Depression in Ambulatory Care and the Role of the Pharmacist

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Educational Objectives

At the completion of this activity, the participant will be able to:

- Examine the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria for major depressive disorder (MDD) and be able to recognize patients at risk
- Explore the Patient Health Questionnaire (PHQ-9) and other screening tools for MDD
- Discuss the medication and monitoring options for MDD to meet the goals of treatment
- Identify the role of the ambulatory care pharmacist as part of a team approach for the care of the MDD patient

Outline

- Introduction
  - Epidemiology
  - Diagnostic criteria
- Screening
- Treatment
- Monitoring
- Role of the Pharmacist

Epidemiology

- Affects over 300 million people worldwide
- Estimated lifetime prevalence: 19.2%
- US 12-month prevalence: 6.7% of adults
  - 7.6% of persons age 12 and older
  - 16.1 million adults
    - 8.5% females
    - 4.7% males
  - Up to 3% of children

World Health Organization. http://www.who.int/mediacentre/factsheets/fs369/en/. Accessed February 26, 2017.; Kessler RC et al. *Psychol Med*. 2010;40(2):225–237.; National Institute of Mental Health. https://www.nimh.nih.gov/health/statistics/prevalence/major-depression-among-adults.shtml. Accessed February 18, 2017.; CDC. https://www.cdc.gov/nchs/fastats/depression.htm. Accessed February 26, 2017.; American Academy of Pediatrics. https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/resilience/Pages/Depression-Fact-Sheet.aspx. Accessed February 27, 2017.

Burden of Depression

- Second leading cause of disability worldwide
- Cost United States an estimated $210.5 billion in 2010
  - Direct health care costs
  - Suicide
  - Lost productivity
- Considered a moderate risk factor for early cardiovascular disease
- Increased risk for other mental illnesses
  - Anxiety disorders 36.6%
  - Mood disorders 13.3%
  - Substance use disorders 5.5%

Global Burden of Disease Study 2013 Collaborators. *Lancet*. 2015;386(9995):743-800.; Greenberg PE, et al. *J Clin Psychiatry*. 2015;76(2):155-62.; Goldstein BI, et al. *Circulation*. 2015;132(10):965-86.; CDC. https://www.cdc.gov/mentalhealth/basics/mental-illness/depression.htm. Accessed February 26, 2017.

DSM-5 Diagnostic Criteria

≥ 5 symptoms lasting at least 2 weeks; at least one in purple

Depressed mood

Loss of interest or pleasure

- Weight/appetite loss or gain
- Insomnia or hypersomnia
- Observable psychomotor agitation or retardation
- Fatigue/loss of energy
- Feelings of worthlessness or guilt
- Inability to concentrate or make decisions
- Recurrent thoughts of death or suicidal ideation

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th Edition. Arlington, VA: American Psychiatric Association; 2013.

Differential Diagnosis

- Bipolar disorder
- Substance-induced mood disorder
- Attention-deficit/hyperactivity disorder
- Adjustment disorder with depressed mood
- Medical conditions
  - Hypothyroidism
  - Multiple sclerosis
  - Stroke

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th Edition. Arlington, VA: American Psychiatric Association; 2013.

Risk Factors

- Family history
- Childhood trauma
- History of other mental health conditions
- Substance abuse
- Chronic health conditions
- Higher rates in
  - Females
  - Young and middle-aged adults
  - Nonwhite persons
  - Undereducated
  - Previously married
  - Unemployed

World Health Organization. http://www.who.int/mediacentre/factsheets/fs369/en/. Accessed February 26, 2017.; National Institute of Mental Health. https://www.nimh.nih.gov/health/statistics/prevalence/major-depression-among-adults.shtml. Accessed February 18, 2017.; Siu L, et al. *JAMA*. 2016;315(4):380-7.

