Behavioral Health is Essential To Health

Prevention Works

Treatment is Effective

People Recover
Clozapine as a Tool in Mental Health Recovery

a scenario-based VIRTUAL GRAND ROUNDS presentation
Through education, training, and resources, SAMHSA’s Recovery to Practice (RTP) program supports the expansion and integration of recovery-oriented behavioral health care delivered in multiple service settings.
About this course

• Continuing education course for clinical decision support in prescribing clozapine

• Focused on a single hypothetical scenario to provide training and decision support for recovery-oriented practice in the treatment of individuals experiencing psychotic symptoms

• CME available: follow prompts on registration page and take and pass the quiz at the end for 1 CME credit
Course objectives

• Explain some of the benefits of clozapine for psychotic symptoms and advancing recovery

• Articulate how shared decision-making has a role in initiating clozapine

• Describe the clozapine Risk Evaluation and Mitigation Strategy (REMS)

• Identify methods for managing treatment of benign ethnic neutropenia (BEN) for primary care and psychiatry providers
1. Meet Robert
2. Working with individuals experiencing psychotic symptoms and schizophrenia
3. Shared decision-making supports for recovery
4. Prescribing clozapine
5. Basics of clozapine Risk Evaluation and Mitigation Strategy (REMS)
6. Robert’s decision to take clozapine
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SAMHSA’s 10 Principles & 4 Dimensions of Recovery in Behavioral Health
Section 1

Meet Robert
Gifts and strengths

• African American young man
• Lives at home with his parents
• Enjoys playing video games
• Employment history working in family business
• Sometimes attends psychiatric rehabilitation program
• Regularly meets with his counselor and psychiatrist
• Gifted writer and aspiring journalist who is considering community college
Robert’s diagnostic experience

- Persecutory delusions
- Social withdrawal
- Difficulty maintaining employment
- Diagnosis of Schizophrenia, Multiple Episodes, currently in partial remission (DSM-5)
- Smokes marijuana occasionally
Robert’s challenges

Recently re-hospitalized for 2 weeks:

• Refused to come out of his room
• Stopped eating and drinking in fear of being poisoned
• Observed to be withdrawn, have little energy, trouble concentrating, and increased depression
• Discharged to home after 12 days stabilization
• Referred to you for care
Review of Robert’s medications

- Robert was appropriately tried on risperidone but had only a partial reduction of delusions
- Switched to olanzapine with no additional improvement
- Developed depressive symptoms and mood lability
- Required a hospitalization
  - Two mood stabilizers added—valproic acid and lamotrigine
  - Anti-anxiety medication added—clonazepam
  - Continued olanzapine

Robert is now on four medications.
Why might clozapine be right for Robert?

• Robert has been prescribed at least two adequate trials of different standard antipsychotic medications (risperidone and olanzapine) but continues to have substantial symptoms that interfere with his daily life—recently severe enough that he required inpatient treatment.

• If he were taking risperidone and olanzapine trials as prescribed, data suggest that he can potentially benefit by a trial of clozapine.

Robert has decided he is ready talk about clozapine.
Forging a partnership

Shared Decision-making

- The shared decision-making process helps forge a partnership between Robert (and his selected supporters such as family members) and his treatment and service providers.

- This partnership facilitates optimal medication and supportive services to treat Robert’s symptoms and assist his recovery.
Section 2

Working with Individuals with Psychotic Symptoms and Schizophrenia
Importance of recovery-oriented approaches

- Foundation of welcoming and genuine positive regard
- Helping Robert and his family understand that it is possible to move forward and achieve goals and dreams
- Acknowledging fears and concerns (including those regarding meds)
- Listening and validating past experiences with mental health treatment informs current approach
- Exploring and believing in Robert’s hopes and dreams creates opportunities for activation and involvement
Doctors have to know that the person needs to live some sort of life, not just give you medicine and you walk away and that’s it.

—Marcus, musician
What is important to Robert?

• What are Robert’s goals?
• What matters to him?
• What are his priorities for treatment?
• Does he want to return to school? Work? Both?
• What things are getting in the way of Robert achieving his goals and having a better quality of life?
• What goals does Robert’s family have for him?
• What matters to them?
Do you have cultural or religious beliefs that influence your ideas or feelings about medication and treatment?
Robert wants his mother and father involved in his treatment.

- How do they see medications making Robert feel?
- How do they talk to Robert about his treatment?
- Do they have questions about the medications?
- How do they feel about supporting Robert in managing his issues?
- Provide unbiased educational materials and where they can find support for themselves.
- Discuss monitoring requirements.
Robert’s current medication concerns

- Medications have partial effectiveness with some **ongoing** symptoms
- Medications causing undesirable side effects
  - Weight gain and potential metabolic problems
  - Drowsiness
  - Dry mouth
  - Others
- Prescribed multi-day dosing
- Prescribed multiple medications (polypharmacy)
In terms of medication, what’s working for you right now?
When people want to be productive in their lives, they need something that doesn’t make them dysfunctional.

