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Standardisation framework for the Maudsley staging method for treatment resistance in depression

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Additional File 1

Generic Name	(UK, unless stated) In weeks on a					Drug ior a	taken t least:	Minimum Dose*	Maximum Dose*	ē	
			dose equal or greater than the minimum dose	Tolerability ^a	Adherence ^b	Response ^c	4 weeks	6 weeks 8 weeks	(mg/day unless stated)	Equal or management of the control o	Equal or greater
	ISED ANTIDEPRESSANT										
	euptake Inhibitors (SSRI)		-		1		1 1				1 1
Citalopram	Cipramil								20	40	
Escitalopram	Cipralex								10	20	
Fluoxetine	Prozac								20	60	
Fluvoxamine	Faverin								100	300	
Paroxetine	Seroxat								20	50	
Sertraline	Lustral								50	200	
Tricyclic Antidepressa	ants (TCA)										
Amitriptyline	Tryptizol								125	200	
Amoxapine									200	300/600 ^H	
Clomipramine	Anafranil								125	250	
Desipramine									125	250	
Dosulepin / Dothiepin	Prothiaden								125	225	
Doxepin	Sinepin								125	300	
Imipramine	Tofranil								125	300	
Lofepramine	Gamanil / Lomont								140	210	
Nortriptyline	Allegron								75	150	
Protriptyline									30	60	
Tianeptine	Stablon (US)								25	50	
Trimipramine	Surmontil								125	300	
Monoamine Oxidase I	nhibitors (MAOI)	1	<u> </u>		<u>i</u>	<u> </u>		<u> </u>	ı İ	i	<u> </u>
Isocarboxazid	. ,								30	60	
Phenelzine	Nardil								45	60/90 ^H	
Tranylcypromine	Parnate								20	-	
Moclobemide	Manerix								300	600	
Selegeline	Eldepryl/Zelapar								6	12	

Generic Name	Brand Names Do (UK, unless stated)			Tolerability & Response	1	Drug tak or at lea	en Minimum st: Dose	Maximum Dose*	ater
		In weeks on a dose equal or greater than the minimum dose	Tolerability ^a	Adherence ^b	Response ^c	4 weeks 6 weeks	(mg/day unless stated)	Dose* (mg/day unless stated))	Equal or greater
Tetracyclic Antidep	ressants (and related)								
Maprotiline	Ludiomil						75	150/225 ^H	
Mianserin	Bolvidon, Norval						30	90	
Mirtazepine	Zispin						30	45	
Nefazadone	Serzone						200	600	
Trazodone	Molipaxin						150	600	
Serotonin-Noradren	naline Reuptake Inhibitors (SNRI)								
Desvenlafaxine	Pristiq (US)						50	400	
Duloxetine	Cymbalta						60	120	
Levomilnacipran	Fetzima (US)						40	120	
Milnacipran	Ixel / Savella (EU / US)						100	200	
Venlafaxine	Efexor						75	375	
Serotonin Modulato	ors & Stimulators								
Vilazodone	Viibryd (US)						10	40	
Vortioxetine	Brintellix						10	20	
Noradrenaline Reup	otake Inhibitors (NRI)	,		,	,	' '	'	,	
Reboxetine	Edronax						8	12	
Viloxazine	Vivalan (US)						200	600	
Noradrenaline &Doj	pamine Reuptake Inhibitors (NDRI)							•	
Bupropion	Zyban						300	400	
Melatonin Agonists	•					• • •	·		
Agomelatine	Valdoxan						25	50	
Other		, ,		•					
Flupentixol	Fluanxol						1	3	

Generic Name	Brand Names (UK, unless stated)	(UK, unless stated) In weeks on a					Drug taken for at least:	Minimum Dose	eater S	aximum Dose*	eater
			dose equal or greater than the minimum dose	Tolerability ^a	Adherence ^b	Response ^c	4 weeks 6 weeks 8 weeks	(mg/day unless stated)	ō	mg/day unless stated)	Equal or gr Augmentat

SECTION B: RECOGNISED AUGMENTATION THERAPIES[†]

First and Second Line Therapies

AripiprazoleAbilifyImage: Composition of the compositio		
Quetiapine Seroquel 150 Risperidone Risperdal 0.5 Lamotrigine Lamictal 200 Lithium Camcolit / Priadel 0.4mr Liothyronine; tri- Textravia 200cc	20	20
Risperidone Risperdal 0.5 Lamotrigine Lamictal 200 Lithium Camcolit / Priadel 0.4mr Liothyronine; tri- Tortrovie 200cm	-	-
Lamotrigine Lamictal 200 Lithium Camcolit / Priadel 0.4mr Liothyronine; tri-	30	300
Lithium Camcolit / Priadel 0.4mr Liothyronine; tri-	3	3
Liothyronine; tri-	40	400
Liothyronine; tri- iodothyronine (T3) Tertroxin 20ug	nmol/l 1.	1.2mmol/l
	g 50	50ug
Buspirone Buspar 15	60	30