Screening

Screening Recommendations

- US Preventive Services Task Force (USPSTF) 2016 Recommendations for Primary Care
  - Depression screening recommended for general adult population and children age 12 and up
    - Including pregnant and postpartum women
    - Insufficient evidence to recommend screening for younger children
  - Adequate systems needed to ensure appropriate follow-up
  - Any positive screening should trigger a full assessment
- Routine suicide risk screening not recommended in the general population

Siu L, et al. *JAMA*. 2016;315(4):380-7.; Siu L, et al. *Ann Int Med*. 2016;164(5):360-6.; U.S. Preventive Services Task Force. https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/suicide-risk-in-adolescents-adults-and-older-adults-screening?ds=1&s=suicide. Accessed February 27, 2016.

Screening Tools

- Adults
  - Patient Health Questionnaire
  - Hospital Anxiety and Depression Scales
- Children and adolescents
  - Patient Health Questionnaire for Adolescents
  - Beck Depression Inventory – primary care version
- Older adults
  - Geriatric Depression Scale
- Postpartum
  - Edinburgh Postnatal Depression Scale

Siu L, et al. *JAMA*. 2016;315(4):380-7.; Siu L, et al. *Ann Int Med*. 2016;164(5):360-6.

Patient Health Questionnaire: PHQ-9

- 9-item self report questionnaire
- Over the past 2 weeks, how often have you been bothered by…
  - Little interest or pleasure in doing things
  - Feeling down, depressed or hopeless
  - Trouble sleeping, or sleeping too much
  - Feeling tired or having little energy
  - Poor appetite or overeating
  - Feeling bad about yourself or that you are a failure
  - Trouble concentrating
  - Moving or speaking slowly or being fidgety and restless
  - Thoughts of hurting yourself
- Rated not at all (0 points), several days (1), more than half the days (2), or nearly every day (3)
- Total score of ≥ 10 has high sensitivity and specificity for major depressive disorder (MDD)

Adapted from Kroenke K, et al. *J Gen Intern Med*. 2001;16(9):606–613.

Patient Health Questionnaire: PHQ-2

- Contains the first 2 questions of the PHQ-9
  - Over the past 2 weeks, how often have you been bothered by…
    - Little interest or pleasure in doing things
    - Feeling down, depressed or hopeless
- Total score ≥ 3 has high sensitivity and specificity for MDD

Adapted from Kroenke K, et al. *Med Care*. 2003;41(11):1284-92.

Depression Screening By Pharmacists

Study	Setting	Number of Participants	Screening Tool	Results
Knox ED, et al. *J Am Pharm Assoc*. 2006;46(4):502-6.	University campus pharmacy	25 out of 35 approached	Zung Self-Rating Depression Scale	• 2 patients were referred for psychiatric assessment • 92% of participants felt "very comfortable" completing the screening • Depression screening implemented thereafter
O'Reilly CL, et al. *Res Social Adm Pharm*. 2015;11(3):364-81.	20 pharmacists in 12 community pharmacies	41 out of 75 approached	BeyondBlue Depression Checklist, PHQ-9, WHO-5	• PHQ-9 was most popular tool amongst pharmacists • Mean interaction time of 16 minutes • 70% were referred to a primary care or mental health specialist
Rosser S, et al. *J Am Pharm Assoc*. 2013;53(1):22-9.	Large grocery chain pharmacy	3,726	PHQ-2 and PHQ-9	• 1.8% screened positive on PHQ-2 - 25% referred to physician • 5 patients referred for urgent treatment due to suicidal thoughts

Treatment

Goals of Treatment

- Acute
  - Response – clinically significant improvement in depressive symptoms (usually ≥50%)
  - Remission – absence of symptoms
- Intermediate
  - Recovery – sustained remission
  - Eliminate residual symptoms
  - Restore prior level of functioning
- Long-term
  - Maintenance to prevent recurrence

Rush AJ, et al. *Neuropsychopharmacol*. 2006;31(9):1841-53.; Baeur M, et al. *World J Biol Psychiatry*. 2013;14(5):334-85.

