Schizophrenia

CPA 2017

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Contents

1 – Assessment & Diagnosis

Diagnosis of Schizophrenia

- **Duration >6 months** → with ≥1 month active-phase sx

5 key features	First-rank sx (Schneider)	Negative sx
• **Delusions** • **Hallucinations** • Disorganized thinking • Grossly disorganized or abn motor behavior • Negative symptoms	• Auditory hallucinations • Somatic hallucinations • **TI/TW/TB** • **Delusional perception**	• **Affecting flattening** • **Avolition** • Alogia • Anhedonia

Diagnosis of Schizophrenia

- Most reliable method of diagnosis
  - **Structured clinical interviews**
  - PLUS information from **multiple informants**
  - PLUS review of previous **medical records**

- Structured clinical interviews (better than unstructured)
  - **DSM5 Structure Clinical Interview** → good reliability
  - **Schedule for Affective Disorders and Schizophrenia for School-Age Children** (most widely used for adolescents)

Methods

- 1) Setup phase
  - Stakeholders
  - Endorsement bodies (CPA, Schizophrenia Society of Canada)
- 2) Adaptation phase
  - NICE, SIGN, APA, AACAP, EPA reviewed
  - English guidelines published after 2010
  - AGREE II tool
  - 3 suitable guidelines
- 3) Working groups
- 4) Finalization phase

[1] Assessment & Care Planning

- Initial comprehensive multidisciplinary assessment
  - Full MSE
  - Risk of suicide, aggression
  - Psychiatric hx, treatment hx
  - Substance use
  - Psychosocial development, neurodevelopment
  - Current functioning
  - Medical hx

- Include collateral information

[2] Assessment of the First Episode of Psychosis

- See new pts **within 2 weeks** of referral
  - Comprehensive assessment
  - Family hx of psychiatric disorders
  - Longitudinal assessment of behavior changes, course of psychosis sx
  - Relationship of substance use to psychotic sx
  - Developmental history → prognostic value
  - Duration of untreated psychosis → prognostic value

- Include family members if possible, with conset

[3] Neuropsychological Assessment

- Neuropsychological testing suggested for:
  - **First episode of psychosis**
  - **Poor response to treatment**

  - Important for treatment + academic planning
  - Robust predictor for overall level of functioning

  - **MATRICS consensus cognitive battery** (US FDA, NIMH)
    - Any mental health professional (ideally neuropsychologist)

[4] Brain Imaging

- Consider on **case-by-case basis** for first episode psychosis
  - Based on aspects of history, neurological exam, neuropsych results
  - If sx of **intracranial pathology**
    - Headaches, N/V, seizure-like activity, later age at onset
  - If sx of **autoimmune encephalitis** → **MRI**
    - Rapid progression of working memory deficits (over <3 mos)
    - New focal CNS findings
    - Unexplained seizures

- Routine neuroimaging **NOT justified** (CT or MRI)
  - Findings do not alter clinical management in meaningful way
  - Risks of radiation exposure, delay in treatment

[5] Genetic Testing

- Consider genetic testing based on Hx + P/E
  - Esp at **first episode of psychosis**
  - Lack diagnostic specificity, but certain copy number variants (CNV)s
    - **Chromosome 22q11** → more prevalent in schizophrenia
    - May help dx rare conditions (with medical/psych implications)
    - May inform psychiatric genetic counselling

- 22q11.2 deletion
  - Of adults with deletion → **25% have schizophrenia**
    - Of population with schizophrenia → **1-2% have deletion**
  - **Similar clinical features** of schizophrenia (vs without deletion)
  - Syndrome → hypernasal speech, learning difficulties, heart defects
  - **Facial features** → long + narrow face, narrow palpebral fissures, flat cheeks, prominent nose, small ears, small mouth, retruded chin

[6] Ongoing Assessment of Positive + Negative Sx

- Assess q3mo in stable pts
  - Use **quantitative measure** for both positive/negative sx
  - Reassess severity **after change in treatment**
  - Important for selecting pts for **clozapine**

- Distinguish negative sx of schizophrenia vs other causes
  - Depression, anxiety, cognitive impairment
  - Neurological disorders, drug SE, substance use

- Scales
  - **PANSS** (Positive and Negative Syndrome Scale)
  - **BPRS** (Brief Psychiatric Rating Scale)
  - **CDSS** (Calgary Depression Scale for Schizophrenia)

[7] Ongoing Assessment of Suicide Risk

- Active reassessment for those at risk
  - Current suicidal ideas, plans, intent (active/passive)
  - Delusions, hallucinations → related to suicide, risk of harm
  - Hopelessness, impulsivity
  - Access to suicide methods (firearms)
  - Reasons for living (responsibility to others, religious beliefs)

- Suicide Risk Assessment Guide
- **Columbia Suicide Severity Rating Scale**
  - Reliable, valid tool → research + clinical settings

[7] Ongoing Assessment of Suicide Risk

- Lifetime risk of suicide in schizophrenia **= 5%**

- Risk factors for suicide in schizophrenia
  - Previous **depressive disorders**
  - Previous **suicide attempts**
  - **Drug** misuse
  - **Poor adherence** to treatment
  - **Agitation** or motor restlessness
  - Fear of **mental disintegration**
  - **Recent loss**
  - **Command hallucinations** (but not hallucinations in general)

[8] Ongoing Assessment of Risk of Aggression

- Detailed assessment
  - Current aggressive/psychotic ideas (physical, sexual, homicide)
  - **Impulsivity, anger management** issues
  - Access to **firearms, weapons**
  - **Specific individuals/groups** whom aggressive expressed towards

- Aggression in schizophrenia
  - Incr rates of **violent crime, suicide, premature mortality**
  - Assoc with **violence, violent offending** (esp **homicide)**
    - Most of excessive risk assoc with **substance abuse comorbidity**
    - More common in **less developed countries**
  - Antipsychotics → **decr risk of violence + crime** (in schizophrenia)

- Clinical features assoc with violence
  - **Psychotic sx** (persecutory ideation)
  - In first episode → **drug misuse, high psychopathology scores**
    - Overall physical violence towards others UNCOMMON

[9] Ongoing Assessment of Substance Use

- Regular assessment of substance use
  - Particular substance (quantity, frequency, pattern, route)
  - Level of dependence, duration of current level of use
  - Impact on **medication adherence**
  - **Readiness to change**
  - Urine toxicology NOT routine → for acute situations, tx planning

- Integrated treatment of psychosis + SUDs
  - Use specified interventions for SUDs

- Screening tools
  - DSM5 recommends **NIDA-Modified ASSIST**

[10] Involvement of Pt in Tx Decision Making

- Shared decision making (initial evaluation + ongoing tx)
  - Differential dx, risks of untreated illness, tx options + risk/benefits
  - Ask pt about **tx-related preferences**
  - Discuss **relapse prevention**

