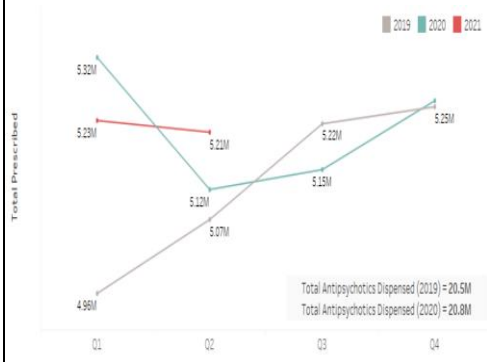
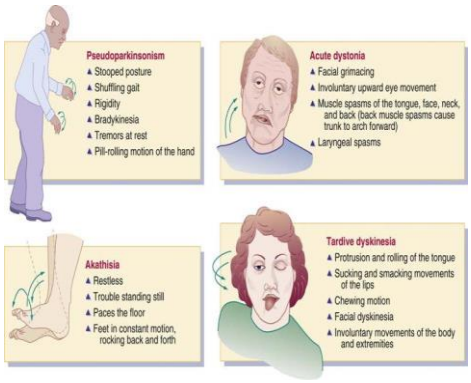
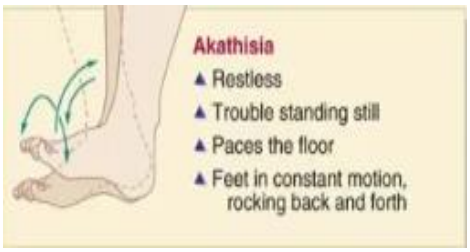
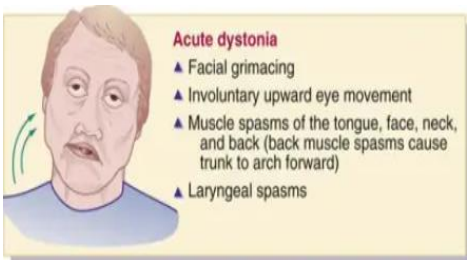
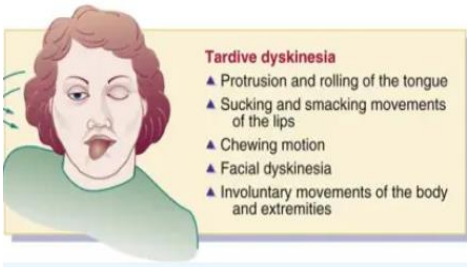
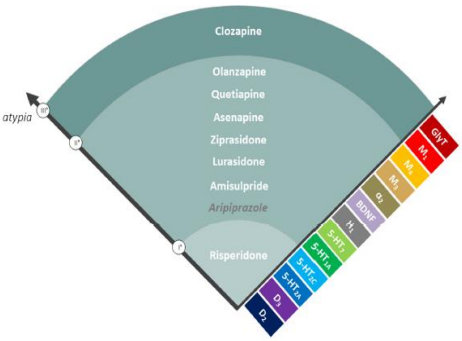
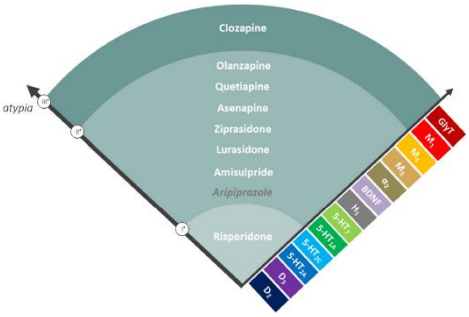
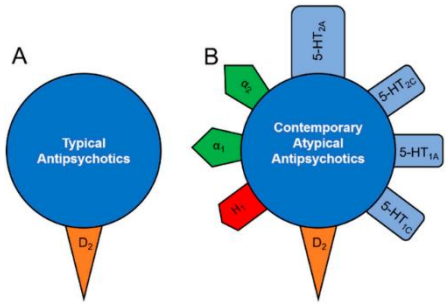
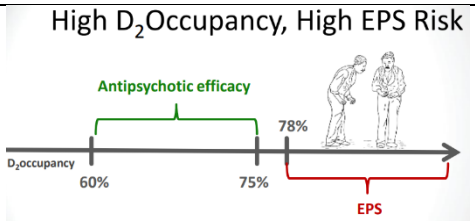
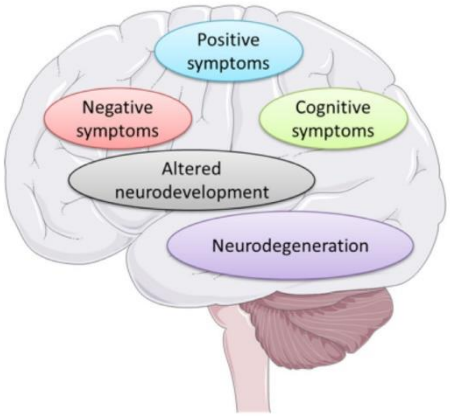
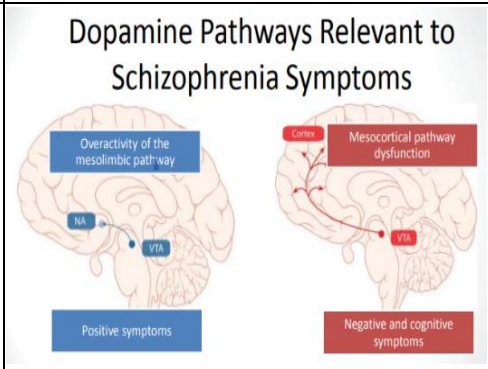
	NP Institute Explainer Video 13 - Atypical v. Typical Antipsychotics: How Do They Work? KOL to Review Content:		
Scene	**Onscreen Images/Footage**	**Description**	**Audio**
Scene 1		*Sponsor Slide*	
	SUPER: Atypical v. Typical Antipsychotics How Do They Work?	Title Slide/Sponsor Slide	Instrumental Music
Scene 2	*Introduction to Antipsychotics*		
Scene 2a **Direction for ART: suggested animations and graphics.** **Please See PowerPoint for full ART/animation direction** **Please recreate this graphic as shown with animation. Include title and source as footnote.**	**Overall Antipsychotic Prescribing and Percent Difference of Total Prescribing: January 2019-June 2021**  Source: Internal ASPE analysis using IQVIA National Prescription Audit, 2015-2021.		Medications known as antipsychotics play a pivotal role in treating various psychiatric conditions and are commonly prescribed to treat different psychiatric illnesses such as schizophrenia, bipolar disorder, or major depression. During the COVID-19 pandemic, total antipsychotics prescribed in long term care facilities for example, increased from 20.5 million to 20.8 million, representing a 1.5 percent increase in prescriptions dispensed from 2019 to 2020 respectively.
Scene 3	*Brief History of Typical and Atypical Antipsychotics With Examples*		
Scene 3a **Please recreate entire graphic and text (using appropriate color schemes) as shown here including source as footnote:**	**FDA-approved Antipsychotics** **First-Generation Antipsychotics** Chlorpromazine Droperidol Fluphenazine Haloperidol Loxapine Perphenazine Pimozide Prochlorperazine Thioridazine Thiothixene Trifluoperazine **Second-Generation Antipsychotics** **Monotherapy** Aripiprazole Asenapine Clozapine Iloperidone Lurasidone Olanzapine Paliperidone Quetiapine Risperidone Ziprasidone **Combination therapy** Olanzapine plus fluoxetine Source: Abou-Setta AM, Mousavi SS, Spooner C, et al. First-Generation Versus Second-Generation Antipsychotics in Adults: Comparative Effectiveness. Rockville (MD): Agency for Healthcare Research and Quality (US); August 2012.		Typical antipsychotics, also known as first-generation antipsychotics, were initially developed in the 1950s, while atypical antipsychotics, or second-generation antipsychotics, gained approval in the 1990s. Clozapine, considered the standard atypical antipsychotic, was discovered in 1959 and is particularly effective for treatment-resistant schizophrenia. Examples of FDA approved first-generation antipsychotics include haloperidol, chlorpromazine, fluphenazine, perphenazine, and thioridazine. Examples of FDA approved second-generation antipsychotics include risperidone, olanzapine, quetiapine, aripiprazole, and clozapine.