Third Line Therapies

Amantadine	Symmetrel	-	300
Cabergoline	Dostinex / Cabaser	2	2
d-cycloserine		1000	1000
Dexamethasone		3	4
Dexamphetamine	Dexedrine	2.5	40
Hyoscine	Buscopan / Kwells	-	-
Ketoconazole	Nizoral	400	800
Mecamylamine		-	10
Methylphenidate	Ritalin/Concerta	20	40
Modafinil	Provigil	100	400
Nemifitide		40 SC	240 SC
Oestrogen		-	-
Omega 3 triglycerides		1000	2000
Pindolol	Visken	7.5	15
Pramipexole	Mirapexin	0.125	5

Generic Name	Brand Names (UK, unless stated)	Dose	Duration In weeks on a		Tolerability & Response		Drug taken or at least:		Maximum Dose*	eater ion
			dose equal or greater than the minimum dose	Tolerability ^a	Adherence ^b	Response ^c	4 weeks 6 weeks 8 weeks	(mg/day unless stated)	mg/day unless stated))	Equal or gr Augmentati

Third line Therapies (continued)

Riluzole	Rilutek			100	200
S-adenosyl-L- methionine				400 IM	1200PO
Testosterone				-	-
Tryptophan				6000	9000
Zinc				25	25
Ziprasidone	Geodon / Zeldox			-	160

Generic Name	Brand Names (UK, unless stated)	Dose	Duration In weeks on a		Tolerability & Response			g take at leas	n Minimum st: Dose	Maximum Dose*	ater
			dose equal or greater than the minimum dose	Tolerability ^a	Adherence ^b	Response ^c	4 weeks	6 weeks	(mg/day unless stated))	o (mg/day unless stated)	Equal or greater
OPTIONAL SECTION	C: OTHER ANTIPSYCHOT	ICS AND MOC	D STABILISERS								
Atypical Antipsychot	ics										
Amisulpiride	Solian								-	-	
Asenapine	Sycrest									20	
Clozapine	Clozaril								-	-	
lloperidone	Fanapt (US / EU)								2	24	
Lurasidone	Latuda								40	80	
Melperone									-	-	
Paliperidone	Invega								-	-	
Sertindole	Serdolect								-	-	
Zotepine	Zoleptil								-	-	
Typical Antipsychotic	cs				. 1	i			i	i	
Chlorpromazine	Largactil	T							-	-	
Fluphenazine	Modecate	1							-	-	
Haloperidol	Haldol								-	-	
Levomepromazine	Nozinan								-	-	
Pericyazine	Neulactil								-	-	
Perphenazine	Fentazine								-	-	
Pimozide	Orap								-	-	
Prochlorperazine	Prochlorperazine								-	-	
Promazine	Sparine								-	-	
Sulpiride	Sulpor/dolmatil								-	-	
Thioridazine	Melleril								-	-	
Trifluoperazine	Stelazine								-	-	
Zuclopenthixol	Clopixol								-	-	
Anticonvulsants	. •				·	i			i	i	
Carbamazepine	Tegretol	T							600	1600	
Gabapentin	Neurontin								-	2400	
Levetiracetam	Keppra								-	4000	
Oxcarbazepine	Trileptal								300	3000	
Phenytoin									300	400	\top

Generic Name	Brand Names (UK, unless stated)	Duration In weeks on a	Tolerability & Response				g tak It lea	en Minimum st: Dose	Maximum Dose*	greater tation
		dose equal or greater than the minimum dose	Tolerability ^a	Adherence ^b	Response ^c	4 weeks	6 weeks	(mg/day unless stated)	o (mg/day o unless stated)	Equal or great Augmentation
Anticonvulsants (conti	inued)	•		•	•			•		
Pregabilin	Lyrica							300	600	
Semisodium Valproate	Depakote / Convulex							-	-	
Sodium Valproate	Epilim							-	-	
Tiagabine	Gabitril							5	45	
Topiramate	Topamax							-	300	
Zonisamide	Zonegran							100	500	

OPTIONAL SECTION D: OTHER REPORTED TREATMENTS FOR DEPRESSION AND RELATED MOOD DISORDERS\$

Allopurinol	Zyloric			-	-	
Amineptine				-	-	
Armodafinil	Nuvigil				150	
Atamoxetine	Strattera			40	120	
Blonanserin	lonasen			-	-	
Bromocriptine				-	-	
Buprenorphine	Subutex /			-	-	
Clonidine	Catapres / Dixarit			-	-	
Clotiapine				-	-	
Dexmethylphenidate	Focalin/ Attenade (US)			5	30	
Etoperidone				-	-	
Focalin/ Attenade (US)	Dexmethylphenidate			5	30	
Hydroxyzine	Atarax / Ucerax			-	-	
Indalpine				-	-	
Inositol	Hexopal			-	12000	
Ketanserin				-	-	
Ketamine				0.5mg/ kg IV	-	
Melatonin				-	-	
Metyrapone	Metopirone			1000	-	
Mifepristone	Mifegyne			-	-	
Mosopramine				-	-	