2 – Pharmacotherapy

Principles of Guideline

- 1) Schizophrenia is a **heterogeneous group** of disorders
- 2) **Psychosis** is common + integral to diagnosis
- 3) **Antipsychotics** → central role
- 4) Psychotic sx can **wax + wane**, influencing tx
- 5) **Other sx domains** can be observed

[A1] Use of Antipsychotics

- Antipsychotic medications **should be recommended**
  - Limited data assessing outcomes
  - Ethical concerns for placebo-controlled trials
  - 3 meta-analysis → modest assoc, limited long-term data
    - **Shorter duration of untreated psychosis**
    - **Improved outcomes**

[A2] Antipsychotic Choice

- Choice of antipsychotic **made together** by pt + physician
  - Included carer if possible, provide information, risk/benefits, SE

- **NO established superior antipsychotic for FIRST-EPISODE**
  - No differences in efficacy or discontinuation rates (FGA vs SGA)
  - SGA better for all-cause discontinuation (NNT = 12)
  - Side effects more pronounced in first-episode (AP-naïve)
  - **Higher response rates** in first-episode (may have ceiling effect)

[A3] Acute Antipsychotic Treatment

- Continue medication for **at least 2 weeks**
  - Unless significant tolerability issues
  - Assess dose + response during early phase
    - If poor response → assess adherence + substance use
  - If **no response after 4 weeks** despite optimization
    - Consider changing antipsychotic
  - If **partial response** → reassess **after 8 weeks**

- Adherence strategies
  - Psychoeducation, simplified dosing, blister packs, dosettes
  - Caregiver support, pill counts, therapeutic drug levels
  - **Earlier LAI use** (not just for non-adherence)

[A4] Antipsychotic Dose + Trial Duration

- Target **lower effective dose range** in first-episode
  - Titrate according to efficacy + tolerability

- Adequate trial = **6 weeks** (at therapeutic dose)
  - "Therapeutic dose" = **≥midpoint of licensed dose range**
  - After initial titration phase of several weeks

- Inadequate trials
  - Inadequate dose, trial duration
  - Medication non-adherence
  - Comorbid substance abuse
  - (determining treatment resistance, clozapine eligibility)

[A5] Antipsychotic Continuation

- **Maintenance tx for ≥18 months** with antipsychotics
  - Following resolutions of **positive sx** of first-episode

- Of first-episode → **1-20% single episode**

- High relapse rates if antipsychotics stopped
  - Despite attaining remission or stabilization with maintenance tx
  - Among tx responders → **82% relapse within 5 years**
    - If NOT taking medication → **5x risk of relapse**

[B1] Acute Exacerbation of Schizophrenia

- Continue med changes **for ≥4 weeks** if acute exacerbation
  - Unless significant tolerability issues
  - If **partial response at 4 weeks** → reassess at **8 weeks**

- Waxing-waning course of schizophrenia
  - APs diminish risk (not eliminate)
  - Worsening sx → **AP non-adherence, substance abuse**
    - Does NOT constitute failed AP trial
    - May consider switch to **depot AP**
  - Relapse can occur without clear risk factors
    - May need higher doses or switch AP
  - If **2 failed** adequate AP trials → **treatment-resistance schizophrenia**
    - **Clozapine** becomes treatment of choice

[C1] Maintenance Antipsychotic Dose

- Risperidone 4-6 mg equivalent (CPZ 300-400 mg)
  - Only empiric way for equivalency → **D2 occupancy neuroimaging**
  - Not possible with some APs due to pharmacology
    - Aripiprazole, clozapine, quetiapine
  - Dosing may be affected by stage of illness, age

[C2] Maintenance Duration of Treatment

- Maintenance AP tx for **at least 2 years**, up to 5+ years
  - Benefit of AP tx in relapse prevention
    - **Lower hospitalization rates**, improved QoL
    - **No sig benefit of SGA vs FGA**
    - But more AP-related SE

- Stabilization does NOT confer immunity to relapse
  - Stabilization with AP for 1 year → **82% relapse after 5 years**

[C3] Maintenance Antipsychotic Delivery

- Option of **oral or depot**, based on pt preference
  - Not always possible (community treatment orders)

- **LAI should be offered to ALL**
  - Earlier use now (not just for non-adherence)
  - **Better symptom control**
  - Superior for **reducing relapse** (6x at 1 year)
  - **Reduced risk of rehospitalization** (1/3 after 7 year)
  - (study efficacy vs effectiveness)

[D1] Clozapine in TRS

- Clozapine should be **offered to all with TRS**
  - Among schizophrenia pts → **25-30% TRS**

- For TRS → **clozapine is ONLY recommended tx**
  - **30-60% response** rate with clozapine
  - High dose AP, switching, combined AP → no consistent evidence
    - May in fact delay clozapine

[E1] Definition of Clozapine-Resistance Schizophrenia

- Treatment-resistance after adequate clozapine trial
  - Persistence of **2+ positive sx of moderate severity**
  - OR persistence of **1+ positive sx of severe severity**

- Adequate trial
  - Oral AP → ≥6 weeks, midpoint dose+
  - Depot AP → ≥6 weeks, steady state
  - Clozapine → **8 weeks, ≥400 mg** (preferably 12 weeks)
    - If once daily → trough levels ≥350 ng/mL (1100 nM/L)
    - If divided doses → trough levels ≥250 ng/mL
  - **Documentation of adherence**
    - Pill counts, dispensing chart review, plasma levels

[E2] Definition of Clozapine-Resistance Schizophrenia

- Strategy for assessment of response to AP
  - Emphasis on **positive sx severity + response**
    - Was used in landmark study of clozapine in TRS
    - Moderate severity on 2/4 BPRS items

[E3] Treatment Options in CRS

- NO recommendations
  - No meta-analyses for clozapine-augmentation
  - **Insufficient evidence** (other APs, ECT in RCTs)

[F1] Aggression + Hostility

- Based on pt preference, pt factors, treatment factors
  - Previous AP tx, SE profiles, medical history
  - If TRS + aggression/hostility → trial of clozapine

- Risk factors for aggression in psychosis
  - **90% with schizophrenia**
  - No systematic analysis for treatment

- Clozapine may be preferred for psychosis + aggression
  - 4 RCTs → all found clozapine superior in tx of aggression
    - Esp if TRS

[F2] Comorbid Depressive Symptoms

- If meets criteria for depressive disorder, **use guidelines**
  - Including use of **antidepressants**

