


[Home](#) > [Journal](#) > [Social Sciences & Humanities](#) > [PSYCH](#)
[Indexing](#) | [View Papers](#) | [Aims & Scope](#) | [Editorial Board](#) | [Guideline](#) | [Article Processing Charges](#)
[PSYCH](#) > Vol.3 No.10, October 2012



A Dimensional Approach to Measuring Antidepressant Response: Implications for Agomelatine

PDF (Size: 140KB) PP. 864-869 DOI: 10.4236/psych.2012.310130

Author(s)

Sidney H. Kennedy, Anna Cyriac

ABSTRACT

Current antidepressant treatments for Major Depressive Disorder (MDD) have limited efficacy and effectiveness. While measurement of response and remission is typically based on overall symptom reduction, the utilization of a dimensional approach, involving mood, cognitive and neurovegetative symptoms, may be more effective in predicting response to different antidepressant classes. In addition to these dimensions, evaluation of function is increasingly recognized as an important patient indicator of antidepressant efficacy. This paper reviews the efficacy of second generation antidepressant classes across the proposed symptom dimensions, and explores the potential benefits of agomelatine. While further research is required, agomelatine generally performed well in the mood dimension including measures of depressed mood, anxiety and anhedonia without inducing emotional blunting. Improvements in daytime alertness and clear thinking, combined with measures of subjective and objective sleep differentiate agomelatine from other currently available antidepressants, and likely contribute to favourable functional outcomes.

KEYWORDS

Symptom Dimensions; Major Depression; Antidepressants

Cite this paper

Kennedy, S. & Cyriac, A. (2012). A Dimensional Approach to Measuring Antidepressant Response: Implications for Agomelatine. *Psychology*, 3, 864-869. doi: 10.4236/psych.2012.310130.

References

- [1] Agosti, V., Stewart, J.W. (1998). Social functioning and residual symptomatology among outpatients who responded to treatment and recovered from major depression. *Journal of Affective Disorders*, 47, 207-210. doi:10.1016/S0165-0327(97)00119-5
- [2] Amado-Boccaro, I., Gougoulis, N., Poirier, L.M., Galinowski, A., & Loo, H. (1992). Effects of antidepressants on cognitive functions: A review. *Neuroscience & Biobehavioral Reviews*, 19, 479-493. doi:10.1016/0149-7634(94)00068-C
- [3] Audinot, V., Mailliet, F., Lahaye-Brasseur, C., Bonnaud, A., Le Gall, A., Amosse, C., Dromaint, S., Rodriguez, M., Nagel, N., Galizzi, J. P., Malpoux, B., Guillaumet, G., Lesieur, D., Lefoulon, F., Renard, P., Delagrangue, P., & Boutin, J.A. (2003). New selective ligands of human cloned melatonin MT1 and MT2 receptors. *Naunyn-Schmiedeberg's Arch Pharmacol*, 367, 553-561. doi:10.1007/s00210-003-0751-2
- [4] Austin, M., Mitchell, P., & Goodwin, G. (2001). Cognitive deficits in depression: Possible implications for functional neuropathology. *British Journal of Psychiatry*, 178, 200-206. doi:10.1192/bjp.178.3.200
- [5] Blier, P., & Blondeau, C. (2011). Neurobiological bases and clinical aspects of the use of aripiprazole in treatment-resistant major depressive disorder. *Journal of Affective Disorders*, 128, S3-S10. doi:10.1016/S0165-0327(11)70003-9
- [6] Bondareff, W., Alpert, M., Friedhoff, A., Richter, E., Clary, C., & Batzar, E. (2000). Comparison of

[Open Special Issues](#)
[Published Special Issues](#)
[Special Issues Guideline](#)
[PSYCH Subscription](#)
[Most popular papers in PSYCH](#)
[About PSYCH News](#)
[Frequently Asked Questions](#)
[Recommend to Peers](#)
[Recommend to Library](#)
[Contact Us](#)

Downloads:	247,323
------------	---------

Visits:	543,122
---------	---------

[Sponsors >>](#)

sertraline and nortriptyline in the treatment of major depressive disorder in late life. *American Journal of Psychiatry*, 157, 729-36. doi:10.1176/appi.ajp.157.5.729

