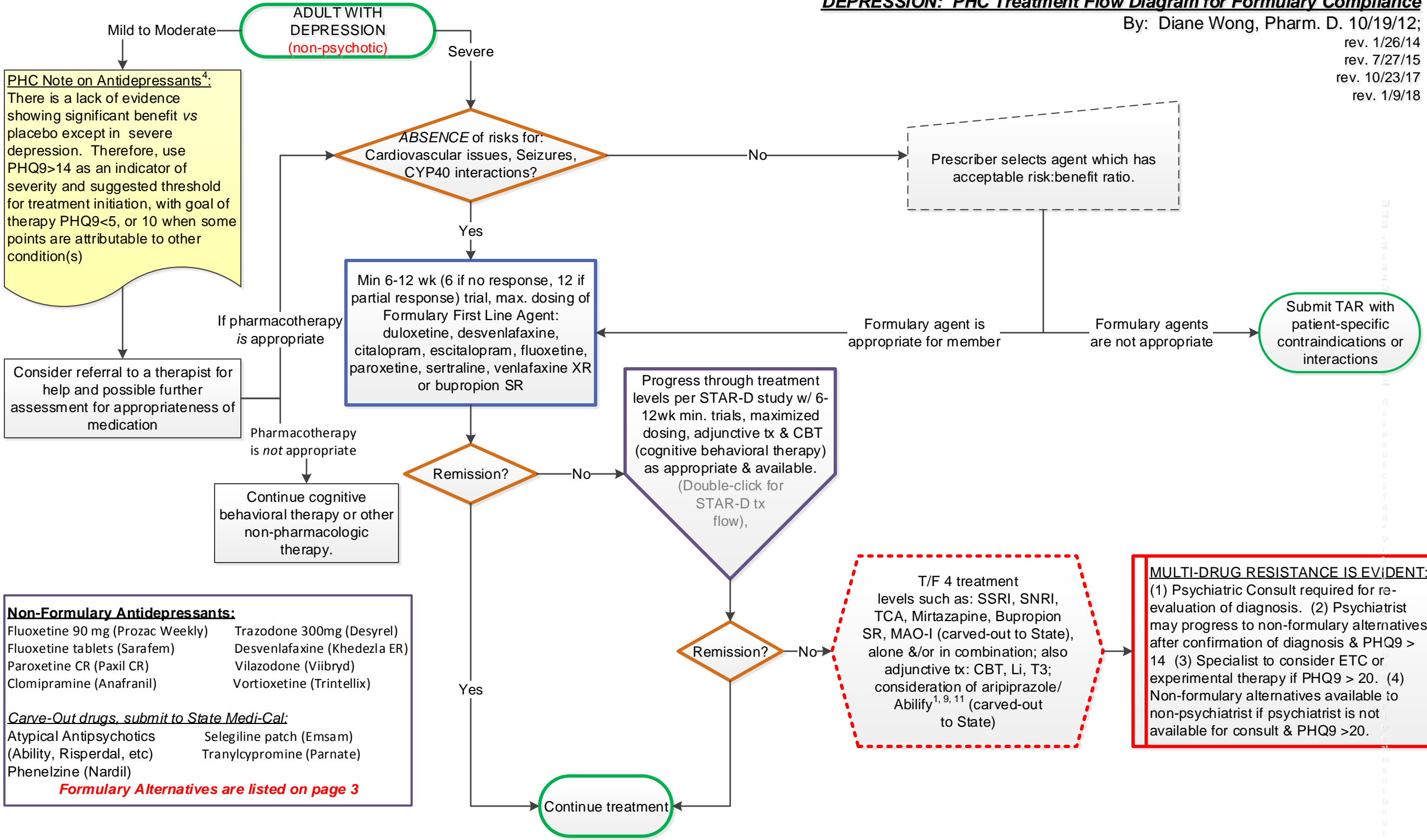


DEPRESSION: PHC Treatment Flow Diagram for Formulary Compliance

By: Diane Wong, Pharm. D. 10/19/12;
 rev. 1/26/14
 rev. 7/27/15
 rev. 10/23/17
 rev. 1/9/18