- Depression COMMON at all stages of schizophrenia
  - Freq **occur prior to onset of psychotic sx**
    - In schizophrenia, first-episode, chronic

3 – Psychosocial Treatments

General Principles of Psychosocial Treatment

- 1) Integration of medical + psychosocial interventions
- 2) Address many aspects of recovery
- 3) Therapeutic alliance can improve engagement/adherence
- 4) Encourage realistically hopeful attitude
- 5) Recovery framework for quality of life
- 6) Shared goals
- 7) Specific skills for effective delivery of interventions
- 8) Support self-management skills
- 9) Address comorbid conditions
- 10) Consider pt + family preferences

Summary of Psychosocial Interventions

Summary of Psychosocial Interventions for Schizophrenia		
Modality	*Recomm.*	*Evidence*
Family Intervention	**OFFER TO ALL**	*Strong, RCT*
Cognitive Behavioral Therapy	**OFFER TO ALL**	*Strong, RCT*
Supported Employment	**OFFER**	*Effective*
Cognitive Remediation	**Consider**	*Limited*
Social Skills Training	**Make available**	*Limited*
Life Skills Training	**Make available**	*Limited*
Patient Education	**Provide**	*Limited*

[1] Family Intervention

- Family intervention should be **offered to all**
  - If close contact with family members
  - Esp if **persistent sx or high risk of relapse** → PRIORITY!
  - Minimum → 10 sessions over 3 months
    - Communication skills, problem solving, psychoeducation
    - Crisis management, relapse prevention
- **STRONG evidence** for efficacy (RCTs)
  - **Reduces sx severity**
  - **Decr hospitalizations**

[2] Supported Employment Programs

- Offer **supported employment programs**
  - To those wishing to find/return to work
  - **MOST EFFECTIVE vocational rehab method**
    - To obtain employment or any occupation
    - More effective than prevocational training to incr employment
  - Individually tailored job development, rapid job search
  - Ongoing job supports, **integration of vocational + MH services**

- Consider occupational/educational/prevocational activities
  - If unable to work or unsuccessful in finding employment

[3] Employment Partnerships

- Mental health services should work with local stakeholders
  - Enable pts to stay in **work or education**
  - Access new **employment, volunteering, education**

- Employment
  - Financial benefits, meaningful activity
  - Sx benefit, psychological well-being

[4] Cognitive Behavioral Therapy for Psychosis

- CBT for psychosis should be **offered to ALL**
  - If **not adequately responding to AP**
  - AND having **persisting sx (incl anxiety, depression)**
  - Can be started during initial, acute or recovery phases
  - Can be done in inpatient settings

- RCT evidence for **EFFECTIVENESS**

[5] CBT should provided by trained therapists

- Follow established protocols with regular supervision
  - Collaborative manner, CBT principles
  - Minimum **16 sessions** (individual or group)

[6] Cognitive Remediation Therapy (CRT)

- CRT may be considered if persisting cognitive difficulties
  - Goal to reduce attention, memory, problem solving deficits
  - **Limited evidence** for effectiveness

[7] Social Skills Training

- Available to those having difficulties with social interaction
  - Incl assoc **stress + anxiety**

- Social skills training
  - Improve interpersonal skills
  - Conversation, making friends, job interviews, assertiveness
  - Verbal/nonverbal aspects of social behavior
  - Modeling, role-playing, behavioral rehearsal
  - Corrective supportive feedback, behavioral homework

- **Limited evidence** of effects
  - ? positive sx, hospitalization, relapse
  - Availability important

[8] Life Skills Training

- Available to those having difficulties with self-care
  - Incl housekeeping, transportation, financial management
  - May have deficits in ADLs/IADLs

- Life skills training
  - Assessment, feedback, structure homework
  - Few RCTs → **not strong evidence** for effectiveness
  - Availability still important

[9] Patient Education

- Appropriate education about schizophrenia + treatment
  - Nature, treatment, recovery → should be integral part of treatment
  - **NO robust effect** on treatment outcomes
    - Symptoms, relapse, rehospitalization, adherence, insight
  - Still provide → ethical concerns
    - Facilitate empowerment, **informed decision making**

New developments

- Insufficient research literature for recommendations
  - Mindfulness interventions
  - Avatar therapy
  - Social cognitive skill training
  - Acceptance & Committeemen Therapy
  - Individual & group peer support
  - Compassion-focused therapy
  - Interventions for common comorbidities (anxiety, depression)

4 – Coexisting Substance Use Disorders

Coexisting Substance Use Disorders

- **Prevalence of SUD** among schizophrenia = **45-47%**
  - (excluding nicotine, caffeine use disorders)

- **Cigarette smoking** among schizophrenia = **60-90%**

- Cannabis, stimulant use → development of psychotic sx
  - Cannabis use → **independent risk factor** (for persistent psychosis)
    - Esp if **genetic risk** for schizophrenia, or **prev psychotic sx**
    - **Regular use in adolescence** → sig incr risk of psychotic sx
      - Even after 1 year of abstinence
      - (presence of psychotic sx does NOT incr risk of cannabis use)
    - Psychosis develops **2.7 years earlier** (vs no cannabis)

Coexisting Substance Use Disorders

- Negative impact on course of schizophrenia
  - More positive sx, more depression
  - Higher rates of non-adherence, higher relapse rates
  - More service utilization

- Unclear effect on neurocognitive effects of psychosis
  - May induce over psychosis in less cognitively vulnerable
  - So potential for improved function with abstinence

- Indictors of underlying psychotic disorder
  - **Persistence** of psychotic sx with abstinence
  - **Sx out of keeping** with type/amount of substance used
  - **Family hx of** schizophrenia
  - **Typical positive sx** of schizophrenia
  - Presence of **negative/cognitive sx**

[1] Non-judgemental, respectful approach

- Flexible, motivational communication → consider
  - Stigma, discrimination assoc with psychosis, substance use
  - Attempts to conceal conditions
  - Fear of being detained, imprisoned, forced treatment
  - Fear of children being taken
  - Fear of being “mad”

[2] Maintain confidentiality, privacy, dignity

- Avoid clinical language without adequate explanation
- Provide independent interpreters
- Aim to preserve **continuity of care**
- Foster therapeutic relationship

[3] Cultural + ethnic sensitivity

- Competent health care professionals
  - Work with families, carers, significant others

[4] Work with local organization

- Local minority, ethnic groups
  - Help support + engage pts with psychosis + coexisting substance use
  - Offer information + training

[5] Offer written + verbal information

- Appropriate to level of understanding
  - About psychosis, substance use
  - Risks assoc with substance use → negative impact on psychosis

[6] Engage families, carers, significant others

- Involve in treatment
  - Offer **family intervention** if living together or close contact with pt
    - Well-established evidence for improving outcomes in scz