Phases of Treatment

- Acute
  - 4-10+ weeks
- Continuation
  - 6-9 months
- Maintenance
  - Usually 2 years or more
  - History of ≥ 3 prior episodes or other risk factors
    - Residual symptoms
    - Early age of onset
    - Family history
  - Patient preference

American Psychiatric Association. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf Accessed February 26, 2017.; Baeur M, et al. *World J Biol Psychiatry*. 2013;14(5):334-85.; Kennedy SH, et al. *Can J Psychiatry*. 2016;61(9):540-60.

Non-Pharmacologic Treatment

- Cognitive Behavioral Therapy
- Interpersonal Therapy
- Mindfulness-based Cognitive Therapy
- Electroconvulsive Therapy (ECT)
- Transcranial Magnetic Stimulation

American Psychiatric Association. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Accessed February 26, 2017.; Kuyken W, et al. *JAMA Psychiatry*. 2016;73(6):565-74.

Antidepressants

- **SSRIs**
  - Fluoxetine
  - Citalopram
  - Sertraline
  - Paroxetine
  - Fluvoxamine
  - Escitalopram
- **SNRIs**
  - Venlafaxine
  - Duloxetine
  - Desvenlafaxine
  - Levomilnacipran
- **MAOIs**
  - Phenelzine
  - Tranylcypromine
  - Transdermal selegiline
- **TCAs**
  - Amitriptyline
  - Nortriptyline
  - Clomipramine
  - Imipramine
  - Doxepin
  - Desipramine
- **Miscellaneous**
  - Bupropion
  - Mirtazapine
  - Trazodone/nefazodone
  - Vilazodone
  - Vortioxetine

Medication Choice

- Overall, all available antidepressants considered equally effective
- First-line – SSRI, SNRI, mirtazapine, or bupropion
  - Canadian guidelines now recommend vortioxetine as an option
- TCAs and MAOIs usually restricted to non-responders due to unfavorable risk/benefit ratio
  - Adverse effects
  - Drug/food interactions

American Psychiatric Association. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf.. Accessed February 27, 2017.; Cleare A, et al. *J Psychopharmacol*. 2015;29(5):459-525.; Baeur M, et al. *World J Biol Psychiatry*. 2013;14(5):334-85.; Kennedy SH, et al. *Can J Psychiatry*. 2016;61(9):540-60.

Individualizing Treatment

- Balance risk vs benefit
- Medication Factors
  - Adverse effect profile
  - Pharmacokinetics
    - Drug interactions
    - Half-life
  - Cost
- Patient factors
  - Patient preference
  - Age – risk of certain adverse effects
    - Suicidality in children and young adults
    - Anticholinergic effects in elderly
  - Prior response to medication
  - Family member response to medication
  - Co-occurring medical and psychiatric disorders
  - Type of depression – specific symptoms
  - Patient's adherence history

American Psychiatric Association. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf.. Accessed March 3, 2017.; Bauer M, et al. *World J Biol Psychiatry*. 2013;14(5):334-85.; Cleare A, et al. *J Psychopharmacol*. 2015;29(5):459-525.; Kennedy SH, et al. *Can J Psychiatry*. 2016;61(9):540-60.

New Antidepressants: Vilazodone

- Efficacy
  - Response rates 40-72% vs 28-55% with placebo
  - Number needed to treat (NNT) = 8
- Mechanism of Action: SSRI and 5-HT_{1A} partial agonist
- Dosing: 10 mg daily titrated at weekly intervals to target dose of 20-40 mg daily
  - Titration necessary to avoid GI adverse effects
  - Dose adjustment required with CYP 3A4 inhibitors or inducers
- Pharmacokinetics
  - Half-life 25 hours
  - Should be given with food to enhance absorption
- Adverse effects
  - Diarrhea: 26-29%
  - Nausea: 22-24%
  - Headache: 15%

Citrome L. *J Affect Dis*. 2016;196:225-33.; Viibryd [package insert]. St. Louis, MO: Forest Pharmaceuticals, Inc; 2011.; Kennedy SH, et al. *Can J Psychiatry*. 2016;61(9):540-60.