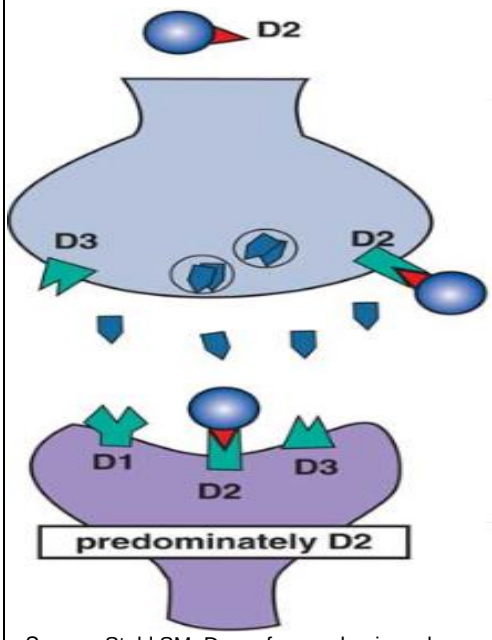
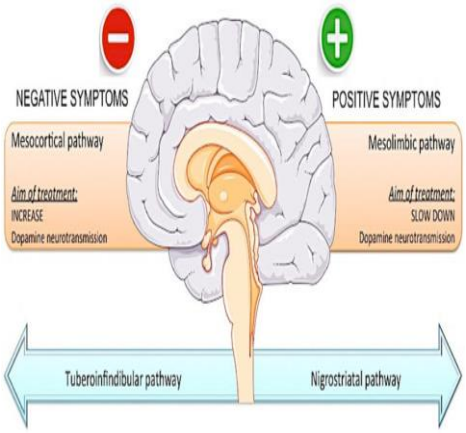
Scene 4	*The Concept of Typicality and Extrapyramidal Symptoms*		
Scene 4a **Please recreate this graphic as shown with animation. Include title and source as footnote.**	**The Concept of Typicality and Extrapyramidal Symptoms**  Source: https://student-nurse-life.com/tag/extrapyramidal-symptoms/		The concept of typical versus atypical antipsychotic was first introduced in the 1960s. Atypicality denotes antipsychotics with lower risks of motor-related adverse effects or extrapyramidal symptoms and hyperprolactinemia. In contrast, typical antipsychotics, by the same definition, are less well-tolerated due to extrapyramidal symptoms and increased risk of hyperprolactinemia. Typical agents are associated with more extrapyramidal symptoms than atypical agents. Extrapyramidal symptoms include dystonia, akathisia, Parkinsonism, and tardive dyskinesia. These symptoms can be very stigmatizing for patients and may require additional treatment.
Scene 4b **Please recreate this graphic as shown with animation. Include title and source as footnote.** **Please recreate this graphic as shown with animation. Include title and source as footnote.**	**Symptoms of Akathisia and Acute Dystonia**   Source: https://student-nurse-life.com/tag/extrapyramidal-symptoms/		Symptoms of akathisia may include restlessness, trouble standing still, pacing of the floor and constant rocking back and forth motion of the feet. Symptoms of acute dystonia may involve grimacing of the face, involuntary eye movements, abnormal posture, and muscle spasms, especially of the tongue, face, neck, and back.

