Duloxetin

for Depression

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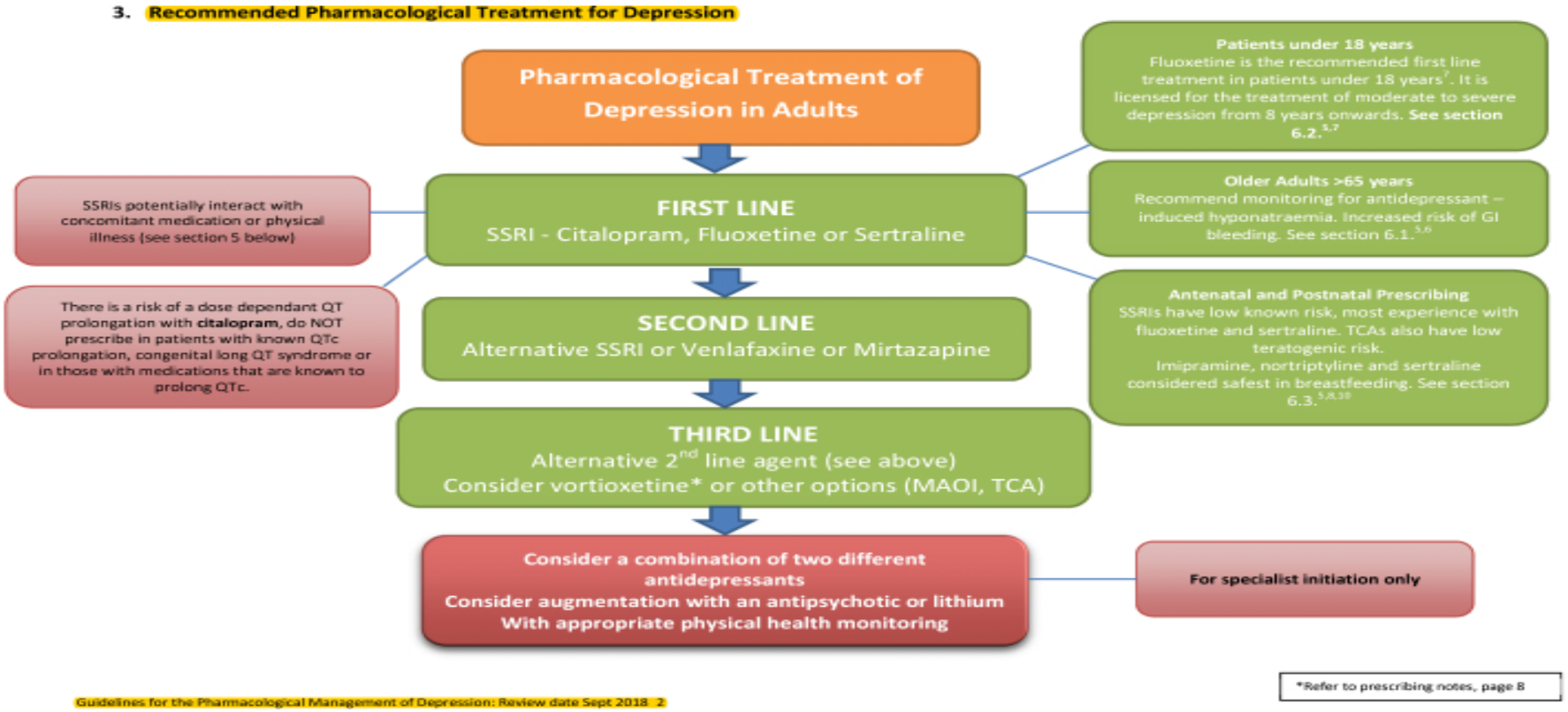
SBMU

Dept of Psychiatry

Prescribing a Psychotropic Agent After Diagnostic Assessment

- Choose a medication based on FDA approval
- Family or personal hx of response
- Adverse effects vs. key symptoms
- Starting dose
- Monitor side effects & clinical response
- Adjust dose if needed

Pharmacological treatment of Depression in Adults



Working in partnership:

Hertfordshire Partnership University NHS Foundation Trust
East and North Hertfordshire Clinical Commissioning Group
Herts Valleys Clinical Commissioning Group

Guidelines on Choice and Selection of Antidepressants for the Management of Depression

Guidelines

Pharmacological treatment recommendations for the unipolar depressive disorder

Guideline organization	First line medication
APA American Psychiatric Association	SSRIs, SNRIs, Mirtazapine, bupropion
CANMAT Canadian Network for Mood and Anxiety Treatments	SSRIs, SNRIs, Mirtazapine, bupropion, vortioxetine
TMAP The Texas Medication Algorithm Project	SSRIs, SNRIs, Mirtazapine, bupropion
RANZCP Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders	SSRIs, Mirtazapine, bupropion