PHC Note on Antidepressants⁴:
 There is a lack of evidence showing significant benefit vs placebo except in severe depression. Therefore, use PHQ9>14 as an indicator of severity and suggested threshold for treatment initiation, with goal of therapy PHQ9<5, or 10 when some points are attributable to other condition(s)

Consider referral to a therapist for help and possible further assessment for appropriateness of medication

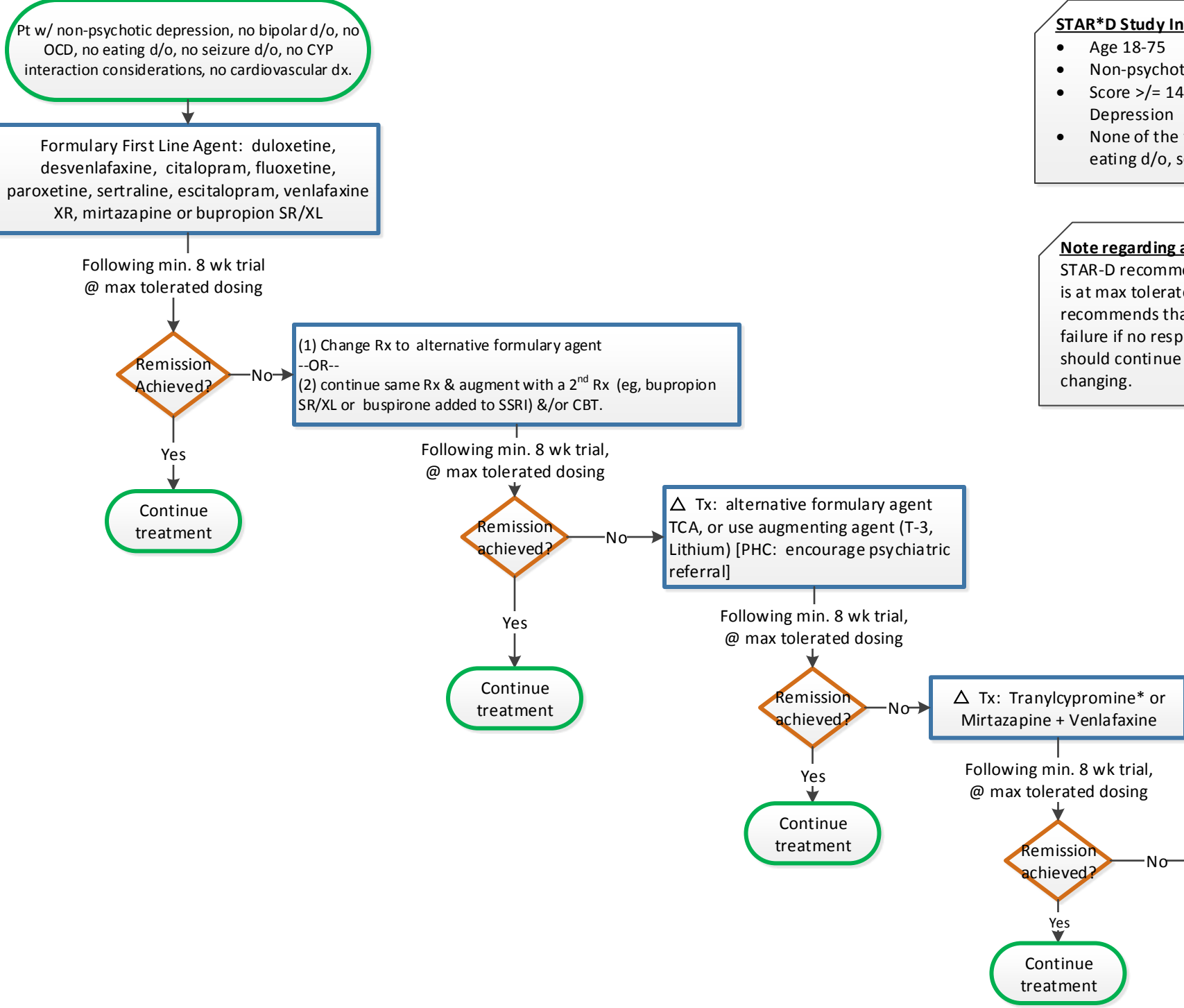
- Non-Formulary Antidepressants:**
- | | |
|----------------------------------|------------------------------|
| Fluoxetine 90 mg (Prozac Weekly) | Trazodone 300mg (Desyrel) |
| Fluoxetine tablets (Sarafem) | Desvenlafaxine (Khedezla ER) |
| Paroxetine CR (Paxil CR) | Vilazodone (Viibryd) |
| Clomipramine (Anafranil) | Vortioxetine (Trintellix) |
- Carve-Out drugs, submit to State Medi-Cal:**
- | | |
|---|---------------------------|
| Atypical Antipsychotics (Ability, Risperdal, etc) | Selegiline patch (Emsam) |
| Phenelzine (Nardil) | Tranylcypromine (Parnate) |
- Formulary Alternatives are listed on page 3**