New Antidepressants: Vortioxetine

- Efficacy
  - Response rates 37.5-68.1% vs 23.0-46.9% with placebo
  - NNT = 9
  - Possible benefit in cognitive functioning
- Mechanism of Action: SSRI, 5-HT_3 and 5-HT_{1A} agonist
- Dosing: 10 mg daily titrated to 20 mg daily
  - Dose adjustment recommended with CYP inducers or CYP 2D6 inhibitors
  - 5 mg dose available for those unable to tolerate higher doses
- Pharmacokinetics
  - Half-life 66 hours
- Adverse Effects
  - Sexual dysfunction: self-report 1-5%, rating scale-based 16-34%
  - Nausea: 21-32%, females > males

Citrome L. *J Affect Dis.* 2016;196:225-33.; Trintellix [package insert]. Deerfield, Il: Takeda Pharmaceuticals America, Inc.; 2016.

New Antidepressants: Levomilnacipran

- Efficacy
  - Response rates 38.4-59.1% vs 29.1-42.2% with placebo
  - NNT = 10
- Mechanism of Action: SNRI
- Dosing: 20 mg daily titrated to 40-120 mg daily
- Pharmacokinetics
  - Half-life 12 hours
- Adverse Effects
  - Nausea: 17%
  - Cardiovascular effects: orthostatic hypotension, tachycardia, palpitations, hypertension

Citrome L. *J Affect Dis.* 2016;196:225-33.; Fetzima [package insert]. Irvine, CA: Allergan USA Inc.; 2017.

When Initial Therapy Fails

- Roughly 55-65% of patients will continue to have symptoms despite treatment
- Chance of response decreases if no improvement seen by 4 weeks
- Re-evaluate
  - Diagnosis
  - Adequacy of treatment (dose, duration)
  - Adherence to treatment
  - Comorbid medical and psychiatric diagnoses
- Treatment options
  - Increase dose of current antidepressant (AD)
    - Minimal adverse effects
    - Some improvement
  - Switch to a different AD
    - Adverse effects
    - No improvement
  - Combine or augment with a second medication (adjunctive medication)
    - Partial response and good tolerability

Cleare A, et al. *J Psychopharmacol.* 2015;29(5):459-525.; Kennedy SH, et al. *Can J Psychiatry.* 2016;61(9):540-60.

Adjunctive Medication Strategies

	Medication
First-Line	aripiprazole, quetiapine, risperidone
Second-Line	brexpiprazole, bupropion, lithium, buspirone, mirtazapine, modafanil, olanzapine, T_3
Third-Line	lamotrigine, stimulants, TCAs, ziprasidone
Experimental	ketamine
Not recommended	pindolol

Cleare A, et al. *J Psychopharmacol.* 2015;29(5):459-525.; Kennedy SH, et al. *Can J Psychiatry.* 2016;61(9):540-60.

FDA-approved Adjunctive Options

- Adjunctive with antidepressants
  - Aripiprazole 2-5 mg/day titrated up to 15 mg/day
  - Quetiapine XR 50 mg/day titrated to 150-300 mg/day
  - Brexpiprazole 0.5-1 mg/day titrated up to 2-3 mg/day
- Treatment-Resistant Depression
  - Olanzapine/fluoxetine 6 mg/ 25 mg QHS titrated to usual max dose of 18 mg/50 mg

Symbyax [package insert]. Indianapolis, IN: Eli Lilly and Company; 2012.; Abilify [package insert]. Tokyo, Japan: Otsuka Pharmaceutical Co, Ltd: 2012.; Seroquel XR [package insert]. Wilmington, DE: Eli Lilly and Company; 2012.; Rexulti [package insert]. Tokyo, Japan: Otsuka Pharmaceutical Co, Ltd; 2017.