Table 1 Recommendations for Switching ADT

Initial Treatment	1rst Intention	2nd Intention
SSRI	- Duloxetine - Venlafaxine	- Other SSRI - Milnacipran - α2-antagonist Agomelatine - Clomipramine
SNRI	- Escitalopram - Sertraline	- Citalopram - Fluoxetine - Fluvoxamine - Paroxetine - Other SNRI - Agomelatine - α2-antagonist - Clomipramine - Imipramine
Tricyclic ADT	- Escitalopram - Duloxetine - Venlafaxine	- Citalopram - Fluoxetine - Fluvoxamine - Paroxetine - Sertraline - Milnacipran - α2-antagonist - Other Tricyclic - Iproniazide
α2-antagonist*	- Escitalopram - Fluoxetine - Paroxetine - Sertraline - Duloxetine - Venlafaxine	- Citalopram - Fluvoxamine - Milnacipran - Agomelatine - Clomipramine

* Switching from an α2-antagonist to another one is not recommended

- Duloxetine hydrochloride (DUL) is an antidepressant included in the pharmacological class of serotonin–norepinephrine reuptake inhibitors approved for the treatment of major depressive disorder, generalized anxiety disorder, diabetic peripheral neuropathic pain, fibromyalgia, and chronic musculoskeletal pain.

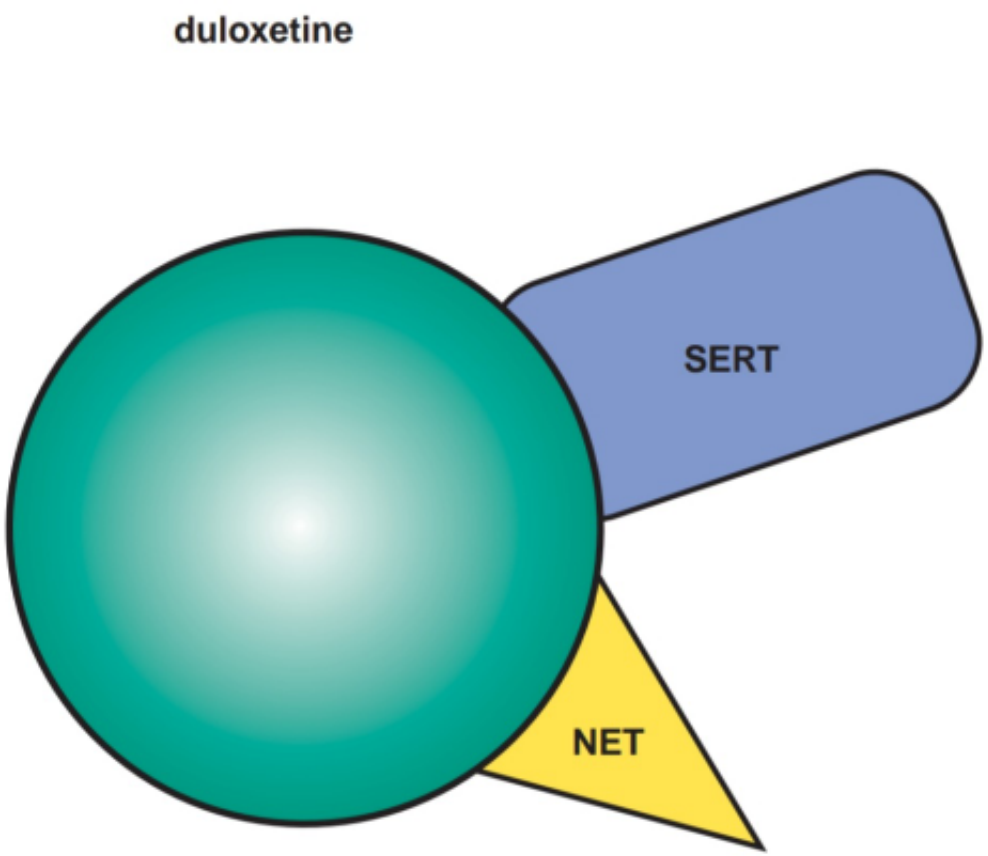


Figure 7-31. Duloxetine. Duloxetine inhibits reuptake of both serotonin (SRI) and norepinephrine (NRI). Its noradrenergic actions may contribute to efficacy for painful physical symptoms. Duloxetine is also an inhibitor of CYP 2D6.