[7] Offer carer's assessment

- <u>For families, carers, significant others</u>
  - Caring, physical, social, MH needs
  - Care plan

[8] Offer written + verbal information to supports

- <u>For families, carers, significant others</u>
  - About nature + treatment of psychosis + substance use
  - How they can support

[9] Do not exclude pts with psychosis because of SUD

- From age-appropriate MH care

[10] Do not exclude SUD pts because of psychosis

- From age-appropriate SUD care

[11] MH HCP should treat both conditions

- Integrated substance use + psychosis tx
  - Provided in MH setting → may lead to be outcomes
    - Compared to parallel or sequential fashion
  - **Specialized concurrent disorder programs** IDEAL
    - If none → **specialized psychosis tx program**
  - Addiction tx beyond typical EPI → NOT more effective
    - Many may stop substance use on own
    - Commonalities between tx (usual vs specialized)
    - Substance use tx not match to stage of change
    - Potential negative sx or cognitive deficits affecting tx
    - Overemphasis on group-based tx

[12] Routinely ask about substance use

- HCP in all settings, pts with known/suspected psychosis
  - Particular substance (quantity, frequency, pattern, route, duration)

[13] Routinely assess for possible psychosis

- HCP in all settings, pts with known/suspected SUDs
  - Seek collateral (if possible, permission)

[14] Offer comprehensive, multidisciplinary assessment

- May take place over several meetings
  - General psych hx
  - Psychosis hx
  - Substance use hx
  - Legal hx
  - Risk assessment

[15] Review change in substance use

- Include changes in effects of substance use over time
  - Patterns of use
  - Mental + physical state
  - Circumstances, treatment
  - Share summary with person

[16] Assess needs of dependent children

- If pt is carer of children or young people

[17] Develop child protection plan if serious concerns

- If pt is carer of children or young people

[18] Assess home situation for vulnerable adults

- If pt is responsible for vulnerable adults
  - Ensure safe-guarding procedures

[19) Assess needs of younger carers or dependents

- Initiate safe-guarding where appropriate

- Consequences of substance use
  - Worsening psychotic sx
  - Tx non-adherence
  - Interactions with prescribed agents
  - Medical comorbidity
  - Incr service utilization
  - **Incr suicides**
  - **Incr violence**
  - Premature death

[20] Monitor physical health

- Consider impact of alcohol + drugs
  - **At least yearly monitoring**
  - More freq if significant physical illness or risk of physical illness

- Pts with schizophrenia → die up to **20 years earlier**
  - Majority due to **cardiovascular factors**
  - Cigarette smoking likely primary modifiable CV risk factor
    - More frequent, smoke more, more often nicotine dependent

[21] Offer help to stop smoking

- Even if previous unsuccessful attempts
  - Consider effect of smoking reduction on **drug metabolism**
    - Esp clozapine, olanzapine (stopping will incr levels)

[22] Smoking cessation strategies

- 1) Nicotine replacement therapy
  - Combination patch + short-acting (inhaler, gum, lozenge, spray)

- **2) Bupropion** → for schizophrenia **(most evidence)**
  - SE → sleep impairment, suicidality, re-emergence of psychotic sx

- 3) Varenicline → greatest efficacy in gen pop
  - Risk of suicidality, re-emergence of psychosis
  - Less evidence → **recommended SECOND** to bupropion

- If bupropion or varenicline
  - Incr risk of adverse neuropsychiatric sx (esp **first 2-3 weeks**)

- If precontemplative/contemplative → use brief MI style

[23] Offer information about local support groups

- To families, carers, significant others

[24] HCPs should seek effective support

- Work in team-based settings
  - Seek supervision
  - Staff support groups

[25] PCP should refer psychosis + SUD to MH

- For assessment + further management

[26] Ensure HCP competent

- In RECOGNITION of pts with psychosis + SUD

[27] HCP should consider supervision, consultation

- For management of psychosis + coexisting SUD
- Consider additional training from specialists

[28] Consider specialist advice, joint management

- If pt with psychosis AND:
  - Severe SUD
  - Multiple moderate SUDs
  - IV substance use
  - Serious social disruption (homelessness, family breakdown)

[29] Coordinate delivery of care + transfer

- To maintain engagement + ongoing care

[30] Offer evidence-based tx for both conditions

[31] Ensure informed consent

- If doubts → assess mental capacity

[32] No superior AP for psychosis + SUD

- SGA may be better tolerated (less EPS)
  - SGA LAI may be better tolerated (vs FGA LAI)
    - No difference demonstrated yet for SGA LAI vs oral
  - CATIE → SGA may have greater benefit for those who discontinue illicit substance use (vs those who continue)

- Clozapine NOT recommended over other APs

- If psychosis does not resolve rapidly with abstinence
  - Follow **first episode guidelines**

- SCZ + AUD → **naltrexone, acamprosate** (disulfiram)
- Cocaine use disorder → TCAs NOT recommended
- Cannabis use disorder → NO benefit non/pharm treatments

Psychosocial Treatments

- Demonstrated efficacy for SUDs → use if available
  - Contingency management
  - CBT/relapse prevention
  - Motivational interviewing
  - Combination CBT + MI
  - Brief intervention
  - Family intervention
  - Assertive community treatment

[33] Do NOT exclude from CM because of psychosis

- Optimal duration uncertain → longer typically better

[34] Substance use services should recognize psychosis

- HCP in substance use treatment services
  - Recognize signs + symptoms of psychosis
  - Able to conduct MH needs + risk assessment
  - Know when to refer to mental health services

[35] Offer MH assessment at substance use treatment

- Comprehensive, multidisciplinary MH assessment
  - In addition to substance use assessment

[36] Collaboration between services

- Substance use + psychosis treatment services
  - Joint meetings
  - Advice, consultation, training for tx of SUD
  - Treatment protocols for schizophrenia + SUD

[37] Inpatient MH → free from cigarettes, drugs, alcohol

- Policies + procedures to promote therapeutic environment

[38] Inpatient MH → assess substance use/withdrawal

- For all pts at point of admission

[39] Inpatient MH drug testing

- Only for **assessment + treatment planning**

[40] Inpatient MH offer NRT

- Even for those who do NOT want to stop smoking
  - Reduce or temporarily stop smoking
  - Detoxication alone does NOT change treatment outcomes for scz
    - Important part of coordinated tx plan

[41] Inpatient MH → Planned Detoxification

- <u>ONLY if:</u>
  - Involvement of **substance use treatment** services
  - **Inpatient setting**
  - Part of overall **coordinated treatment plan**