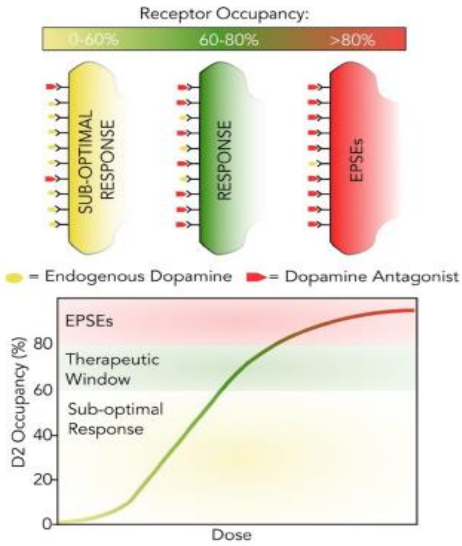
Scene 4c **Please recreate this graphic as shown with animation. Include title and source as footnote.** **Please recreate this graphic as shown with animation. Include title and source as footnote.**	**Symptoms of Pseudoparkinsonism and Tardive Dyskinesia**   Source: https://student-nurse-life.com/tag/extrapyramidal-symptoms/		Pseudoparkinsonism symptoms, include stooped posture, shuffling gait, tremors at rest, rigidity of skeletal muscles, and bradykinesia or slow movements. Tardive dyskinesia can persist even after stopping medications and involves protrusion and rolling of the tongue, chewing motion, sucking, and smacking of the lips, and facial dyskinesia or involuntary and repetitive movements of the mouth and face.
Scene 5	*Other Potential Side Effects and Warnings Associated With Antipsychotics*		
Scene 5a Suggested B roll here or stock footage	B-roll or stock footage https://www.shutterstock.com/video/clip-1102864473-portrait-depressed-woman-sits-on-bed-mess		Both typical and atypical agents carry the risk of neuroleptic malignant syndrome, a rare but potentially fatal condition characterized by symptoms such as rigidity, tremor, fever, and altered mental status. Antipsychotics also have warnings for cardiotoxic effects, such as QTc prolongation and arrhythmias. Other warnings include the potential for seizures and increased mortality risk in older individuals with dementia.
Scene 6	*Definition and Characteristics* of *Typical and Atypical Antipsychotics*		