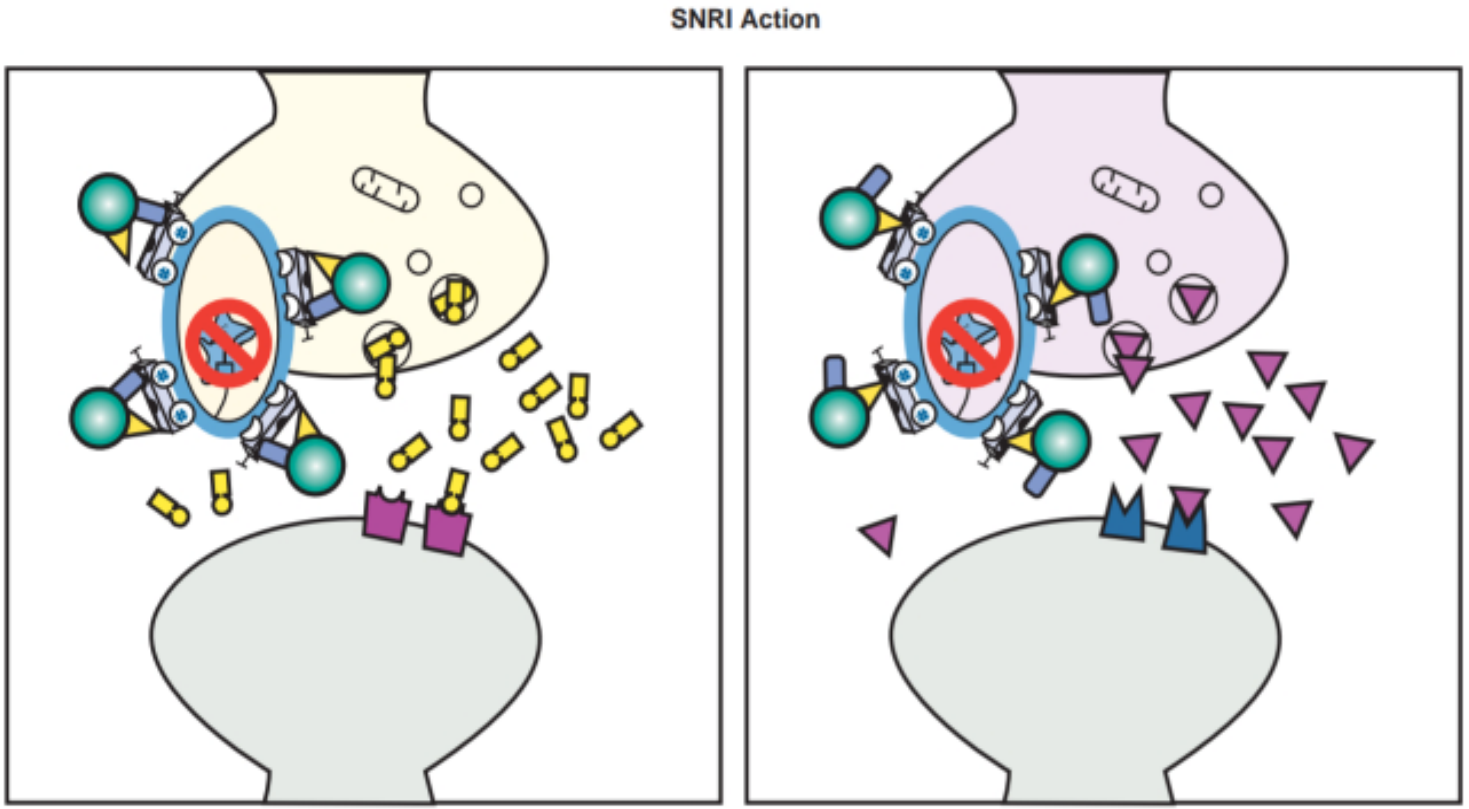


Figure 7-33. SNRI actions. In this figure, the dual actions of the serotonin–norepinephrine reuptake inhibitors (SNRIs) are shown. Both the serotonin reuptake inhibitor (SRI) portion of the SNRI molecule (left panel) and the norepinephrine reuptake inhibitor (NRI) portion of the SNRI molecule (right panel) are inserted into their respective reuptake pumps. Consequently, both pumps are blocked, and the drug mediates an antidepressant effect.

- Since DUL is extensively metabolized by the liver, any degree of hepatic insufficiency is a contraindication to treatment.

- The drug is generally safe and well tolerated across all approved indications in adults at doses ranging from 60 to 120 mg/day.
- The most commonly reported adverse reactions (≥5% and at least twice the incidence of placebo patients) were nausea, dry mouth, somnolence, constipation, decreased appetite, and hyperhidrosis, which occurred mainly in the early stages of the assumption and disappeared after the first weeks of treatment.

- In the longerterm therapy (for at least 6 months to 1 year), frequent treatment emergent adverse events observed in adult patients were palpitations, blurred vision, vertigo, weight gain/loss, chills/rigors, and pruritus.

- Regarding cardiovascular safety, a pooled analysis of clinical trials on MDD showed that DUL had modest effects on heart rate and blood pressure and no clinically meaningful effect on electrocardiogram (ECG) profiles; the cardiovascular effects of DUL were comparable with other antidepressants

- Overall, DUL is considered to be relatively safe in the case of overdose, but the possibility of fatal outcomes increases with concomitant assumption of multiple drugs.
- Symptoms of DUL overdose are somnolence, hypotension or hypertension, vomiting, tachycardia, syncope, serotonin syndrome, seizures, and coma.

- Duloxetine has not been recommended as a routine first-line acute treatment for major depression.

frontiers in Psychiatry

REVIEW
published: 25 October 2019
doi: 10.3389/fpsyt.2019.00772

Duloxetine in Psychiatric Disorders: Expansions Beyond Major Depression and Generalized Anxiety Disorder

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Antidepressants: Ranking of Side Effects

Class	Drug	Insomnia	Sedation	Headache	Tremor	Dry Mouth	Sweating	Nausea	Diarrhea	Constipation	Fatigue	Anxiety	Sexual Dysfunction
SSRI	Citalopram												
	Escitalopram												
	Fluoxetine												
	Fluvoxamine												
	Paroxetine												
	Sertraline												
SNRI	Duloxetine												
	Venlafaxine												
	Desvenlafaxine												
Others	Bupropion												
	Mirtazapine												