Brexpiprazole

- Also approved for treatment of schizophrenia
- Efficacy for MDD
  - Response rates of 23.0-23.4% vs 14.3-15.7% with placebo
  - NNT = 11-13
- Mechanism of action: partial agonist at D_2 and 5-HT_{1A}
- Pharmacokinetics
  - $T_{1/2}$ = 91 hours
  - Metabolized by CYP 3A4 and 2D6
- Adverse effects
  - Akathisia – 6-14%
  - Weight gain
    - 30% gained clinically significant levels of weight (≥ 7%) in long-term studies

McKeage K. *CNS Drugs.* 2016;30(2):91-9.; Rexulti [package insert]. Tokyo, Japan: Otsuka Pharmaceutical Co, Ltd; 2017.

Monitoring

Adverse Effects

- Cardiovascular
  - Hypertension – SNRIs, bupropion
  - Hypertensive crisis – MAOIs
  - Orthostatic hypotension – TCAs, trazodone, MAOIs
  - Arrhythmias – TCAs, citalopram
- Anticholinergic – TCAs
- Neurologic
  - Headache – SSRIs, SNRIs, bupropion
  - Seizures – TCAs, bupropion

American Psychiatric Association. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Accessed February 28, 2017.

Adverse Effects

- Sexual dysfunction – both sexes
  - Less frequent with bupropion, mirtazapine, nefazodone, vilazodone?, vortioxetine?
  - May be more frequent with paroxetine and escitalopram
  - Types of effects
    - Hypoarousal
    - Anorgasmia
    - Priapism
- Weight gain – especially with paroxetine, mirtazapine and TCAs
- Gastrointestinal (nausea)
  - Typically starts early on and dissipates within first few weeks
- Sedation – TCAs, trazodone, mirtazapine, paroxetine
- Insomnia, restlessness – SSRIs, SNRIs, bupropion
- Suicidality – NNH 143

American Psychiatric Association. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf Accessed February 28, 2017.; Kennedy SH, et al. *Can J Psychiatry*. 2016;61(9):540-60.; Mayo Clinic. http://www.mayoclinic.org/diseases-conditions/depression/in-depth/antidepressants/art-20049305. Accessed February 28, 2017.

Monitoring for Adverse Effects

- Symptom/adverse effect diary
- Open dialogue with physicians about adverse effects
  - Some will go away on their own
  - Some can be mediated by careful titration or changing time of day
- Hypertensive crisis
  - Throbbing headache
  - Palpitations
- Serotonin syndrome
  - Mental status changes
  - Agitation
  - Myoclonus and hyperreflexia
  - Fever and diaphoresis
  - Shivering
  - Ataxia
  - Diarrhea

Krishnan KR. *J Clin Psychiatry*. 2007;68(suppl 8):35-41.; Mayo Clinic. http://www.mayoclinic.org/diseases-conditions/depression/in-depth/antidepressants/art-20049305. Accessed February 28, 2017.

Drug Interactions

- Pharmacodynamic
  - Serotonin syndrome
  - Hypertensive crisis
  - Bleeding
  - QT_c Prolongation
- Pharmacokinetic
  - CYP 450
  - Impaired absorption

Drug Interactions

- Serotonin syndrome (SSRIs, SNRIs, MAOIS, TCAs)
  - Tramadol
  - Meperidine
  - Antipsychotics
  - Dextromethorphan
  - **Linezolid**
- QTc prolongation - especially **citalopram and escitalopram**
  - Antipsychotics
    - **Quetiapine**
  - **Methadone**
  - Amiodarone
  - Sotalol
  - Levofloxacin
  - Moxifloxacin
  - Risk Scoring Tool available
    - Tisdale et al. *Circ Cardiovasc Qual Outcomes*. 2013;6:479-87.

American Psychiatric Associationhttp://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Accessed February 28,2017.; Citalopram [package insert]. St. Louis, MO: Forest Laboratories, Inc.; 2012.; Kennedy SH, et al. *Can J Psychiatry*. 2016;61(9):540-60.; Tisdale JE. *Can Pharm J*. 2016;149:139-52.