Scene 6a **Please recreate this graphic as shown with animation. Include title and source as footnote.**	**The Spectrum of Atypia: A New Classification for Atypical Antipsychotics**  Source: Carli M, Kolachalam S, Longoni B, et al. Atypical Antipsychotics and Metabolic Syndrome: From Molecular Mechanisms to Clinical Differences. Pharmaceuticals (Basel). 2021;14(3):238. Published 2021 Mar 8. doi:10.3390/ph14030238		The newly proposed classification system for atypical antipsychotics is based on the concept of spectrum atypia.. Researchers developed this concept in hopes of distinguishing the diversity among atypical agents in terms of their efficacy and motor and endocrine-related side effects. The spectrum ranges from the least atypical agent (or level 1) to the most atypical agent (or level 3), with all the other atypical agents falling within the extremes of this spectrum (or level 2).
Scene 6b **Please recreate this graphic as shown with animation. Include title and source as footnote.**	**The Spectrum of Atypia: A New Classification for Atypical Antipsychotics contd.**  Source: Carli M, Kolachalam S, Longoni B, et al. Atypical Antipsychotics and Metabolic Syndrome: From Molecular Mechanisms to Clinical Differences. Pharmaceuticals (Basel). 2021;14(3):238. Published 2021 Mar 8. doi:10.3390/ph14030238		This proposed spectrum includes the molecular targets of atypical agents, starting with dopamine (D2) and serotonin 5-HT2A and C receptors, which are shared targets among all atypical antipsychotics. It also includes muscarinic (M1) receptors and glycine transporter activity (GlyT), as seen with the mechanism of clozapine. Level 1 and level 2 agents involve additional targets like histaminergic (H1) and alpha receptors, along with brain-derived neurotrophic factor (BDNF).

Scene 7	*Mechanism of Action of Typical and Atypical Antipsychotic Medications*		
Scene 7a **Please recreate this graphic as shown with animation. Include title and source as footnote.**	**Mechanism of Action of Antipsychotics**  Source: Grinchii D, Dremencov E. Mechanism of Action of Atypical Antipsychotic Drugs in Mood Disorders. *International Journal of Molecular Sciences*. 2020; 21(24):9532. https://doi.org/10.3390/ijms21249532		Atypical antipsychotics differ in terms of efficacy and potential side effects based on their affinity for serotonergic 5HT2A/D2 and 5HT2C/D2 receptors, as well as their fast dissociation from the D2 receptor. They are categorized as weak dopaminergic D2 receptor blockers, and their mechanism extends beyond dopamine D2 antagonism to involve other receptors, particularly serotonin (5HT2A) receptors.
Scene 7b **Please recreate this graphic as shown with animation. Include title and source as footnote.**	 Source: Kapur S, Zipursky R, Jones C, Remington G, Houle S. Relationship between dopamine D(2) occupancy, clinical response, and side effects: a double-blind PET study of first-episode schizophrenia. Am J Psychiatry. 2000;157(4):514-20		In contrast, typical antipsychotics work by inhibiting dopaminergic neurotransmission, with optimal efficacy achieved by blocking around 72% of the brain's dopamine D2 receptors. Additionally, they also affect noradrenergic, muscarinic, and histaminergic systems.