0-9% 10-29% ☒30 %

*Based on unadjusted rates from Product Monographs

Table 3 Recommendations for clinical dimensions of major depressive disorder

Dimension	First Intention	Second Intention
With marked anhedonia	SSRI or SNRI	α2-antagonist or agomelatine
With marked psychomotor retardation	SNRI, SSRI	Tricyclic or α2 antagonists
With marked sleep disturbances	SSRI or SNRI or α2-antagonist or agomelatine	Tricyclic ADT
With atypical features (hyperphagia, hypersomnia)	SSRI or SNRI	Tricyclic or agomelatine
With psychotic features	SNRI in monotherapy or SSRI in combination with an atypical antipsychotic	SSRI, tricyclic ADT or α2-antagonist, in monotherapy or in combination with AAP
With anxious features	SSRI or SNRI or α2 antagonist	Tricyclic ADT
With high suicidal risk	SSRI or SNRI or α2 antagonist	Tricyclic ADT or potentiation strategies with lithium or AAP

AAP Atypical Antipsychotic, *SNRI* Dual serotonin and norepinephrine reuptake inhibitors, *SSRI* Selective serotonin reuptake inhibitors

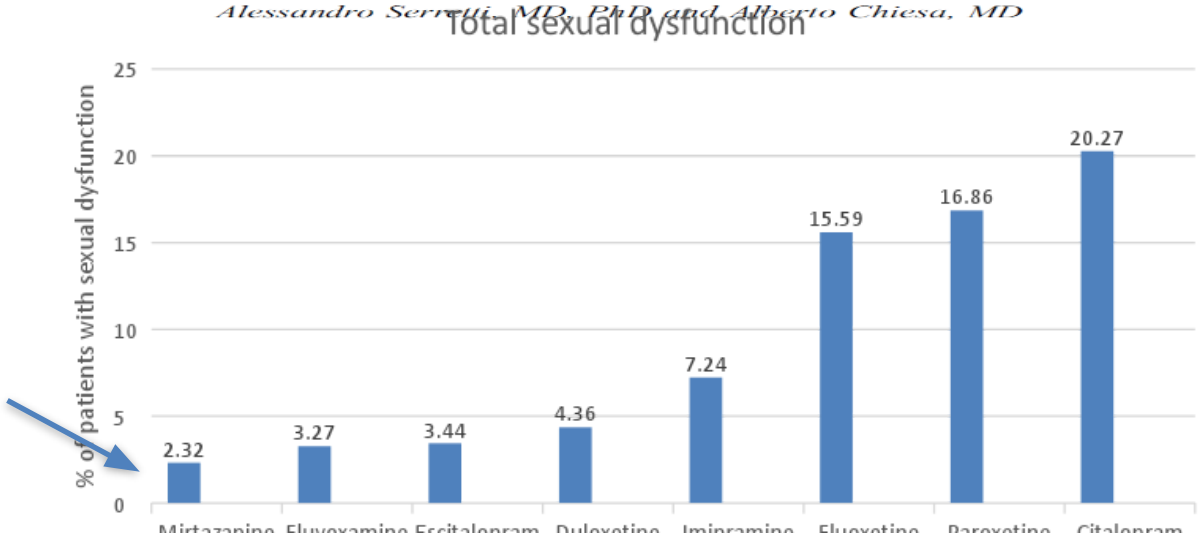
Less sexual dysfunction

Journal of Clinical Psychopharmacology REVIEW ARTICLE Italy

Treatment-Emergent Sexual Dysfunction Related to Antidepressants

A Meta-Analysis

Alessandro Serretti, MD, PhD and Alberto Chiesa, MD



Serretti A, Chiesa A. Treatment-emergent sexual dysfunction related to antidepressants: a meta-analysis. Journal of clinical psychopharmacology. 2009 Jun 1;29(3):259-66.

Bennabi et al. BMC Psychiatry (2019) 19:262
https://doi.org/10.1186/s12888-019-2237-x