- [7] Brodbeck, J., Abbott, R.A., Goodyer, I.M., & Croudace, T.J. (2011). General and specific components of depression and anxiety in an adolescent population. *BMC Psychiatry*, 11, 191. doi:10.1186/1471-244X-11-191
- [8] Cipriani, A., La Ferla, T., Furukawa, T.A., Signoretti, A., Nakagawa, A., Churchill, R., & Barbui, C. (2010). Sertraline versus other anti-depressive agents for depression. *Cochrane Database of Systematic Reviews*, 1.
- [9] Conradi, H. J., Ormel, J., & de Jonge, P. (2010). Presence of individual (residual) symptoms during depressive episodes and periods of remission: A 3-year prospective study. *Psychological Medicine*, 8, 1-10.
- [10] Corruble, E., Belaidi, C., & Goodwin, G. (2011). P02-24-Agomelatine versus escitalopram in major depressive disorders: A randomized double-blind, long term study focusing on sleep satisfaction and emotional blunting. *European Psychiatry*, 26, 619. doi:10.1016/S0924-9338(11)72325-2
- [11] Cunningham, L., Borison, R., Carman, J., Chouinard, G., Crowder, J.E., Diamond, B.I., Fischer, D.E., & Hearst, E. (1994). A comparison of venlafaxine, trazodone, and placebo in major depression. *Journal of Clinical Psychopharmacology*, 15, 30-40.
- [12] Di Giannantonio, M., Di Iorio, G., Guglielmo, R., De Berardis, D., Conti, C.M., Acciavatti, T., Cornelio, M., & Martinotti, G. (2011). Major depressive disorder, anhedonia and agomelatine: An open-label study. *Journal of Biological Regulators & Homeostatic Agents*, 25, 109-114
- [13] Demyttenaere, K. (2011). Agomelatine: A narrative review. *European Neuropsychopharmacology*, 21, S703-S709. doi:10.1016/j.euroneuro.2011.07.004
- [14] Doraswaimy, P., Krishnan, K., Oxman, T., Jenkyn, L.R., Coffey, D.J., Burt, T., & Clary, C.M. (2003). Does antidepressant therapy improve cognition in elderly depressed patients? *Journals of Gerontology*, 12, 1137-1144.
- [15] Dunner, D.L., & Dunbar, G.C. (1992). Optimal dose for paroxetine. *Journal of Clinical Psychiatry*, 53, 21-26.
- [16] Farabaugh, A.H., Bitran, S., Witte, J., Alpert, J., Chuzi, S., Clain, A.J., & Papakostas, G. I. (2010). Anxious depression and early changes in the HAMD-17 anxiety-somatization factor items and antidepressant treatment outcome. *International Clinical Psychopharmacology*, 25, 214-217. doi:10.1097/YIC.0b013e328339fbbd
- [17] Fava, M., Rush, A.J., Alpert, J.E., Balasubramani, G.K., Wisniewski, S.R., Carmin, C.N., Biggs, M.M., Zisook, S., Leuchter, A., Howland, R., Warden, D., & Trivedi, M.H. (2008). Difference in treatment outcome in outpatients with anxious versus nonanxious depression: A STAR*D report. *American Journal of Psychiatry*, 165, 342-351. doi:10.1176/appi.ajp.2007.06111868
- [18] Fekadu, A., Wooderson, S. C., Rane, L. J., Markopoulou, K., Poon, L., Cleare, A. J. (2011). Long-term impact of residual symptoms in treatment-resistant depression. *Canadian Journal of Psychiatry*, 56, 549-557.
- [19] Fossati, P., Amar, G., Raoux, N., Ergis, A., & Alligaire, J. (1999). Executive functioning and verbal memory in young patients with unipolar depression and schizophrenia. *Psychiatry Research*, 89, 171-187. doi:10.1016/S0165-1781(99)00110-9
- [20] Furlan, P., Kallan, M., Ten, T., Pollock, B. G., Katz, I., & Lucki, I. (2001). Cognitive and psychomotor effects of paroxetine and sertraline on healthy elderly volunteers. *American Journal of Geriatric Psychiatry*, 9, 429-437.
- [21] Gualtieri, C., & John, L. (2007). Bupropion normalizes cognitive performance in patients with depression. *Medscape General Medicine*, 9, 22.
- [22] Hale, A., Corral, R. M., Mencacci, C., Ruiz, J. S., Severo, C. A., & Gentil, V. (2010). Superior antidepressant efficacy results of agomelatine versus fluoxetine in severe MDD patients: A randomized, double-blind study. *International Clinical Psychopharmacology*, 25, 305-314. doi:10.1097/YIC.0b013e32833a86aa
- [23] Hamilton, M. (1959). The assessment of anxiety states by rating. *British Journal of Medical Psychology*, 32, 50-55. doi:10.1111/j.2044-8341.1959.tb00467.x