QT_c Prolongation With Citalopram and Escitalopram

- Citalopram – FDA warning
  - Maximum dose lowered to 40 mg/day
  - Maximum dose 20 mg/day
    - Age >60 years
    - Hepatic impairment
    - Concurrent use of moderate-strong CYP2C19 inhibitors
    - CYP2C19 poor metabolizers
- Escitalopram – Medicines and Healthcare Products Regulatory Agency (UK) warning
  - Maximum dose 10 mg/day for those >65 years

Celexa [package insert]. St. Louis, MO: Forest Pharmaceuticals, Inc; 2012. . Cleare A, et al. *J Psychopharmacol.* 2015;29(5):459-525.; Kennedy SH, et al. *Can J Psychiatry.* 2016;61(9):540-60.

Drug Interactions

- Hypertensive crisis (MAOIs)
  - Tyramine containing foods
  - Pseudoephedrine
  - Phenylephrine
  - Dextromethorpan
- Bleeding (SSRIs, SNRIs)
  - Anticoagulants
  - Antiplatelets
  - NSAIDs

American Psychiatric Association. *Practice Guideline for the Treatment of Patients With Major Depressive Disorder*, 3rd Edition. Washington, DC: American Psychiatric Association; 2010.

Pharmacokinetic Drug Interactions: CYP 450

Minimal/Low Potential	Moderate Potential	High Potential
• Citalopram • Desvenlafaxine • Escitalopram • Mirtazapine • Venlafaxine	• Aripiprazole (2D6, 3A4 substrate) • Bupropion (2D6 inhibitor) • Duloxetine (2D6 inhibitor, 1A2 substrate) • Levomilnacipran (3A4 substrate) • Olanzapine (1A2 substrate) • Sertraline (2D6 inhibitor) • Vilazodone (3A4 substrate) • Vortioxetine (2D6 substrate)	• Fluoxetine (2D6, 2C19 inhibitor) • Fluvoxamine (1A2, 2C19, 3A4 inhibitor) • Paroxetine (2D6 inhibitor) • Quetiapine (3A4 substrate)

Kennedy SH, et al. *Can J Psychiatry.* 2016;61(9):540-60.

Role of the Pharmacist

APhA Foundation White Paper on Pharmacist Role in Depression Management

- Identifying those at risk
- Providing patient education
  - What the medication is used for
  - How to take it
  - What to expect (time to onset of effect, adverse effects)
  - Emphasize value of early treatment and importance of adherence
  - Provide depression symptom checklist/rating scale
- Collaboration and communication with providers
- Increase awareness of the pharmacist's role

APhA Foundation. http://www.aphafoundation.org/sites/default/files/ckeditor/files/WhitePaper-PharmacistRoleManagingDepression-APhAFoundation-2009(1).pdf. Accessed February 28, 2017.

What Do Patients Want to Know?

- Balance of benefit and harm information
  - Written information largely focuses on negative effects
- Information about
  - Indications
  - Benefits
  - Likely duration of treatment
    - At least 4-6 months after symptom resolution
  - Adverse effects

Haw C, Stubbs J. *J Affect Dis* 2011;128(1-2):165-70.

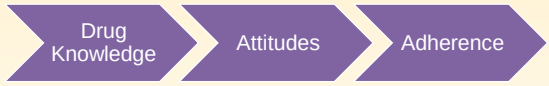
Optimizing Medication Adherence

- Non-adherence to antidepressants 50-75%
- Adherence and discontinuation associated with amount of information given to patient
- Patients more likely to adhere to medication regimens if clinicians ask about adverse effects and medication-related concerns

Hassan AK, et al. *Int J Clin Pharm*. 2016;38:429-37.; Sun GC, et al. *Perspect Psych Care*. 2011;47(1):13-22.; Rickles NM, et al. *J Am Pharm Assoc*. 2006;46(1):25-32.; Brown C, et al. *J Fam Pract* 2007;65(5):356-63.