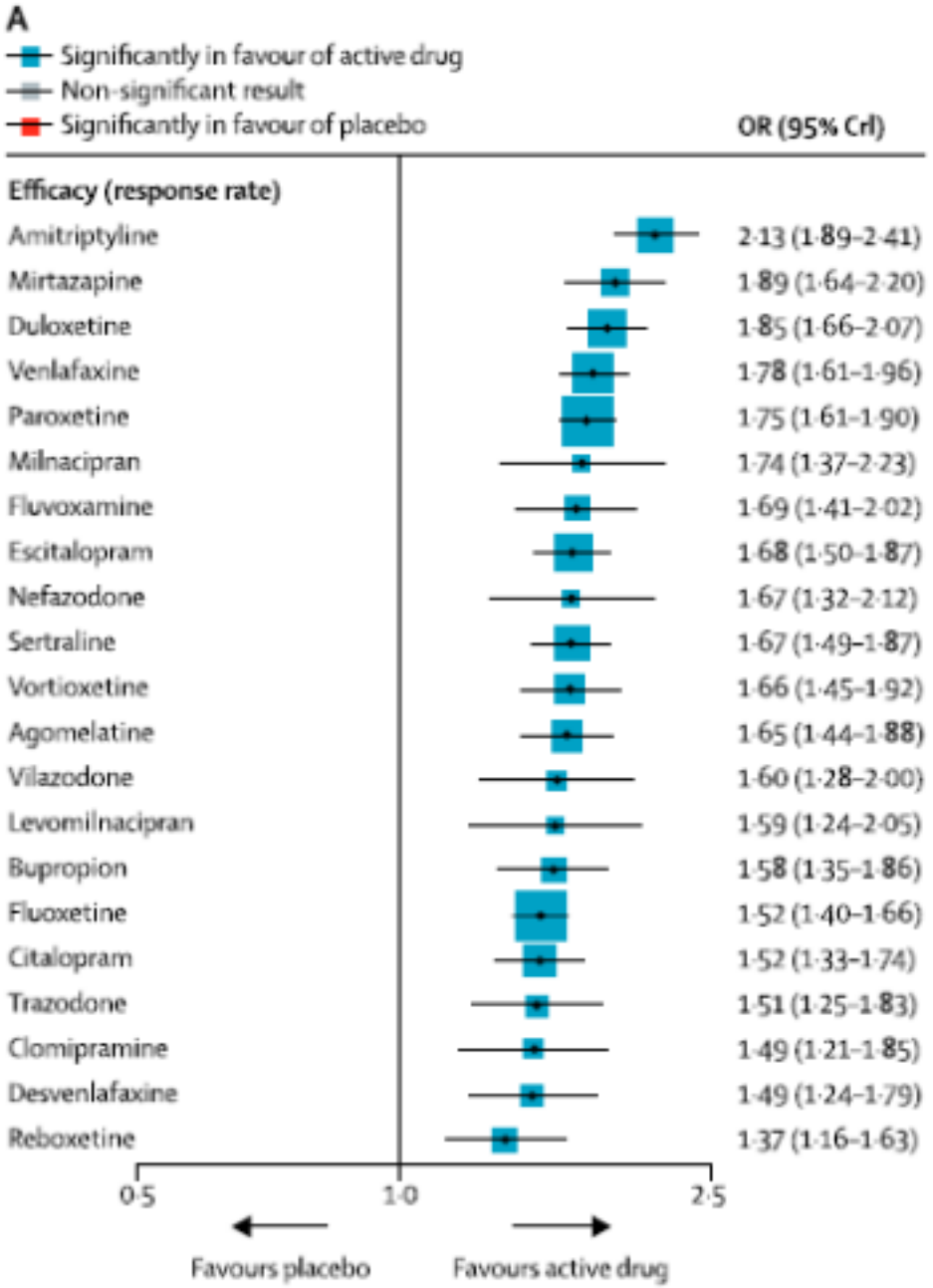
BMC Psychiatry

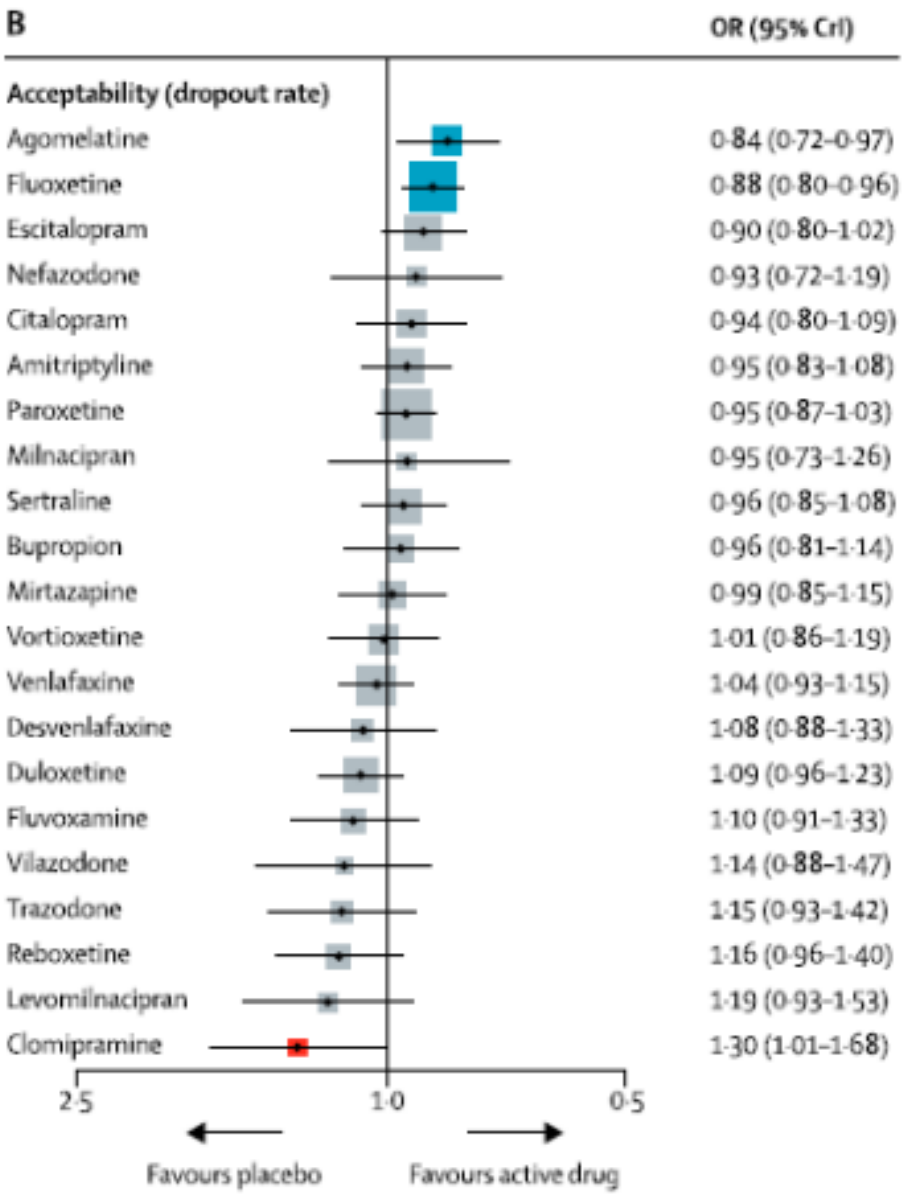
RESEARCH ARTICLE Open Access

Clinical guidelines for the management of treatment-resistant depression: French recommendations from experts, the French Association for Biological Psychiatry and Neuropsychopharmacology and the fondation FondaMental

D. Bennabi[1,18*], T. Charpeaud[2], A. Yrondi[3], J.-B. Genty[4], S. Destouches[4], S. Lancrenon[4], N. Alaïli[5], F. Bellivier[5], T. Bougerol[6], V. Camus[7], J.-M. Dorey[8,9,10], O. Doumy[11], F. Haesebaert[12], J. Holtzmann[6], C. Lançon[13], M. Lefebvre[12], F. Moliere[14], I. Nieto[5], C. Rabu[15], R. Richieri[13], L. Schmitt[3], F. Stephan[16], G. Vaiva[17], M. Walter[16], M. Leboyer[15], W. El-Hage[7], P.-M. Llorca[2], P. Courtet[14], B. Aouizerate[8,9,10] and E. Haffen[1]

FIGURE 3. Forest Plots of Network Meta-Analysis of All Trials for Efficacy (A) and Acceptability (B)





Antidepressants were compared with placebo, which was the reference compound. OR=odds ratio. CrI=credible interval. A color version of the figure, as originally published, appears in the online version of this article (focus.psychiatryonline.org).

FIGURE 4. Head-to-Head Comparisons for Efficacy and Acceptability of the 21 Antidepressants

Efficacy (response rate) | Comparison | Acceptability (dropout rate)