- [24] Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery & Psychiatry*, 23, 56-62. doi:10.1136/jnnp.23.1.56
- [25] Harmer, C.J., Shelley, N.C., Cowen, P.J., & Goodwin, G.M. (2004). Increased positive versus negative affective perception and memory in healthy volunteers following selective serotonin and norepinephrine reuptake inhibition. *American Journal of Psychiatry*, 7, 1256-1263. doi:10.1176/appi.ajp.161.7.1256
- [26] Harmer, C.J., de Bodinat, C., Dawson, G.R., Dourish, C.T., Waldenmaier, L., Adams, S., Cowen, P.J., & Goodwin, G.M. (2011). Agomelatine facilitates positive versus negative affective processing in healthy volunteer models. *Journal of Psychopharmacology*, 25, 1159-1167. doi:10.1177/0269881110376689
- [27] Joyce, P.R., Mulder, R.T., McKenzie, J.M., Luty, S.E., & Cloninger, C.R. (2004). Atypical depression, atypical temperament and a differential antidepressant response to fluoxetine and nortriptyline. *Depression and Anxiety*, 19, 180-186. doi:10.1002/da.20001
- [28] Kasper, S., Hajak, G., Wulff, K., Hoogendijk, W.J., Montejo, A.L., Smeraldi, E., Rybakowski, J.K., Quersalva, M.A., Wirz-Justice, A.M., Picarel-Blanchot, F., & Baylé, F.J. (2010). Efficacy of the novel antidepressant agomelatine on the circadian rest-activity cycle and depressive and anxiety symptoms in patients with major depressive disorder: A randomized, double-blind comparison with sertraline. *Journal of Clinical Psychiatry*, 71, 109-120. doi:10.4088/JCP.09m05347blu
- [29] Keller, M. B., Lavori, P. W., Friedman, B., Nielsen, E., Endicott, J. et al. (1987). The longitudinal follow-up evaluation: A comprehensive method for assessing outcome in prospective longitudinal studies. *Archives of General Psychiatry*, 44, 540-548. doi:10.1001/archpsyc.1987.01800180050009
- [30] Keltner, N. L., McAfee, K. M., & Taylor, C. L. (2002). Mechanisms and treatments of SSRI induced sexual dysfunction. *Perspectives in Psychiatric Care*, 38, 111-116. doi:10.1111/j.1744-6163.2002.tb00665.x
- [31] Kendell, R. E. (1975). *The role of diagnosis in psychiatry*. Oxford: Blackwell Scientific Publications.
- [32] Kennedy, S. H., & Emsley, R. (2006). Placebo-controlled trial of agomelatine in the treatment of major depressive disorder. *European Neuropsychopharmacology*, 16, 93-100. doi:10.1016/j.euroneuro.2005.09.002
- [33] Kennedy, S.H., Rizvi, S., Fulton, K., & Rasmussen, J. (2008). A double-blind comparison of sexual functioning, antidepressant efficacy, and tolerability between agomelatine and venlafaxine XR. *Journal of Clinical Psychopharmacology*, 28, 329-333. doi:10.1097/JCP.0b013e318172b48c
- [34] Kennedy, S.H., & Rizvi, S.J. (2009). Emerging drugs for major depressive disorder. *Expert Opinion on Emerging Drugs*, 14, 439-453. doi:10.1517/14728210903107751
- [35] Kennedy, S.H., & Rizvi, S.J. (2010). Agomelatine in the treatment of major depressive disorder: Potential for clinical effectiveness. *CNS Drugs*, 24, 479-499. doi:10.2165/11534420-000000000-00000
- [36] Korszun, A., Moskvina, V., Brewster, S., Craddock, N., Ferrero, F., Gill, M., Jones, I.R., Jones, L.A., Maier, W., Mors, O., Owen, M.J., Preisig, M., Reich, T., Rietschel, M., Farmer, A., & McGuffin, P. (2004). Familiality of symptom dimensions in depression. *Archives of General Psychiatry*, 61, 468-474. doi:10.1001/archpsyc.61.5.468
- [37] Laux, G. (2011). P02-52—The antidepressant efficacy of agomelatine in daily practice: Results of the non-interventional study VIVALDI. *European Psychiatry*, 26, 647. doi:10.1016/S0924-9338(11)72353-7
- [38] Lemoine, P., Guilleminault, C., & Alvarez, E. (2007). Improvement in subjective sleep in major depressive disorder with a novel antidepressant, agomelatine: Randomized, double-blind comparison with venlafaxine. *Journal of Clinical Psychiatry*, 68, 1723-1732. doi:10.4088/JCP.v68n1112
- [39] Liemburg, E., Aleman, A., Bous, J., Hollander, K., & Knegtering, H. (2011). An open randomized pilot trial on the differential effects of aripiprazole versus risperidone on anhedonia and subjective well-being. *Pharmacopsychiatry*, 44, 109-113. doi:10.1055/s-0031-1271688
- [40] Loo, H., Hale, A., & D'haenen, H. (2002). Determination of the dose of agomelatine, a melatonergic agonist and selective 5-HT(2C) antagonist, in the treatment of major depressive disorder: A placebo-controlled dose range study. *International Clinical Psychopharmacology*, 17, 239-247. doi:10.1097/00004850-200209000-00004