T/F 4 treatment levels such as: SSRI, SNRI, TCA, Mirtazapine, Bupropion SR, MAO-I (carved-out to State), alone &/or in combination; also adjunctive tx: CBT, Li, T3; consideration of aripiprazole/ Abilify^{1,9,11} (carved-out to State)

MULTI-DRUG RESISTANCE IS EVIDENT:
 (1) Psychiatric Consult required for re-evaluation of diagnosis. (2) Psychiatrist may progress to non-formulary alternatives after confirmation of diagnosis & PHQ9 > 14 (3) Specialist to consider ETC or experimental therapy if PHQ9 > 20. (4) Non-formulary alternatives available to non-psychiatrist if psychiatrist is not available for consult & PHQ9 >20.

Treatment Algorithm based on STAR*D prospective trial, through 4 treatment changes³

PHC Note on Antidepressants⁴:
 There is a lack of evidence showing significant benefit vs placebo except in severe depression. Therefore, use PHQ9>14 as an indicator of severity and suggested threshold for treatment initiation, with goal of therapy PHQ9<5, or 10 when some points are attributable to other condition(s)



- STAR*D Study Inclusion Criteria:**
- Age 18-75
 - Non-psychotic major depression
 - Score >= 14 on Hamilton Rating Scale for Depression
 - None of the following: bipolar d/o, OCD, eating d/o, seizure d/o

Note regarding adequate trial durations:
 STAR-D recommends a minimum 8 wk trial once pt is at max tolerated dose. PHC Subcommittee recommends that 6 wk is adequate to determine failure if no response present; if partial response, should continue tx x 12 wks before considering changing.

Multi-drug tx-resistance:
 No specific STAR*D recommendations after 4 treatment failures...refer to PHC F/NF Decision Tree.
 (double-click to return to previous flow)

PHC Formulary Antidepressants

TCAS	<p><u>Formulary, no restrictions:</u></p> <table border="0"> <tr> <td>Amitriptyline (Elavil)</td> <td>Imipramine HCL (Tofranil only, not pamoate/PM)</td> </tr> <tr> <td>Desipramine (Norpramin)</td> <td>Nortriptyline (Pamelor)</td> </tr> <tr> <td>Doxepin (Sinequan)</td> <td>Protriptyline (Vivactil)</td> </tr> </table>	Amitriptyline (Elavil)	Imipramine HCL (Tofranil only, not pamoate/PM)	Desipramine (Norpramin)	Nortriptyline (Pamelor)	Doxepin (Sinequan)	Protriptyline (Vivactil)
Amitriptyline (Elavil)	Imipramine HCL (Tofranil only, not pamoate/PM)						
Desipramine (Norpramin)	Nortriptyline (Pamelor)						
Doxepin (Sinequan)	Protriptyline (Vivactil)						
SSRIs	<p><u>Formulary, no restrictions:</u></p> <table border="0"> <tr> <td>Citalopram</td> <td>Paroxetine</td> </tr> <tr> <td>Escitalopram</td> <td>Sertraline</td> </tr> <tr> <td>Fluoxetine</td> <td>Fluvoxamine</td> </tr> </table>	Citalopram	Paroxetine	Escitalopram	Sertraline	Fluoxetine	Fluvoxamine
Citalopram	Paroxetine						
Escitalopram	Sertraline						
Fluoxetine	Fluvoxamine						
SNRIs	<p><u>Formulary, no restrictions:</u></p> <p>Venlafaxine ER capsules (generic Effexor XR)</p> <p>Venlafaxine IR tablets (generic Effexor)</p> <p><u>Formulary, with restrictions:</u></p> <p>Desvenlafaxine Succinate ER (generic for Pristiq) – Limited to 1 per day</p> <p>Duloxetine – limited to 2 per day</p>						
OTHER	<p><u>Formulary, no restrictions:</u></p> <p>Trazodone 50, 100 & 150mg (Generic Desyrel, immediate release)</p> <p><u>Formulary, with restrictions:</u></p> <p>Bupropion, immediate release, limited to 3 per day (TID dosing)</p> <p>Bupropion SR, limited to 2 per day (BID dosing)</p> <p>Bupropion XR, limited to 1 per day (QD dosing)</p> <p>Mirtazapine, limited to 1 per day</p> <p>Nefazodone, limited to ages 18 and older</p>						