Agom	0.22* (0.55–0.92)	0.80* (0.54–1.15)	0.89† (0.66–1.18)	0.52* (0.42–0.77)	0.62† (0.47–0.82)	0.90* (0.70–1.27)	0.85‡ (0.68–1.05)	0.65† (0.52–0.87)	0.75* (0.52–1.05)	0.81* (0.63–1.05)	0.76* (0.44–1.44)	0.81* (0.65–1.00)	0.51* (0.35–0.80)	0.86* (0.66–1.13)	0.63* (0.48–0.88)	0.24† (0.58–0.91)	1.24‡ (0.75–2.15)
0.96* (0.76–1.24)	**Amit**	1.00‡ (0.78–1.58)	1.23* (0.96–1.64)	0.79† (0.60–1.05)	0.87† (0.66–1.15)	1.15* (1.05–1.26)	1.18† (0.99–1.47)	0.97* (0.76–1.24)	1.00‡ (0.84–1.65)	1.12* (0.89–1.42)	0.98‡ (0.62–1.55)	1.02† (0.95–1.34)	0.74† (0.53–1.13)	1.16* (0.97–1.47)	0.96* (0.70–1.30)	1.02* (0.83–1.26)	1.72† (1.00–3.02)
0.82† (0.59–1.30)	0.86‡ (0.62–1.31)	**Bupr**	1.11‡ (0.76–1.67)	0.71† (0.49–1.07)	0.78‡ (0.53–1.18)	1.23* (0.84–1.82)	1.07‡ (0.76–1.50)	0.87‡ (0.59–1.30)	1.00‡ (0.66–1.49)	1.01* (0.70–1.47)	0.89‡ (0.52–1.54)	1.02‡ (0.73–1.43)	0.67‡ (0.42–1.08)	1.03‡ (0.75–1.56)	0.87† (0.57–1.30)	0.92‡ (0.66–1.30)	1.55‡ (0.85–2.84)
1.13* (0.88–1.47)	1.17* (0.93–1.49)	1.30† (0.88–1.93)	**Cita**	0.66† (0.47–0.87)	0.70* (0.51–0.95)	1.09* (0.85–1.42)	0.99* (0.76–1.21)	0.78* (0.59–1.05)	0.89* (0.64–1.23)	0.91* (0.68–1.21)	0.79‡ (0.49–1.37)	0.94* (0.71–1.17)	0.60* (0.41–0.87)	0.97† (0.76–1.25)	0.77* (0.53–1.13)	0.83‡ (0.64–1.07)	1.40‡ (0.78–2.48)
1.20* (0.93–1.59)	1.24* (0.98–1.58)	1.37† (0.93–2.04)	1.06* (0.82–1.38)	**Clom**	1.10* (0.80–1.51)	1.31* (1.27–2.21)	1.49† (1.16–1.90)	1.22† (0.88–1.67)	1.46* (1.00–1.92)	1.41* (1.05–1.92)	1.24‡ (0.76–2.00)	1.42† (1.12–1.79)	0.96‡ (0.62–1.42)	1.53† (1.15–1.96)	1.21† (0.83–1.73)	1.39† (0.99–1.97)	2.20† (1.22–3.90)
1.09* (0.83–1.47)	1.10* (0.84–1.42)	1.21‡ (0.81–1.81)	0.97* (0.71–1.32)	0.88‡ (0.66–1.18)	**Dulo**	1.19* (1.10–2.03)	1.37* (1.06–1.73)	1.12* (0.80–1.53)	1.28‡ (0.91–1.75)	1.30* (0.96–1.77)	1.13‡ (0.69–1.85)	1.30* (1.02–1.61)	0.86‡ (0.57–1.29)	1.38† (1.04–1.80)	1.10† (0.76–1.55)	1.18† (0.92–1.49)	1.99† (1.13–3.57)
0.90* (0.73–1.14)	0.93* (0.74–1.17)	1.03‡ (0.70–1.51)	0.79* (0.62–0.97)	0.75* (0.58–0.97)	**Esci**	0.87* (0.70–1.09)	0.77* (0.59–0.96)	0.81* (0.59–1.11)	0.83* (0.63–1.08)	0.72‡ (0.45–1.18)	0.83† (0.60–1.05)	0.55* (0.37–0.81)	0.88* (0.63–1.12)	0.70* (0.48–1.00)	0.75* (0.60–0.94)	0.71‡ (0.51–1.25)	
1.20* (0.95–1.48)	1.25* (1.06–1.48)	1.38† (0.97–1.97)	1.06* (0.82–1.35)	1.00‡ (0.81–1.24)	1.14* (0.90–1.44)	1.34* (1.15–1.55)	**Fluo**	0.82* (0.66–1.04)	0.94* (0.72–1.20)	0.92* (0.72–1.16)	0.83‡ (0.54–1.30)	0.95* (0.83–1.09)	0.61* (0.44–0.90)	1.02† (0.84–1.21)	0.81* (0.60–1.09)	0.87† (0.70–1.08)	1.46‡ (0.85–3.53)
1.20* (0.93–1.61)	1.25* (0.99–1.59)	1.38† (0.93–2.07)	1.06* (0.82–1.38)	1.00‡ (0.76–1.32)	1.14* (0.85–1.54)	1.34* (1.03–1.75)	1.00* (0.80–1.25)	**Fluv**	1.14* (0.84–1.58)	1.16* (0.85–1.57)	1.03‡ (0.63–1.71)	1.15* (0.90–1.48)	0.77† (0.51–1.17)	1.23* (0.94–1.63)	0.99‡ (0.69–1.47)	1.06* (0.80–1.38)	1.78‡ (1.00–3.24)