—Linda, mother of one

Experiences of people who use clozapine
Section 3

Shared Decision-making
Supports for Recovery
The importance of shared decision-making in your prescribing practices

Shared decision-making

• Ensures that individuals have full information about the various options for treatment and the pros and cons of each
• Puts the individual’s values, goals, and preferences at the forefront of treatment decisions
• Increases the individual’s ownership of treatment decisions
• May improve follow-through with decisions made
• Enhances the partnership between provider and the person
What is Shared Decision-making?

- Supported Deliberation
- 2 Experts 2 Perspectives
- “Truly” Informed Consent
- Clarifying Values/Preferences

Shared Decision
Stages of Conversation

Choices talk

Options talk

Decision talk

What supports are needed by Robert and his family?

Discuss with Robert and his family what supports they need to fulfill the clozapine monitoring requirements.

For example,

- Having a familiar staff member go with them to the first blood draw for testing
- Acknowledge any concerns (e.g., some people do not like needles)
What non-medication supports do you and your family need or want to support your recovery?
Incorporating non-medication treatment options

Clozapine can be an extremely effective medication:

- Essential to remember it is only a piece of any treatment plan
- Medication is often not the most important piece
- Incorporate strategies to address Robert’s physical wellness and intellectual, social, and occupational well-being
I had been in group, individual therapy, behavioral therapy. With clozapine, I was able to stay even and calm enough that I could use those skills and tools. Before, I was just all over the charts.

—Sondra, peer specialist
How do we know we are using shared decision-making effectively?

• How do we know whether things are:
  – Getting better?
  – Getting worse?
  – Staying the same?

• Are we following up on the shared decision?

• Are we using decision aids and additional resources to support deliberation?

ASK: How might we know? How can we track change?
Experiences of people who use clozapine

Working, having a car, having a life—it makes a big difference when you feel okay. One day at a time is good, but it sure is nice that a week from now I’ll still be feeling good.

—Sondra, peer support specialist
Section 4

Prescribing Clozapine
When is clozapine indicated?

• Clozapine is used for treatment of refractory schizophrenia and bipolar disorder with two unsuccessful trials of other antipsychotic medications

• Intolerable side-effects to other antipsychotic agents:
  – Neuroleptic-induced movement disorders
  – Psychosis in Parkinson’s Disease

• Psychogenic polydipsia (excessive thirst)

• Suicidality

• Aggression and violence
What are the expected outcomes of clozapine?

- Clozapine reduces suicidal behavior in people who have schizophrenia or schizoaffective disorder.¹

- Clozapine has been shown to improve daily living as measured by:
  - Ability to care for own needs with less assistance, live in more independent settings
  - Return to community life with social participation

- Clozapine was more effective for people with schizophrenia who prospectively failed to improve with an atypical antipsychotic than switching to another newer atypical antipsychotic.²
Ron

Experiences of people who use clozapine

I used to have delusions and really bizarre thinking, but the clozapine has actually helped me get through and it is working for me.

—Ron, crossing guard
Side effects of clozapine

Some of the undesirable side effects:

- Weight gain
- Drowsiness and fatigue
- Drooling or dry mouth
- Increased sweating
- Seizures
- Obsessive-compulsive behaviors
- Other
I take clozapine at night so it helps me sleep. I wake up the next morning and have coffee and I feel much better after a good night’s sleep.

—Marcus, musician
Balancing safety with efficacy

Optimizing benefits by:

• Educating the person and their support system on why clozapine is being recommended

• Discussing the benefits and risks, as well as how blood monitoring can decrease new/further risks

• Providing them with tools to be aware of metabolic issues

• Achieving adequate clozapine plasma levels (>350 ng/ml) and dosing

• Incorporating recovery supports (e.g., family and group therapy, supported employment)
Clozapine can cause severe neutropenia. Individuals with neutropenia may have no symptoms or may have any of the following:

- Flu-like symptoms
- Fever or chills
- Abdominal pain
- Extreme weakness/tiredness
- Pain/burning when urinating
- Wounds take a long time to heal
- Unusual vaginal discharge/itching
- Sores, pain in/around rectal area
- Sores, ulcers inside mouth/gums/skin
- Infections: skin, throat, urinary tract, vaginal, pneumonia, any other infection

Individuals should understand the importance of reporting any of these symptoms to their doctor.
White blood cells (WBCs) are immune system cells

- Protect against infectious agents and foreign invaders
- Short life span

Neutrophils (granulocytes)

- Subtype of WBCs; first line of defense when infection strikes; kill bacteria and fungi

Absolute neutrophil count (ANC)

- Number of WBCs that are neutrophils
- Neutropenia is defined as ANC < 1,500/μL in Caucasians
Severity of neutropenia relates to the relative risk of infection

- Mild (1,000 to 1,500/μL)
- Moderate (500 to 1,000/μL)
- Severe (<500/μL)
When should someone *not* take clozapine?