References:

1. American Psychiatric Association (APA). *Practice guideline for the treatment of patients with major depressive disorder*. 3rd ed. Arlington (VA): American Psychiatric Association (APA); 2010 Oct. 152 p. [1170 references]
2. Epilepsy.com/Professionals. Epilepsy Foundation, n.d. Web. *Epilepsy and Seizure Information for Healthcare Professionals* : Oct.-Nov. 2012. <<http://www.professionals.epilepsy.com/>>.
3. Gaynes, Bradley N., et al. *The STAR*D Study: Treating Depression in the Real World*. *Cleveland Clinic Journal of Medicine*, 2008, vol 75, no 1, pp 57-66.
4. Kirsch, I, et al. *Initial Severity and Antidepressant Benefits: A Meta-Analysis of Data Submitted to the Food and Drug Administration*, PLoS Medicine, 2008; vol 5, no 2, pp 260-268.
5. PL Detail-Document, Antidepressants and Cardiovascular Risk. *Pharmacist's Letter/Prescriber's Letter* 2010;26(2):260207.
6. PL Detail-Document, Celexa (Citalopram) and QT Interval Prolongation. *Pharmacist's Letter/Prescriber's Letter* 2011;27(10):271002.
7. PL Detail-Document, Comparison of Commonly Used Antidepressants. *Pharmacist's Letter/Prescriber's Letter* 2008;24(5):24059
8. PL Detail-Document, Depression and Heart Disease. *Pharmacist's Letter/Prescriber's Letter* 2009;25(1):250104
9. PL Detail-Document, Treatment Resistant Depression: An Update. *Pharmacist's Letter/Prescriber's Letter* 2009; 25(5):250510.
10. RxList.com. WebMD, n.d. Web. 19 Oct. 2012. <<http://www.rxlist.com/>>.
11. Weber, J, et al. *Aripiprazole: In Major Depressive Disorder*. *CNS Drugs*, 2008, 22(10):807-13; <http://www.ncbi.nlm.nih.gov/pubmed/18788833>
12. Brause, D, *Slight risk of QT-interval prolongation found with two antidepressants*; Mescap Online www.medscape.com/viewarticle/791429
13. Dailymed.com, NIH, Web 6-5-17, https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=0a541d20-5466-433b-a104-40a7b2296076#Section_5.9
14. Zhang, L, et al. *QT effects of duloxetine at supratherapeutic doses: a placebo and ositive controlled study*. *J Cardiovasc Pharmacol*. 2007 Mar; 49(3):146-53; abstract <https://www.ncbi.nlm.nih.gov/pubmed/17414226>
15. Wernicke, J, et al. *An evaluation of the cardiovascular safety profile of duloxetine: findings from 42 placeo-controlled studies*. *Drug Safety*, 2007;30(5):437-55; abstract <https://www.ncbi.nlm.nih.gov/pubmed/17472422>