1.07* (0.80–1.44)	1.11* (0.86–1.43)	1.25† (0.81–1.85)	0.94* (0.71–1.26)	0.89† (0.67–1.19)	1.01‡ (0.74–1.38)	1.19* (0.90–1.58)	0.89* (0.70–1.13)	0.89† (0.67–1.17)	**Miln**	1.03* (0.75–1.37)	0.82‡ (0.56–1.44)	1.02‡ (0.80–1.31)	0.67† (0.45–1.03)	1.08* (0.82–1.44)	0.86* (0.60–1.25)	0.93* (0.71–1.22)	1.56‡ (0.85–2.84)
0.93* (0.73–1.21)	0.97* (0.77–1.21)	1.07‡ (0.73–1.57)	0.82* (0.65–1.05)	0.78* (0.59–1.01)	0.88* (0.67–1.16)	1.04* (0.83–1.32)	0.78* (0.61–0.99)	0.78* (0.58–1.04)	0.87* (0.65–1.15)	**Mirt**	0.87† (0.55–1.41)	1.00* (0.82–1.23)	0.66* (0.45–0.96)	1.06* (0.84–1.35)	0.85* (0.62–1.12)	0.91* (0.73–1.13)	1.53‡ (0.89–2.72)
1.15* (0.96–1.76)	1.19* (0.80–1.78)	1.32† (0.80–2.20)	1.03‡ (0.67–1.54)	0.96‡ (0.63–1.45)	1.09‡ (0.71–1.68)	1.28* (0.86–1.94)	0.96‡ (0.66–1.40)	0.95‡ (0.63–1.45)	1.07‡ (0.70–1.67)	1.23* (0.82–1.85)	**Nefa**	1.05‡ (0.74–1.78)	0.75‡ (0.49–1.32)	1.23† (0.77–1.90)	0.98‡ (0.57–1.64)	1.04‡ (0.66–1.65)	1.76‡ (0.90–3.58)
1.01* (0.82–1.24)	1.05* (0.89–1.23)	1.16† (0.83–1.64)	0.89* (0.72–1.08)	0.84‡ (0.68–1.03)	0.95‡ (0.76–1.15)	1.13* (0.93–1.35)	0.84* (0.73–0.96)	0.84* (0.67–1.04)	0.94† (0.75–1.18)	1.02* (0.85–1.30)	0.88‡ (0.60–1.27)	**Paro**	0.58* (0.46–0.74)	1.08* (0.88–1.28)	0.85† (0.63–1.15)	0.91* (0.77–1.07)	1.53‡ (0.90–2.66)
1.44* (1.02–2.04)	1.50† (1.07–2.07)	1.65† (1.05–2.60)	1.27† (0.92–1.75)	1.20‡ (0.84–1.70)	1.36† (0.95–1.95)	1.60* (1.14–2.23)	1.20† (0.88–1.62)	1.20‡ (0.83–1.71)	1.35† (0.92–1.95)	1.56* (1.09–2.17)	1.25† (0.77–2.01)	1.43† (1.05–1.94)	**Rebo**	1.61† (1.09–2.34)	1.28† (0.82–2.01)	1.38† (0.94–1.99)	2.32† (1.24–4.41)
1.07* (0.85–1.37)	1.11* (0.93–1.35)	1.23‡ (0.86–1.79)	0.95† (0.76–1.18)	0.90‡ (0.71–1.13)	1.02‡ (0.75–1.37)	1.20* (0.97–1.48)	0.89‡ (0.70–1.09)	0.89† (0.70–1.13)	1.00‡ (0.77–1.30)	1.15* (0.93–1.43)	0.93‡ (0.63–1.37)	1.07* (0.90–1.26)	0.75† (0.54–1.04)	**Sert**	0.80* (0.58–1.11)	0.86* (0.70–1.06)	1.45‡ (0.84–2.54)
1.36* (0.99–1.87)	1.41† (1.06–1.86)	1.59† (1.04–2.39)	1.27* (0.88–1.65)	1.21‡ (0.83–1.64)	1.28† (0.93–1.76)	1.51* (1.12–2.04)	1.13† (0.82–1.46)	1.13‡ (0.82–1.55)	1.27* (0.91–1.76)	1.47* (1.09–1.94)	1.18† (0.75–1.84)	1.35* (1.04–1.75)	0.94† (0.66–1.33)	1.29† (0.95–1.67)	**Traz**	1.07† (0.77–1.47)	1.80‡ (0.98–3.18)
1.01* (0.82–1.26)	1.05* (0.82–1.27)	1.16† (0.82–1.65)	0.90* (0.72–1.13)	0.85† (0.67–1.06)	0.95‡ (0.72–1.21)	1.13* (0.93–1.37)	0.84† (0.73–0.97)	0.84* (0.66–1.07)	0.95* (0.73–1.23)	1.05* (0.85–1.33)	0.88‡ (0.59–1.30)	1.01† (0.86–1.17)	0.73† (0.53–0.97)	0.94* (0.78–1.13)	0.75† (0.57–0.98)	**Venl**	1.63† (1.11–2.86)
0.73† (0.42–1.26)	0.76† (0.44–1.29)	0.83‡ (0.45–1.54)	0.64† (0.37–1.11)	0.61† (0.35–1.05)	0.69‡ (0.40–1.20)	0.81† (0.47–1.39)	0.60† (0.38–1.02)	0.60† (0.36–1.05)	0.68† (0.39–1.20)	0.78† (0.45–1.36)	0.63† (0.33–1.18)	0.72† (0.43–1.22)	0.51† (0.28–0.92)	0.68† (0.39–1.16)	0.54† (0.30–0.95)	0.72* (0.43–1.19)	**Vort**