**Physiological interactions**
- Prescribing contraindications
- Boxed warning

**Drug interactions**
- CYP450 interactions

**Social factors**
- Need for continuous blood monitoring
- Pregnancy and lactation risk
- Informed choice
Strategic discontinuation of clozapine

Reasons for discontinuation

• Side effects
• Lifestyle/social factors

Physical effects of discontinuing clozapine

• Discontinuation syndrome: delirium, agitation, confusion, and diaphoresis (sweating)
Why has clozapine been under-prescribed?

- Among certain ethnic groups, a significant proportion of people have a lower baseline neutrophil count called *benign ethnic neutropenia* (BEN).
- Until the change in prescribing guidelines in 2015, this prevented many individuals from being prescribed clozapine because of neutropenia and the other concerns clozapine raised for providers.
What is benign ethnic neutropenia (BEN)?

What is BEN?

- A phenotype observed in certain ethnic groups with ANCs lower than “standard” laboratory ranges for neutrophils

- **Phenotype**: a visible or observable trait

- **Neutropenia**: low white blood cell count

Most commonly observed in individuals of African descent (~50%), some Middle Eastern ethnic groups and other groups with darker skin (~38%)
How does BEN present?

Neutropenia as confirmed via

- Blood test
- **NO** history of repeated or severe infections

Clinically different from other neutropenia such as congenital neutropenia, cyclic neutropenia, chronic idiopathic neutropenia, neutropenia secondary to other conditions
Can an individual with BEN take clozapine safely?

- **DARC** gene polymorphism is implicated in BEN of African ancestry.
- Individuals with BEN are otherwise healthy with no increased risk of infections or clozapine-induced neutropenia.

It should be noted that BEN is clinically different from other neutropenias.
What informs a “Yes” or “No” decision for clozapine pharmacotherapy for people with BEN?

**Yes:** Based on whether the individual meets the clinical criteria for clozapine treatment

**No:** If the individual does not meet the criteria or has a contraindication for clozapine treatment

**Individual with BEN:** In addition to above, apply clozapine REMS guidelines for ANC monitoring among people with BEN
Section 5

Basics of the Clozapine Risk Evaluation and Mitigation Strategy (REMS)
Risk Evaluation & Mitigation Strategy (REMS) guidelines

- Clozapine is now managed through one entity
- Certification for prescribers, designees, and pharmacies
- New thresholds for clozapine discontinuation
- Provisions for BEN populations
- Only ANC levels reported
- Prescribers can continue treatment with rationale
- National Non-rechallenge Master File (NNRMF) is discontinued
- Agranulocytosis no longer in terminology
In October 2015, the FDA released new neutropenia monitoring guidelines and a streamlined REMS program.

According to the new guidelines, ONLY absolute neutrophil count (ANC) will be monitored. There are two ANC monitoring algorithms:

- **For general population patients** (i.e., those without BEN), interrupt treatment if neutropenia is suspected to be clozapine-induced for ANC less than 1,000 cells per microliter.

- **For patients with BEN**, interrupt treatment if neutropenia is suspected to be clozapine-induced for ANC less than 500 cells/microliter.
New REMS guidelines around neutropenia

Before starting clozapine treatment, baseline ANC must be:

- At least 1,500/µL for the general population
- At least 1,000/µL for people with BEN

*Neutropenia is an abnormally low concentration of neutrophils (a type of white blood cell) in the blood.*
Ron

Experiences of people who use clozapine

I go to the hospital once a month to have my white blood count checked. I do it before I refill the prescription. It’s no big deal to me.

—Ron, crossing guard
For more information or to certify with clozapine REMS

Detailed information about the clozapine REMS Program and certification:

www.clozapinerems.com
Phone: 844-267-8678
Fax: 844-404-8876
Section 6

Robert’s Decision to Take Clozapine
After the first 6 months, Robert reports the following:

- His delusions have greatly decreased.
- His anxiety has lowered and his mood is more stable.
- He feels less withdrawn and more communicative with family.
- He has been able to make friends and has begun looking for a new job.
- The biggest negative was the weekly blood draws. They have been changed to every other week.
- Another negative was feeling sedated for the first several months.
The clozapine has really stabilized my life.... It has given me a lot of self confidence—in my job in particular.

—Sondra, peer support specialist
How will a person know clozapine is working?

- It will probably take several weeks to see big enough changes in a person’s symptoms to decide if clozapine is the right medication for them.
- A person may eventually experience the following:
  - Hallucinations, disorganized thinking, and delusions may improve in the first 1–2 weeks.
  - Sometimes these symptoms do not completely go away.
  - Motivation and desire to be around other people can take at least 1–2 weeks to improve.
  - Symptoms continue to get better the longer a person takes clozapine.
  - It may take 2–3 months before a person can get the full benefit of clozapine.
Experiences of people who use clozapine

It’s not going to work overnight; not going to work for a month and then you can stop taking the medication. Once you’re in, you’re in for a long time.

—Marcus, musician
For more information on prescribing clozapine, BEN, REMS guidelines, and shared decision-making, review the supplemental resources attached to this course.
RTP discipline-based curricula

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