Scene 8	*Etiology of Schizophrenia Symptoms and MOA of Antipsychotics*		
Scene 8a **Please recreate this graphic as shown with animation. Include title and source as footnote.**	**Etiology of Schizophrenia Symptoms**  Source: https://www.researchgate.net/figure/An-Overview-to-Symptoms-and-Etiology-of-Schizophrenia-Schizophrenia-is-a-complex-and_fig1_322256052		Dopamine plays a critical role in schizophrenia, a psychiatric disorder characterized by positive symptoms of hallucinations, delusions, and negative symptoms of apathy, and cognitive impairment.
Scene 8b **Please recreate this graphic as shown with animation. Include title and source as footnote.**	 Source: https://psychopharmacologyinstitute.com/publication/mechanism-of-action-of-antipsychotic-agents-2094		Reduced cortical dopamine release is linked to cognitive impairment and negative symptoms, while abnormalities or excess in striatal dopamine contribute to positive symptoms. Blocking striatal dopamine D2 receptors is essential for symptom relief, especially positive symptoms. However, antipsychotics can impact other receptors, including serotonin, histamine, acetylcholine, and norepinephrine, thus affecting their efficacy and potential for side effects.

Scene 9	*Efficacy of Typical and Atypical Antipsychotics in Treating Various Psychiatric Conditions*		
Scene 9a **Please recreate this graphic as shown with animation. Include title and source as footnote.**	**Antipsychotic binding at the Dopamine D2 receptor**  Source: Stahl SM. Drugs for psychosis and mood: unique actions at D3, D2, and D1 dopamine receptor subtypes. CNS Spectrums. 2017;22(5):375-384. doi:10.1017/S1092852917000608		All approved antipsychotics bind to dopamine D2 receptors at therapeutic doses, which is crucial for their effectiveness.
Scene 9b **Please recreate this graphic as shown with animation. Include title and source as footnote.**	**Dopaminergic Hypothesis of Schizophrenia**  Source: https://www.researchgate.net/figure/An-Overview-to-Symptoms-and-Etiology-of-Schizophrenia-Schizophrenia-is-a-complex-and_fig1_322256052		Atypical antipsychotics have broader efficacy than typical ones, treating various psychiatric symptoms including positive, negative, mood, and suicidal symptoms. Their diverse mechanism of action and ability to target multiple receptors and neutrophils may lead to synaptic plasticity in the brain over time. Typical agents primarily target positive symptoms through dopamine D2 receptor blockade.

Scene 9c **Please recreate this graphic as shown with animation. Include title and source as footnote.**	 Source: Kaar SJ, Natesan S, McCutcheon R, Howes OD. Antipsychotics: Mechanisms underlying clinical response and side-effects and novel treatment approaches based on pathophysiology. Neuropharmacology. 2020;172:107704. doi:10.1016/j.neuropharm.2019.107704		Studies show that achieving dopamine D2 receptor blockade above 50% occupancy is crucial for a higher chance of clinical response. However, occupancy exceeding approximately 85% increases the risk for extrapyramidal symptoms in schizophrenia. In addition, a therapeutic range of 60% to 80% D2 occupancy is suggested to increase the chances of eliciting a clinical response and reduce potential for extrapyramidal symptoms. Currently, only clozapine and aripiprazole, a partial dopamine agonist, are the exception to this pattern.

Scene 10	*Considerations and Conclusion*		
Scene 10a Suggested B roll here or stock footage	B-roll or Stock footage https://www.shutterstock.com/image-photo/one-person-answering-question-about-clozapine-1864354120 B-roll or stock footage https://www.shutterstock.com/image-photo/one-person-answering-question-about-clozapine-1865171983 B-roll or stock footage https://www.shutterstock.com/video/clip-1065349579-during-visit-young-female-doctor-white-coat		For atypical agents such as olanzapine and clozapine which carry greater risk for metabolic syndrome, clinicians are encouraged to look for ways at preventing or reducing these effects either by recommending physical exercise, and diet, which have shown some effectiveness when implemented in feasible and affordable ways for patients. Clinicians are also encouraged to weigh both the benefits and tolerability of these medications, as current options for individualized treatment rely on careful clinical observation and assessment, especially for agents like clozapine which has increased monitoring parameters due to increased risk for agranulocytosis and myocarditis.
Scene 10b Suggested B roll here or stock footage	B-roll or stock footage https://www.shutterstock.com/video/clip-25541747-researcher-wet-plant-seedling-biological-research-genetic		Emerging treatment options based on pharmacogenetic tests or biomarkers may hold promise for personalized antipsychotic selection; however, their implementation remains limited.

References:

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12. Solmi M, Murru A, Pacchiarotti I, et al. Safety, tolerability, and risks associated with first- and second-generation antipsychotics: a state-of-the-art clinical review. *Ther Clin Risk Manag.* 2017;13:757-777. Published 2017 Jun 29. doi:10.2147/TCRM.S117321