- [41] McCabe, C., Mishor, Z., Cowen, P.J., & Harmer, C.J. (2010). Diminished neural processing of aversive and rewarding stimuli during selective serotonin reuptake inhibitor treatment. *Biological Psychiatry*, 67, 439-445. doi:10.1016/j.biopsych.2009.11.001
- [42] McKnight, P.E., & Kashdan, T.B. (2009). The importance of functional impairment to mental health outcomes: A case for reassessing our goals in depression treatment research. *Clinical Psychology Review*, 29, 243-259. doi:10.1016/j.cpr.2009.01.005
- [43] McMakin, D.L., Olino, T.M., Porta, G., Dietz, L.J., Emslie, G., Clarke, G., Wagner, K.D., Asarnow, J.R., Ryan, N.D., Birmaher, B., Sham-seddeen, W., Mayes, T., Kennard, B., Spirito, A., Keller, M., Lynch, F.L., Dickerson, J.F., & Brent, D.A. (2012). Anhedonia predicts poorer recovery among youth with selective serotonin reuptake inhibitor treatment resistant-depression. *Journal of the American Academy of Child and Adolescent Psychiatry*, 51, 404-411. doi:10.1016/j.jaac.2012.01.011
- [44] Mendels, J., Johnston, R., Mattes, J., & Riesenberg, R. (1993). Efficacy and safety of b.i.d. doses of venlafaxine in a dose-response study. *Psychopharmacology Bulletin*, 29, 169-174.
- [45] Millan, M.J., Gobert, A., Lejeune, F., Dekeyne, A., Newman-Tancredi, A., Pasteau, V., Rivet, J.M., & Cussac, D. (2003). The novel melatonin agonist agomelatine (S20098) is an antagonist at 5-hydroxytryptamine_{2C} receptors, blockade of which enhances the activity of frontocortical dopaminergic and adrenergic pathways. *Journal of Pharmacology and Experimental Therapeutics*, 306, 954-964. doi:10.1124/jpet.103.051797
- [46] Montejo, A., Majadas, S., Rizvi, S., & Kennedy, S.H. (2011). The effects of agomelatine on sexual function in depressed patients and healthy volunteers. *Human Psychopharmacology-Clinical and Experimental*, 26, 537-542. doi:10.1002/hup.1243
- [47] Montgomery, S.A., & Asberg, A. (1979). A new depression scale designed to be sensitive to change. *The British Journal of Psychiatry*, 134, 382-389. doi:10.1192/bjp.134.4.382
- [48] Montgomery, S.A., & Kasper, S. (2007). Severe depression and antidepressants: Focus on a pooled analysis of placebo-controlled studies on agomelatine. *International Clinical Psychopharmacology*, 22, 283-291. doi:10.1097/YIC.0b013e3280c56b13
- [49] Olie, J.P., & Kasper, S. (2007). Efficacy of agomelatine, a MT₁/MT₂ receptor agonist with 5-HT_{2C} antagonistic properties, in major depressive disorder. *International Journal of Neuropsychopharmacology*, 10, 661-673.
- [50] Opbroek, A., Delgado, P.L., Laukes, C., McGahuey, C., Katsanis, J., Moreno, F.A., & Manber, R. (2002). Emotional blunting associated with SSRI-induced sexual dysfunction. Do SSRIs inhibit emotional responses? *International Journal of Neuropsychopharmacology*, 5, 147-151. doi:10.1017/S1461145702002870
- [51] Ossewaarde, L., Verkes, R.J., Hermans, E.J., Kooijman, S.C., Uner, M., Tendolkar, I., van Wingen, G.A., & Fernandez, G. (2011). Two-week administration of the combined serotonergic-noradrenergic reuptake inhibitor duloxetine augments functioning of mesolimbic incentive processing circuits. *Biological Psychiatry*, 70, 568-574. doi:10.1016/j.biopsych.2011.03.041
- [52] Nierenberg, A.A., & Wright, E.C. (1999). Evolution of remission as the new standard in the treatment of depression. *Journal of Clinical Psychiatry*, 60, 7-11.
- [53] Novotny, V., & Pecena, J. (2011). Agomelatine—First results from trial VALID in Slovakia. *International Journal of Psychiatry in Clinical Practice*, 33-34.
- [54] Papakostas, G.I., & Larsen, K. (2011). Testing anxious depression as a predictor and moderator of symptom improvement in major depressive disorder during treatment with escitalopram. *European Archives of Psychiatry and Clinical Neuroscience*, 261, 147-156. doi:10.1007/s00406-010-0149-3
- [55] Parker, G., Wilhelm, K., Mitchell, P., Roy, K., & Hadzi-Pavlovic, D. (1999). Subtyping depression: Testing algorithms and identification of a tiered model. *Journal of Nervous and Mental Disease*, 187, 610-617. doi:10.1097/00005053-199910000-00004
- [56] Perry, P.J. (1996). Pharmacotherapy for major depression with melancholic features: Relative efficacy of tricyclic versus selective serotonin reuptake inhibitor antidepressants. *Journal of Affective Disorders*, 39, 1-6. doi:10.1016/0165-0327(96)00014-6
- [57] Porter, R., Gallagher, P., Thompson, J., & Young, A. (2003). Neuro-cognitive impairment in drug-free patients with major depressive disorder. *British Journal of Psychiatry*, 182, 214-220. doi:10.1192/bjp.182.3.214