Drugs are reported in alphabetical order. Data are ORs (95% CrI) in the column-defining treatment compared with the row-defining treatment. For efficacy, ORs higher than 1 favour the column-defining treatment (ie, the first in alphabetical order). For acceptability, ORs lower than 1 favour the first drug in alphabetical order. To obtain ORs for comparisons in the opposite direction, reciprocals should be taken. Significant results are in bold and underscored. The certainty of the evidence (according to GRADE) was incorporated in this figure (appendix pp 231–65). OR=odds ratio. CrI=credible interval. Agom=agomelatine. Amit=amitriptyline. Bupr=bupropion. Cita=citalopram. Clom=clomipramine. Dulo=duloxetine. Esci=escitalopram. Fluo=fluoxetine. Fluv=fluvoxamine. Miln=milnacipran. Mirt=mirtazapine. Nefa=nefazodone. Paro=paroxetine. Rebo=reboxetine. Sert=sertraline. Traz=trazodone. Venl=venlafaxine. Vort=vortioxetine. *Moderate quality of evidence. †Low quality of evidence. ‡Very low quality of evidence. A color version of the figure, as originally published, appears in the online version of this article (focus.psychiatryonline.org).

Comparative Efficacy and Acceptability of 21 Antidepressant Drugs for the Acute Treatment of Adults With Major Depressive Disorder: A Systematic Review and Network Meta-Analysis

Andrea Cipriani, Toshi A Furukawa, Georgia Salanti, Anna Chaimani, Lauren Z Atkinson, Yusuke Ogawa, Stefan Leucht, Henricus G Ruhe, Erick H Turner, Julian P T Higgins, Matthias Egger, Nozomi Takeshima, Yu Hayasaka, Hissei Imai, Kiyomi Shinohara, Aran Tajika, John P A Ioannidis, John R Geddes