[42] Inpatient MH → do NOT discharge b/c substances

- Do not discharge solely because of substance use

[43] Inpatient MH → if discharged

- Ensure:
  - Identified **care coordinator**
  - **Care plan** → psychosis + SUD needs
  - Information about **overdose risk**
    - Esp opioids/benzos that have been reduced/stopped

5 – Pharmacotherapy in Children & Youth

Pharmacotherapy in Children & Youth

- Schizophrenia spectrum disorders
  - Often have onset in **adolescence**
  - Significantly interfere with normal **developmental trajectory**

- Psychotic experiences
  - May be **normal variant in very young children**
  - May be manifestation of medical etiology or other psychiatric cause
    - Primary mood, anxiety disorder, OCD, PTSD
  - **If transient/attenuated psychotic sx**
    - May be at high risk for **developing psychosis + schizophrenia**

- Semistructured interviews
  - **Schedule for Affective Disorders and Schizophrenia for School-Age Children**
  - **Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS)**

Pharmacotherapy in Children & Youth

- Childhood-onset schizophrenia (age <12)
  - Rare → 1.6 – 1.9 per 100,000

- Early-onset schizophrenia
  - Rapid incr prevalence **after age 14** → esp **males**
  - **25% of all psychiatric admission** age 10-18
  - Similar phases to adult-onset → but **more severe psychopathology**
    - If untreated → major morbidity
  - **Higher suicide risk**
  - May have poorer prognosis
    - 30% requiring long-term intensive support
    - Also if low premorbid social function, insidious onset, lower intellectual function, negative symptoms

Pharmacotherapy in Children & Youth

- Treatment → psychosocial + pharmacological
  - Limited, but increasing, evidence for APs in children + youth
  - Heightened vigilance to confirm dx
    - Higher medical + psychiatric morbidity due to scz
    - More sensitive to medication SE (metabolic, EPS)

General Principles of Care

- Expertise working with youth + families
- Ongoing assessment of capacity to make tx decisions
- Tx decisions in partnership with youth + caregiver
- Foster autonomy + active participation
- Ongoing psychoeducation
- Address impact of barriers (comorbidity, stigma)
- Consider developmental level, emotional maturity, cognitive capacity, sensory deficits, language development
- Culturally competent setting
- Maintain continuity of care
- Consistency of therapeutic relationships

First Episode Psychosis

- [1] Urgently refer first episode MH service
  - All children + youth with **sustained psychotic sx (>4 weeks)**
  - Earlier detection + shorter duration of untreated psychosis
    - Benefits to executive function
    - Improved positive outcomes with longitudinal follow-ups

- [2] APs for first episode with psychiatric consultation
  - **Should NOT be started in primary care**
    - Done in consultation with psychiatrist with C&A training
    - Biopsychosocial management plan
  - Increasing prescription **of APs in C&A (often off label)**
    - Often for non-psychotic, non-bipolar disorders
    - Risk of side effect + burden

First Episode Psychosis

- [3] Offer APs in conjunction with psychosocial tx
  - For first episode → APs + psychological/psychosocial tx

- One-third of adults with SCZ → **onset before age 18**
  - Early onset → **worse prognostic factors**
    - More severe expression of illness
    - Lower premorbid social/emotional adjustment
    - More negative sx, cognitive impairments
    - Longer treatment delays
  - **Antipsychotics as effective as with adults**
    - Offer once diagnosis confirmed

First Episode Psychosis

- [4] Choose AP jointly with pt + parents/carers
  - If younger children → with just parents/carers
  - Provide **age-appropriate information**, risk/benefits, SE
    - Metabolic, EPS, CV, hormonal, drug interactions
  - Monitoring paramount
  - **No superior antipsychotic agent/formulation**
    - (except clozapine)

First Episode Psychosis

- [5] Clinical situations where ECG suggested
  - Specified by Health Canada drug monograph
  - **Specific cardiovascular risk** on physical exam (high BP)
  - **Personal hx of CVD**
  - Family hx of **premature sudden cardiac death, prolonged QT**

- Schizophrenia spectrum disorders → **2-3x mortality**
  - Regardless of age at onset
  - Mostly related to **CV illness or obesity-related cancer**
  - APs contribute to CV morbidity/mortality
    - Duration of lifetime exposure

First Episode Psychosis

- [6] Explicit individual therapeutic trial of APs
  - Most/least tolerable side effects
  - Expected benefits/risks, indications for changes
  - Start with **lower dose** than lowest licensed adult range
  - Justify/record reasons for dosages if above recommended
  - Rationale for medication changes/continuation
  - Trial = **optimal dose for 4-6 weeks**

First Episode Psychosis

- [7] Monitoring of physical health + AP effects
  - Clearly establish between primary + specialty care
    - Standardized scales → incr effectiveness, decr nonadherence
  - Early-onset psychosis → **more vulnerable than adults**
    - More severe illness, neurodevelopmental deficits
    - Incr risk of adverse events (related to pharmacotherapy)
  - May have **potential positive response at lower doses**
    - Slow dosing, target to efficacy (not weight)
    - Avoid abrupt switches (minimize rebound phenomena)
  - Treatment resistance → lack of satisfactory improvement
    - **After 6-8 weeks** of adequate dose (consider confounders)

First Episode Psychosis

- [8] Discuss nonprescribed therapies
  - That pt, parents or carers wish to use (complementary therapies)
    - Discuss safety, efficacy, possible interference
  - **Lack of alliance** → may predict poor engagement
    - Nonadherence, rehospitalization, severity of sx, dropout rates
    - Youth esp vulnerable to drop-out in first years

First Episode Psychosis

- [9] Discuss substance use
  - Cannabis, alcohol, tobacco, drugs, prescription meds
    - Possible interference with non/pharm tx
  - Stimulants, cannabis
    - Harmful effects across spectrum of psychotic disorders
    - Trigger onset, worsens psychotic sx, precipitate relapse
    - **Any use of cannabis → 40% greater risk** of psychotic disorder
  - Nicotine, alcohol → incr morbidity risks
    - Cardiovascular illness, obesity-related cancer

- [10] Do NOT initiate regular combined APs
  - Only short periods when changing medication
  - No evidence in youth

Early Post-Acute Period

- [11] Review AP meds regularly
  - Benefits, side effects
- [12] Make plans for recovery + possible future care
  - Early period of recovery, reflect on episode + impact
  - Realistically optimistic approach
- [13] Inform high relapse risk if medication stopped
  - High relapse risk **within 1-2 years** after acute episode
- [14] Discontinue/taper AP gradually
  - Monitor regularly for relapse

Early Post-Acute Period

- [15] Continue to monitor after discontinue/taper
  - Monitor regularly for relapse far **at least 2 years**
  - **80% relapse** within 5 years of initial remitted episode
    - Non-adherence → sig predictor
  - **Repeated relapses**
    - Incr risk of persistent psychotic sx
    - Decr gray matter
    - May decr response to medication
    - May negatively influence goal attainment (esp if younger)