Nimodipine	Nimotop				-	180	

Generic Name	Brand Names (UK, unless stated)	Dose	Duration Tolerability & Respon In weeks on a		Tolerability & Response			g tak at lea	en Minimum st: Dose	ater	Maximum Dose*	ater	_ u
			dose equal or greater that the minimum dose	Tolerability ^a	Adherence ^b	Response ^c	4 weeks	6 weeks	(mg/day unless stated)	Equal or greater	(mg/day unless stated)	Equal or greater	Augmentation
Other reported trea	tments (continued)		·		i		<u> </u>		·				
Nomifensine									-		-		
Orphenadrine	Biorphen / Disipal								-		=		
Pergolide									-		-		
Perospirone	Lullan								-		-		
Pipradrol									-		-		
Prazosin	Hypovase								-		-		
Propranolol	Inderal								-		-		
Pyrovalerone									-		-		
Rasagiline	Azilect								-		-		
Remoxipride									-		-		
Ritanserin	Tisterton (US)								-		-		
Ropinirole	Adartrel / Requip								-		-		
Rotigotine	Neupro								-		-		
Seteperone									-		-		
Setiptiline									-		-		
St John's Wort									-		-		
Tamoxifen									10		140		
Tandospirone									-		-		
Teniloxazine									-		-		
Thyroxine (T4)	Eltroxine								-		-		
Tofenacin									-		-	П	
Yohimbine									-		30	П	
Zimelidine									-		-		

ECT					-	-	
rTMS					-	-	
VNS					-	-	
Bright Light					-	-	

tDCS						

Notes: The MTI is developed primarily for treatment resistant depression in "unipolar" depression. For purposes of the Maudsley Staging Method, treatments in Section A count towards antidepressant treatments and those in Section B towards augmentation treatments. Where two antidepressants are used in combination, count both as antidepressant trials under Section A. Although some combinations of antidepressants are more frequently used (e.g. venlafaxine plus mirtazapine, MAOI + TCA, SSRI + NRI) no specific weighting for these combinations is used for rating the Maudsley Staging Method. Section C (Other Antipsychotics/Mood Stabilisers) and Sections D (Other Reported Treatments For Mood Disorders) are optional and included for purposes of clinical utility. The list of drugs is deliberately inclusive so that all previous treatments can be assessed, and thus includes many that are not licenced or recommended for the treatment of depression; in addition, some have now been withdrawn in some countries. Inclusion does not indicate evidence of efficacy or a recommendation to prescribe. Prescribers should always check doses of treatments with which they are not familiar. The MTI will be updated in line with the Maudsley Prescribing Guidelines to maintain evidence base for inclusion in Sections A and B, and for new additions to Sections C and D: please contact authors for updated versions

*Dose ranges are taken from the following sources in order of preference: Maudsley Prescribing Guidelines, British National Formulary and manufacturer's SPC. Dose ranges may refer to other indications where not well established for depression. Plasma levels are used for lithium in preference to dosage. Minimum or maximum undefined where left empty.

- † Included as first, second or third line augmentation strategies for TRD within Maudsley Prescribing Guidelines (Taylor et al 2015)
- ‡ Not currently included in Maudsley Prescribing Guidelines; therefore, not scored for purposes of the Maudsley Staging Method
- a enter free text, or use Clinical Global Impression Treatment Related Adverse Effects (AEs) Index: 1, no AEs; 2, AEs do not significantly interfere with patient's functioning; 3, AEs significantly interfere with patient's functioning; 4, AEs outweigh therapeutic effect.
- b enter free text, or estimate percentage of doses that were taken. To be defined as an adequate trial adherence of at least 75% is needed.
- c enter free text, or use response based on Clinical Global Impression Scale: 1, very much improved; 2, much improved; 3, minimally improved; 4, no change; 5, minimally worse; 6, much worse; or 7, very much worse.
- H dose in hospitalised patients; for consistency use the lower dose to determine whether maximum dose has been used
- PO oral: IM intramuscular: IV intravenous.

Physical treatment abbreviations: ECT – electroconvulsive therapy; rTMS – repetitive transcranial magnetic stimulation; VNS – vagus nerve stimulation; tDCS – transcranial direct current stimulation. Under dose and duration, a description of relevant parameters for each modality of treatment should be recorded, including where appropriate: bilateral v unilateral; frequency and total number of applications; intensity (e.g. electricity dose or length of seizure); and brain area targeted. No minimum criteria are stated due to current absence of sufficient evidence.

CGI scale based on Guy W, editor. ECDEU Assessment Manual for Psychopharmacology, 1976. Rockville, MD, U.S. Department of Health, Education, and Welfare