PTCE DIRECTIONS IN Pharmacy

Optimizing Medication Adherence



Sun GC, et al. *Perspect Psychiatr Care*. 2011;47(1):13-22.; Young, HN, et al. *J Gel Intern Med*. 2006;21(11):1172-7.

PTCE DIRECTIONS IN Pharmacy

Improving Medication Attitudes

- Rickles, et al.
  - 63 patients presenting with new AD prescription
  - 3 monthly telephone calls from pharmacists
  - Results
    - Patients who gave more feedback to RPh had:
      - Better AD knowledge ($P \leq .05$)
      - More positive AD beliefs ($P \leq .05$)
      - More positive perceptions of progress ($P \leq .001$)

Rickles NM, et al. *J Am Pharm Assoc*. 2006;46(1):25-32.

PTCE DIRECTIONS IN Pharmacy

Treatment Expectations

- Most ADs work by increasing availability of certain chemicals in the brain (serotonin, norepinephrine, dopamine)
- 60-70% of patients respond to the first AD they try
- ADs take <u>at least</u> 3-4 weeks to achieve full therapeutic benefit
- Patients should continue taking their AD for at least 6-9 months to minimize risk of relapse

U.S. Food and Drug Administration. http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm095980.htm. Accessed March 4, 2017.

PTCE DIRECTIONS IN Pharmacy

Importance of Adherence

- Don't stop taking your antidepressants or change the dose on your own
- Depression may return if ADs are stopped too soon
- Discontinuation symptoms
  - **F**lu-like symptoms (headache, chills)
  - **I**nsomnia
  - **N**ausea
  - **I**mbalance/dizziness
  - **S**ensory disturbances (paresthesias, "electric shock-like" sensations)
  - **H**yperarousal
  - Others: anxiety, irritability, lightheadedness

American Psychiatric Association; http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Accessed February 28, 2016.; Kennedy SH, et al. *Can J Psychiatry*. 2016;61(9):540-60.

PTCE DIRECTIONS IN Pharmacy

Pharmacist Medication Management

- Project ImPACT: Depression, Asheville North Carolina
  - 130 patients in 2 ambulatory care clinics
  - Face-to-face visits with pharmacist care manager once per month-quarterly for a year
    - Intake interview to obtain medical history
    - Formulated treatment plan and communicated to primary care physician
    - Educated patient and assessed for adherence
  - PHQ-9 completed at baseline and each follow-up visit
  - Results
    - 80% had a decrease in PHQ-9 scores
      - 68% considered responders
      - 56% achieved remission
    - Annual medical costs decreased
    - Employers continued to offer the program after the study ended

Finley PR, et al. *J Am Pharm Assoc*. 2011;51(1):40-9.

PTCE DIRECTIONS IN Pharmacy

Conclusion

- Major depressive disorder is a common and debilitating illness
- Multiple screening tools exist to aid in identifying patients in need of treatment
- Pharmacists can be implemental in screening for this disorder, recommending appropriate pharmacotherapy and monitoring for treatment response

Additional Resources

- US Preventive Services Task Force Recommendations for Primary Care Practice
  - https://www.uspreventiveservicestaskforce.org/Page/Name/recommendations
- Substance Abuse and Mental Health Services Administration
  - https://www.samhsa.gov/
- American Academy of Pediatrics Mental Health Initiatives
  - https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Mental-Health/Pages/default.aspx
- MacArthur Foundation Initiative on Depression and Primary Care
  - https://www.macfound.org/networks/initiative-on-depression-primary-care/details
- Patient Health Questionnaire Screeners
  - http://www.phqscreeners.com/
- Mayo Clinic: Tips for Coping with Antidepressant Side Effects
  - http://www.mayoclinic.org/diseases-conditions/depression/in-depth/antidepressants/art-20049305
- College of Psychiatric and Neurologic Pharmacists
  - http://cpnp.org/
- National Alliance on Mental Illness
  - http://www.nami.org/
- Credible Meds – QTc prolonging medications lists
  - https://crediblemeds.org/

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