- Intensive psychosocial tx + low dose AP → effective
  - Maintenance of medication superior in preventing relapse
  - Many will require lifelong maintenance tx

Subsequent Acute Episodes or Schizophrenia

- [16] Offer AP + psychological interventions
  - Family intervention + individual CBT

- [17] Offer AP or review existing meds
  - Similar criteria to starting treatment

- **80%** for first episode **relapses within 5 years** of remission
  - Specialized programs effective at preventing relapse
    - Combination approach:
    - Outreach, CBT, medication, family support, education

Hospital Care

- [18] Age/developmental appropriate hospital care if needed

Management of Acute Aggression or Agitation

- [19) HCP are trained/competent if using sedation/restraints
- [20] Careful using high-potency AP as urgent sedation
  - Esp if AP naïve → higher risk of **EPS, acute dystonic reactions**
- [21] After urgent discussion, opportunity to discuss
- Start with non-pharm, minimize use of meds/restraints
  - **Benzos (PO/IM)** → rapid onset, good safety profile
    - Risk of **paradoxical response** in young people
  - **Antipsychotics** → may be preferred for confirmed SCZ
  - Insufficient evidence for antihistamines

Promoting Recovery + Future Care in Primary Care

- [22] Coordinate for **at least yearly** monitoring
  - Higher risk of CVD (vs gen pop)

- SGA/FGA → mostly used **OFF LABEL** in C&A (Canada)
  - **Aripiprazole APPROVED** for tx of SCZ under age 18

- SGA side effects
  - **Weight gain/metabolic** → OLANZAPINE, clozapine, quetiapine
  - **EPS, akathisia** → RISPERIDONE, olanzapine, aripiprazole
  - Sialorrhea, sedation, sexual dysfunction, prolonged QTc

Intervention for Non-Responders

- [23] Offer clozapine if non-response to 2 adequate trials
  - **2 different APs**, each for **6-8 weeks**
  - Treatment resistance → lack of satisfactory improvement
    - Investigate other causes of non-response

- Clozapine → superior efficacy for TRS in C&A too
  - Often incr clinical response after **6-8 months**
  - **Benefits sustained** in long-term maintenance studies (2-9 years)
  - Hematological risks → transient/mild, rare
  - Metabolic abnormalities → comparable to olanzapine

6 – Psychosocial Treatment in Children & Youth

Recommendations

- [1] Work in partnership with parents + carers
  - Consider developmental level, emotional maturity, cognitive capacity
- [2] Atmosphere of hope + optimism, focus on recovery
- [3] Take time to build relationship
- [4] Advise parents/carers about right to own assessments
- [5] Trained/skilled HCP, know legal/ethic considerations
  - Confidentiality, information sharing

Recommendations

- [6] Foster pt autonomy, self-management
  - Offer access to peer support
- [7] Maintain continuity of therapeutic relationships
- [8] Ensure all involved understand confidentiality/limits
  - Privacy, safety, dignity respected
- [9] Discuss involvement of parents/carers
  - Depending on developmental level, repeat at intervals
- [10] Communicate clearly, consider pt factors
  - Use communication aids if necessary

Recommendations

- [11] Use interpreters if necessary

- [12] Clinicians should gain cultural competence
  - Or seek advice/supervision for HCP with experience

Family Intervention

- [13] Offer family intervention to **ALL FAMILIES**
  - For preventing + reducing relapse
  - **Start ASAP** → acute phase, inpatient settings, or later

- [14] Preferably include pt with SCZ
  - 10+ sessions, over 3-12 months
    - Preference single-family vs multifamily group intervention
  - Focus on relationship between pt with SCZ and parent/carer
    - Communication skills, problem solving, psychoeducation
    - Crisis management + recovery

- Family interventions → among most evidence-based
  - Important for recovery of pt + family

Cognitive Behavioral Therapy

- [15] Offer CBT to promote recovery in C&A
  - With **persistent positive + negative sx**
  - Those **in remission**

- [16] Deliver CBT by trained therapists, effective protocols
  - Regular supervision, **minimum 16 sessions**

- Studies for CBT in first episode psychosis
  - In late-teens, young adults → **strong benefit**
  - Group CBT may be more beneficial (vs individual, limited evidence)
    - Take **pt preference**

Supported Employment/Education Programs

- [17] Offer supported employment
  - To those **who wish to work** (if above compulsory school age)

- [18] Principles of supported employment programs
  - Goal is **regular/competitive work** → NO exclusions
  - MH team to work with supported employment team
  - Consider **personal job preferences**
  - Offer counselling on **social benefits**
  - **Rapid job search** (no prevocational training needed)
  - **Job specialist** → develop close ties with employers
    - Negotiates accommodations, develops new positions
    - Offer continuous support

Supported Employment/Education Programs

- [19) Liaise with school/educational authority
  - Ensure ongoing education provided (subject to consent)

- [20] Consider supported education programs
  - Wish to complete degree or to obtain training before employment
  - Have special educational needs
  - Need specific education-related accommodations

- [21] Same principles as supported employment programs
  - Regular education/training is goal → NO exclusions
  - MH team works with supported education team
  - Pt preferences considered
  - Rapid return to school
  - Educational specialist support

Supported Employment/Education Programs

- [22] If programs not available, work with local stakeholders
  - MH services (incl those representing minority group)
  - Enable stay in school/work, new opportunities

- Employment + education → essential to recovery
  - Supported employment → most effective vocational rehab model to obtain competitive employment
  - Supported education → less studied, but promising

Psychoeducation

- [21] Provide information to pt + parents/carers
  - About illness, treatment
  - Relevant information about groups, resources, organizations

- NO evidence of impact on critical outcomes
  - Symptoms, relapse, rehospitalization, adherence, insight
  - BUT facilitates **empowerment, informed decisions**

Cognitive Remediation

- [24] Consider if persisting cognitive difficulties

- Insufficient evidence for strong recommendation
  - Can decr cognitive deficits impacting social function
    - Attention, memory, problem-solving
  - Benefits when offered with other psychosocial tx, in groups

Social Skills Training

- [25] If stress/anxiety related to social interaction
  - May improve negative sx
  - Interpersonal skills related to social situations
    - Conversation skills, making friends, assertiveness
  - Similar to adult social skills training

7 – Individuals with High Risk of Psychosis

Individuals at High Risk of Developing Psychosis

- Prodromal phase (pre-psychotic)
  - **80-90% pts** retrospectively report prodromal period
    - Problems thinking, feeling, behaving → change in function
  - 3 at-risk subgroups (Clinical High Risk, CHR)

