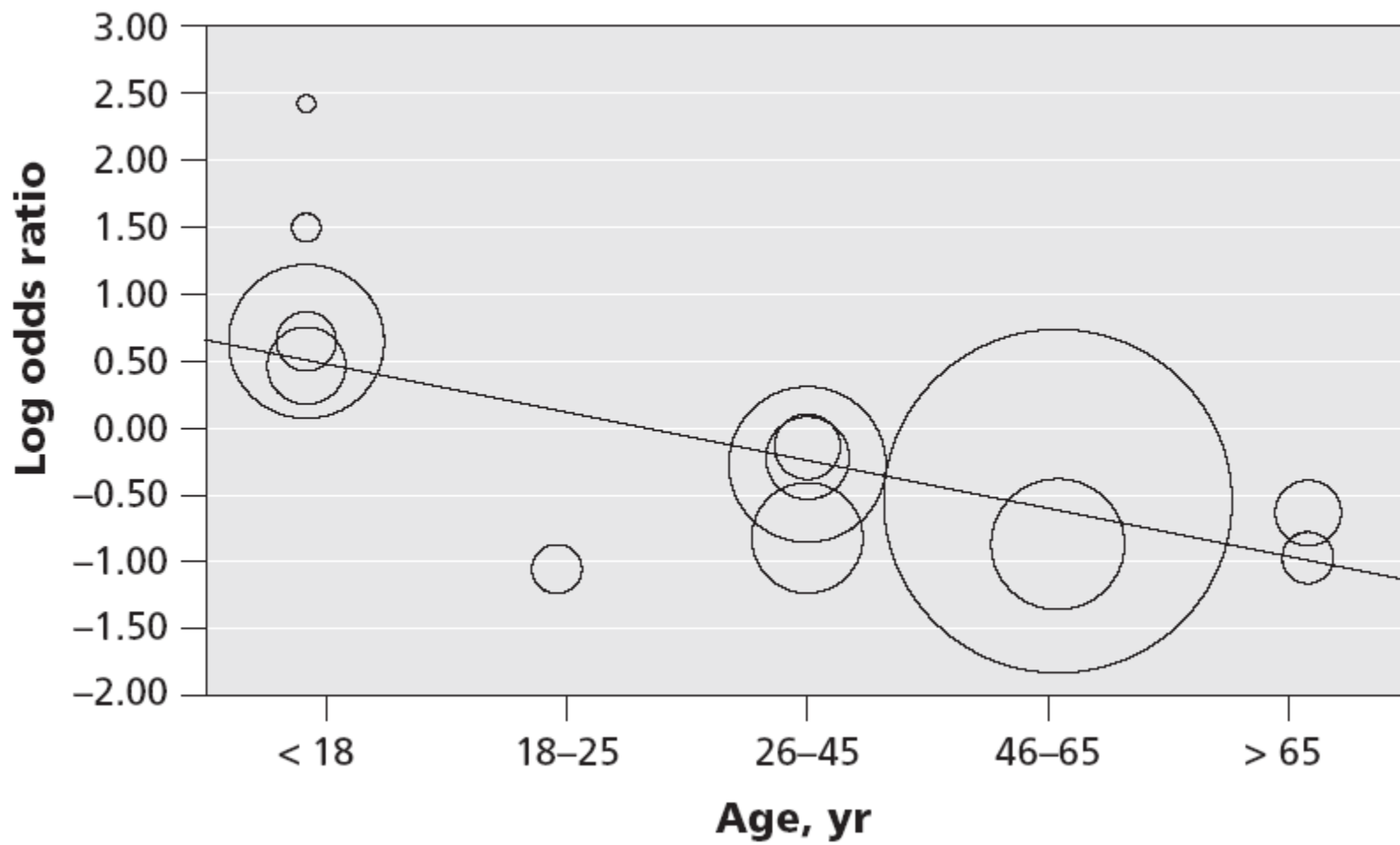
“It is unclear whether the use of selective serotonin reuptake inhibitors (SSRIs) and other antidepressant drugs reduce the risk of suicide in people with depression. We explored the association between exposure to SSRIs and risk of suicide completion or attempt.”

“We conducted a systematic review of observational studies that reported completed or attempted suicide in depressed individuals who were exposed to SSRIs compared with those who were not exposed to antidepressants.”



Group; study	Age, yr	Odds ratio (95% CI)
Adolescents		
Olfson et al. ⁴⁴	6–18	11.26 (0.97–130.70)
Olfson et al. ⁴⁵	6–18	1.91 (0.90–4.07)
Sondergard et al. ⁴⁸	10–17	4.47 (0.95–20.96)
Tiihonen et al. ⁴⁹	10–19	1.91 (1.43–2.55)
Valuck et al. ⁵⁰	12–18	1.59 (0.89–2.82)
<i>Overall</i>		1.92 (1.51–2.44)
		$I^2 = 0.0\%$
Adults		
Gibbons et al. ⁴³	18–25	0.35 (0.14–0.85)
Gibbons et al. ⁴³	26–45	0.44 (0.29–0.65)
Gibbons et al. ⁴³	46–65	0.42 (0.30–0.58)
Olfson et al. ⁴⁴	19–64	0.87 (0.44–1.73)
Olfson et al. ⁴⁵	19–64	0.80 (0.74–1.38)
Sondergard et al. ⁴⁷	56*	0.58 (0.50–0.66)
Tiihonen et al. ⁴⁹	38*	0.76 (0.57–1.10)
<i>Overall</i>		0.57 (0.47–0.70)
		$I^2 = 52.5\%$
Elderly		
Gibbons et al. ⁴³	≥ 65	0.38 (0.16–0.91)
Rahme et al. ⁴⁶	75*	0.53 (0.27–1.06)
<i>Overall</i>		0.46 (0.27–0.79)
		$I^2 = 0.0\%$





PRINCIPI GENERALI (II)

- ❑ Riconoscere la Depressione Maggiore
- ❑ Trattare farmacologicamente i soggetti con depressione maggiore di intensità media-grave
- ❑ Particolare “attenzione” agli anziani (rischio di suicidio – situazione di vita)
- ❑ Particolare “attenzione” ai giovani (rischio di suicidio – effetto collaterale del trattamento)
- ❑ In termini di efficacia gli antidepressivi non sono tutti uguali. Le evidenze suggeriscono che alcuni antidepressivi non andrebbero prescritti in prima battuta nei soggetti con depressione maggiore (reboxetina, duloxetina).
- ❑ Le evidenze suggeriscono che la sertralina è una valida prima battuta nei soggetti con depressione maggiore (escitalopram).
- ❑ Attenzione alla “adesione” al trattamento (è una frequente ragione di non-risposta agli antidepressivi)
- ❑ Nei soggetti in trattamento da anni che stanno bene prendere in considerazione la possibilità di sospendere la terapia (non bruscamente, vedi anamnesi)