- [58] Quera-Salva, M.A., Hajak, G., Philip, P., Montplaisir, J., Keufer-Le Gall, S., Laredo, J., & Guilleminault, C. (2011). Comparison of agomelatine and escitalopram on nighttime sleep and daytime condition and efficacy in major depressive disorder patients. *International Clinical Psychopharmacology*, 26, 252-262. doi:10.1097/YIC.0b013e328349b117
- [59] Racagni, G., Riva, M.A., Molteni, R., Musazzi, L., Calabrese, F., Popoli, M., & Tardito, D. (2011). Mode of action of agomelatine: Synergy between melatonergic and 5-HT_{2c} receptors. *The World Journal of Biological Psychiatry*, 12, 574-587. doi:10.3109/15622975.2011.595823
- [60] Raskin, J., Wiltse, C.G., Siegal, A., Javaid, S., Xu, J., Dinkel, J.J., Rotz, B.T., & Mohs, R.C. (2007). Efficacy of duloxetine on cognition, depression, and pain in elderly patients with major depressive disorder: an 8-week, double-blind, placebo-controlled trial. *American Journal of Psychiatry*, 164, 900-909. doi:10.1176/appi.ajp.164.6.900
- [61] Sheehan, D.V., Harnett-Sheehan, K., & Raj, B.A. (1996). The measurement of disability. *International Clinical Psychopharmacology*, 11, 89-95. doi:10.1097/00004850-199606003-00015
- [62] Silverstone, P.H., Entsuah, R., & Hackett, D. (2002). Two items on the Hamilton Depression rating scale are effective predictors of remission: Comparison of selective serotonin reuptake inhibitors with the combined serotonin/norepinephrine reuptake inhibitor, venlafaxine. *International Clinical Psychopharmacology*, 17, 273-280. doi:10.1097/00004850-200211000-00002
- [63] Snaith, R.P., Hamilton, M., Morley, S., Humayan, A., Hargreaves, D., & Trigwell, P. (1995). A scale for the assessment of hedonic tone the Snaith-Hamilton Pleasure Scale. *British Journal of Psychiatry*, 67, 99-103. doi:10.1192/bjp.167.1.99
- [64] Souery, D., Oswald, P., Massat, I., Bailer, U., Bollen, J., Demyttenaere, K., Kasper, S., Lecrubier, Y., Montgomery, S., Serretti, A., Zohar, J., & Mendlewicz, J. (2007). Clinical factors associated with treatment resistance in major depressive disorder: Results from a European multicenter study. *Journal of Clinical Psychiatry*, 68, 1062-1070. doi:10.4088/JCP.v68n0713
- [65] Stahl, S.M., Fava, M., Trivedi, M.H., Caputo, A., Shah, A., & Post, A. (2010). Agomelatine in the treatment of major depressive disorder: An 8-week, multicenter, randomized, placebo-controlled trial. *Journal of Clinical Psychiatry*, 71, 616-626. doi:10.4088/JCP.09m05471blu
- [66] Stein, D.J., Ahokas, A.A., & de Bodinat, C. (2008). Efficacy of agomelatine in generalized anxiety disorder: A randomized, double-blind, placebo-controlled study. *Journal of Clinical Psychopharmacology*, 28, 561-566. doi:10.1097/JCP.0b013e318184ff5b