- 1) Attenuated Positive Symptom Syndrome (APSS)
  - Non-psychotic-level disturbances (TF, TC, perceptual abn), **past year**
  - **MOST common syndrome observed**

- 2) Brief Intermittent Psychotic Symptom Syndrome (BIPS)
  - 1+ positive psychotic sx, but **too brief**

- 3) Genetic Risk & Deterioration (GRD)
  - **Functional decline + genetic risk**

Clinical High Risk for Psychosis

- 2 measures for CHR
  - **CAARMS** (Comprehensive Assessment of At-Risk Mental States)
  - **SIPS** (Structured Interview of Prodromal Syndromes)
    - SIPS most commonly used in NA

- Those meeting CHR criteria → **helping seeking, age 13-30**
  - Often multiple concerns, **attenuated positive symptoms**
  - Often **comorbid dx** (esp anxiety, depression)
  - Often **sig negative sx** → functional impairment
  - May have been present for some time, recently worsened
  - Those help-seeking → higher risk than positive screens

Recommendations

- [1] Refer potential pts for comprehensive assessments
  - If **distressed or decline in social functioning**, with either:
    - Transient/attenuated **psychotic sx**, or suggestive psychotic sx
    - OR **1º relative** with psychosis/schizophrenia/schizotypy
  - Refer without delay → specialist MH services, EPI

- [2] Assessment done by psychiatrist/specialist
  - May do both CAARM/SIPS and comorbidity assessment
  - Of identified CHR → **73% with comorbid axis I dx**
    - Most commonly **depression**

- [3] Offer individual CBT ± family intervention

Recommendations

- [4] Offer interventions for presenting problem
  - Comorbidity common in CHR
    - **Depression 40%**, anxiety, substance use
    - Does NOT appear to incr **risk of transition** to psychosis
    - Tx can relieve distress + improve function

- [5] Offer interventions to prevent functional impairment
  - Decline in function or cognitive impairment
    - Often present before + worsen until onset of psychosis
  - Functional deficits may **predict conversion** to psychosis

Recommendations

- [6] Interventions can prevent/delay first episode in CHR
  - Psychological interventions (esp CBT), pharmacotherapy
    - Decr risk 64% at 6 months, 56% at 12 months

- [7] Treatments should be monitor by MH specialist
  - Psychiatrist, clinical psychologist, equivalent MHCP
  - Deliver evidence-based tx with **high fidelity**

- [8] Staged interventional model for adult CHR
  - **Least restrictive treatment** as first choice
  - If psychological tx ineffective, and severe attenuated psychotic sx
    - Complement with **low-dose SGA**
    - Aim to achieve **symptomatic stabilization**
  - Long-term AP for primary prevention NOT recommended

Recommendations

- [9] Regular monitoring for persistent prodromal symptoms
  - If continued sx, impaired function, or distressed
    - BUT cannot clearly dx psychosis → **monitor for up to 3 years**
    - Use structured/validated assessment tools
  - Frequency/duration of monitoring:
    - Severity + frequency of sx
    - Level of impairment/distress
    - Degree of family disruption/concern
  - If asked to be discharged
    - Offer follow-up, option to self-refer
    - Ask GP to continue monitoring

- 2.5 year longitudinal follow-up study
  - 71% did not convert, but 1+ positive sx in 43% at 1 yr, 41% at 2 yr

8 – Comprehensive Community Treatment

Need for organized mental health system

- Accessible community MHT
- High-security forensic services
- Supported living arrangement
- Supports for families
- Evidence-based coordinate specialty care programs
  - First-episode psychosis services
  - Assertive community treatment programs

Conceptualization of Recovery

- 1) Subjective experience (pt centered)
  - "Way of living a satisfying, hopeful and contributing life even with limitations caused by illness"
  - **CHIME framework** (5 key recovery processes)
    - Connectedness, hope, identity, meaning, empowerment
  - Facilitates shared decision making → no tools in schizophrenia

- 2) Symptomatic ± functional recovery (outcome centered)
  - Symptom remission, vocational functioning, independent living, peer relationships

Recommendations

- [1] Offer comprehensive range of care across all phases
  - Should be **population-based**
  - Outpt clinics, community MHTs, acute inpt, community residential
    - TRS programs, ACT teams, EPI
    - Alternatives to acute inpt, residential, occupation, rehabilitation
  - Optimal evidence-based treatment = **COST-EFFECTIVE**

- [2] Offer full range of interventions
  - Competent delivery of all offered interventions **(FIDELITY)**
    - Provincial Technical Assistance Centres (PTACs)
  - Emphasis on **engagement** (vs risk management)
  - **Least restrictive** + stigmatizing environment
  - **Diversity-related practices** for inclusion

Recommendations

- [3] Community MHT serving a defined population
  - Available to all pts with SCZ, other severe mental disorders, families
  - CMHTs should cover **1.5% of population**
    - High-intensity (ACT) → 10% of pts (1 staff per 10 pts)
    - Medium-intensity → 20% of pts (1 staff per 20 pts)
    - Intensive case management → 70%
    - Standard case management for majority (1 staff per 80 pts)

- [4] Improve experience of care
  - Work in partnership with pts + carers
  - Atmosphere of hope, recovery-orientation
  - Building supportive relationships
  - Foster autonomy, self-management, shared decision making

Recommendations

- [5] Communication with Diverse Backgrounds & Carers
  - Minimize clinical language
  - Information in appropriate language
  - Use interpreters
  - Offer list of local education providers

Specific systemic recommendations

- [6] Assertive Community Treatment
  - ACT for pts with **serious mental disorder** (incl schizophrenia)
    - High use of inpatient services
    - Residual psychotic sx
    - Hx of poor engagement
    - Leading to frequent relapse or social breakdown
  - Team-based + outreach approach, high staff:pt ratio

  - **EFFECTIVE**
    - **Decr rehospitalization** rates
    - Improve **housing + occupational function**
    - Improves **QoL + service satisfaction**
    - Does NOT lead to different improvement in clinical state or costs

Specific systemic recommendations

- [7] Intensive Case Management
  - Consider for those **likely to disengage** from treatment/services
    - High staff:pt ratio, assistance with daily living skills
    - Caseloads NOT shared between clinicians in ICM (vs ACT)
  - Mixed results on case management outcomes

- [8] First Episode Psychosis Models of Care
  - Evidence-based coordinated multidisciplinary specialized service
    - Engagement, assertive outreach
    - Family involvement + interventions
    - Psychological interventions + informed care
    - Vocational/educational interventions
    - Access to antipsychotic meds
  - First Episode Psychosis Fidelity Scale (FEPS-FS)