- [67] Stein, D.J., & Kennedy, S.H. (2011). Efficacy of the novel antidepressant agomelatine for anxiety symptoms within depression. *European College of Neuropsychopharmacology Annual Meeting*, Paris, 5 September 2011.
- [68] Uher, R., Farmer, A., Maier, W., Rietschel, M., Hauser, J., Marusic, A., Mors, O., Elkin, A., Williamson, R.J., Schmael, C., Henigsberg, N., Perez, J., Mendlewicz, J., Janzing, J.G., Zobel, A., Skibinska, M., Kozel, D., Stamp, A.S., Bajs, M., Placentino, A., Barreto, M., Mc-Guffin, P., & Aitchison, K.J. (2008). Measuring depression: Comparison and integration of three scales in the GENDEP study. *Psychological Medicine*, 38, 289-300. doi:10.1017/S0033291707001730
- [69] Uher, R., Maier, W., Hauser, J., Marusic, A., Schmael, C., Mors, O., Henigsberg, N., Souery, D., Placentino, A., Rietschel, M., Zobel, A., Dmitrzak-Weglarz, M., Petrovic, A., Jorgensen, L., Kalember, P., Giovannini, C., Barreto, M., Elkin, A., Landau, S., Farmer, A., Aitchison, K.J., & McGuffin, P. (2009). Differential efficacy of escitalopram and nortriptyline on dimensional measures of depression. *British Journal of Psychiatry*, 194, 252-259. doi:10.1192/bjp.bp.108.057554
- [70] Wade, A.G., Fernández, J.L., François, C., Hansen, K., Danchenko, N., & Despiegel, N. (2008). Escitalopram and duloxetine in major depressive disorder: A pharmacoeconomic comparison using UK cost data. *Pharmacoeconomics*, 26, 969-981. doi:10.2165/00019053-200826110-00008
- [71] Waldinger, M.D., Zwinderman, A.H., & Olivier, B. (2003). Antidepressants and ejaculation: A double-blind, randomized, fixed-dose study with mirtazapine and paroxetine. *Journal of Clinical Psychopharmacology*, 23, 467-470. doi:10.1097/01.jcp.0000088904.24613.e4
- [72] Warden, D., Trivedi, M. H., Wisniewski, S. R., Davis, L., Nierenberg, A. A., Gaynes, B. N., & Rush, A. J. (2007). Predictors of attrition during initial (citalopram) treatment for depression: A STAR*D report. *American Journal of Psychiatry*, 164, 1189-1197. doi:10.1176/appi.ajp.2007.06071225
- [73] Zajecka, J., Schatzberg, A., Stahl, S., Shah, A., Caputo, A., & Post, A. (2010). Efficacy and safety of agomelatine in the treatment of major depressive disorder: A multicenter, randomized, double-blind,

- [74] Zigmond, A.S., & Snaith, R.P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica*, 67, 361-370. doi:10.1111/j.1600-0447.1983.tb09716.x
- [75] Zimmerman, M., Ruggero, C.J., Chelminski, I., Young, D., Posternak, M.A., Friedman, M., Boerescu, D., & Attiullah, N. (2006). Developing brief scales for use in clinical practice: the reliability and validity of single-item self-report measures of depression symptom severity, psychosocial impairment due to depression, and quality of life. *Journal of Clinical Psychiatry*, 67, 1536-1541. doi:10.4088/JCP.v67n1007