Specific systemic recommendations

- [9] Assess first episode psychosis without delay
  - **50% of new referrals should be seen within 2 weeks**
    - If unavailable, refer to other urgent care services
  - Negative outcomes assoc with **untreated psychosis**
    - 15-29% attempt suicide
    - Aggression + violence common
  - Long-term outcomes of **duration of untreated psychosis**
    - Longer → poorer outcome

- [10] Early intervention accessible to all
  - Regardless of age or duration of untreated psychosis
    - Mean age of onset → M age 21.4, F age 27.4
    - **27% of women have onset after age 35**

Specific systemic recommendations

- [11] Crisis Resolution + Home Treatment Teams (AHBT)
  - Offer if severity of acute episode exceeds capacity of EPI services
  - Not widely adopted in Canada (policy in England)

- [12] Crisis House or Acute Day Facilities
  - Acute community tx with crisis resolution, home treatment teams
    - Consider **before admission** to inpt unit
    - OR means to **timely discharge** from inpt units
  - Consider crisis house or acute day facilities (less evidence)

- [13] Hospitalization
  - Consider impact on person, carers
  - If unavoidable → ensure suitable setting (age, gender, vulnerability)

Specific systemic recommendations

- [14] Supported employment
  - Also **individual placement & support (IPS)**
  - Approach to vocational rehabilitation
  - More effective than prevocational training

- [15] Supported housing + LTC
  - Pts shall live in housing of **their choice**
    - Supported community housing available to all
    - Role of non-institutional residential facilities
    - LTC facilities should be home-like settings
  - **Housing First** → applied to homeless
    - Access to good hosing, supplement to rent, support by ACT/ICM
    - Better housing outcomes, community function, QoL

Specific systemic recommendations

- [16] Peer Support & Self-Management
  - May improve service user experience, QoL **(low quality evidence)**
    - Peer support worker → trained, recovered, stable, supported
- [17] Return to Primary Care
  - If responded effectively → option to return to primary care
- [18] Relapse & Re-referral to Secondary Care
  - If established dx of psychosis/schizophrenia
- [19) Transfer between Health Regions
  - If movement catchments → meeting for transition plan
  - **Active approach to continuity of care**

9 – Physical Health & Drug Safety

Antipsychotic Dosing & Polypharmacy

- High-dose + combination APs → may increase harm
  - High-dose ceiling effect (max occupancy of D2 receptors)
  - No evidence for **polypharmacy** (but may useful in tx-refractory)

- Lowest effective dosage (begin at lower end)
  - Control sx, reduce relapse, minimize SE, optimize well-being
  - Adequate duration of treatment → **minimum 2 weeks**

- [1] Work together to find appropriate med + dose
  - Consider pt preference

- [2] Combination AP NOT routine
  - Discuss risk/benefits with pt

Cardiovascular Health + Metabolic Syndrome

- Incr risk of premature death with major mental illness
  - Severe mental illness → **2-3x higher mortality, 10-20 less years**
    - Higher rates of **known risk factors** (smoking, diet, sedentary)
    - **Medications** → weight gain, DLD, abn glucose metabolism
    - Reduced access or bias to **health care resources**

- CV conditions → **major part of excess mortality**
  - Sig modifiable risk factors
    - BP control, glycemic control, correction of lipid abn
    - Smoking cessation, incr physical activity, weight control
  - **Metabolic syndrome** → higher rates in long-term mental illness
    - Central obesity, HTN, hyperglycemia, low HDL, incr TG
  - First-episode → sig metabolic abn EARLY into illness

Cardiovascular Health + Metabolic Syndrome

- [3] Offer combined health eating + exercise program
- [4] Routine monitoring of weight, CV, metabolic indicators
- [5] Suggested monitoring schedule
  - Sig metabolic abn early → important initial + follow-up screening
- [6] Local arrangements for physical health monitoring
- [7] Primary health care monitoring annually
  - Incl cardiovascular risk assessment

Cardiovascular Health + Metabolic Syndrome

- [5] Suggested monitoring schedule

Suggested Metabolic Syndrome Monitoring Schedule				
Test	**Baseline**	**At 1 mo**	**At 3 mo**	**Yearly**
Personal + family medical hx	**B**	**-**	**-**	**Y**
Smoking history	**B**	**-**	**3**	**Y**
H & P for EPS	**B**	**1**	**3**	**Y**
BMI, weight, waist circumference	**B**	**1**	**3**	**Y**
BP	**B**	*PRN*	**3**	**Y**
HbA1c, fasting glucose	**B**	*PRN*	**3**	**Y**
Lipids (random, fasting)	**B**	*PRN*	**3**	**Y**
Prolactin	*PRN*	*PRN*	*PRN*	*PRN*

Preventing + Management of Metabolic SE

- Long-term AP adds to risk of diabetes
  - With AP initiation
    - Incr appetite, early incr TG, DLD, glucose dysregulation
    - Early weight gain → can continue for months-years
    - May promote tx refusal, decr self-esteem, stigma
    - Other physical problems
      - OA, OSA, gallbladder disease, obesity-related cancers

- CATIE → **olanzapine** = greatest metabolic + CV risk
  - Rates of tx discontinuation due to weight gain
    - Olanzapine 9.2%, quetiapine 3.6%, ziprasidone 3.2%
    - Risperidone 1.8%, perphenazine 1.1%
  - Clozapine average weight gain (less than olanzapine)

Preventing + Management of Metabolic SE

Risk of Clinically Significant Weight Gain	Antipsychotics
Higher (>24%)	• Chlorpromazine • Clozapine • Olanzapine
Intermediate (10-24%)	• Lurasidone • Quetiapine • Risperidone • Paliperidone • Perphenazine • Other FGAs
Lower (<12%)	• Aripiprazole • Asenapine • Ziprasidone

Preventing + Management of Metabolic SE

- Weight change varies even among same AP
  - Need to be careful even with low risk APs
- Mechanism of weight gain → UNKNOWN
  - May be due to binding affinity to **H1 receptors**
    - Assoc with eating behaviors, sensation of satiety
- Proactive, preventative approach (diet + exercise)
  - No specific intervention recommend (promising results)
  - Unclear if specific metabolic monitoring clinics improve outcomes
- Metformin (well investigated in first episode)
  - May have **sig weight loss within 3 months** of starting
  - Also decr rate of **new-onset diabetes** if dysglycemia

Preventing + Management of Metabolic SE

- [8] Consider lifestyle interventions if weight gain on APs
- [9] Consider metformin if weight gain on APs
- [10] If sig metabolic SE, follow relevant guidelines
  - Rapid/excessive weight gain, abn lipid levels, glucose problems
  - Canadian guidelines on obesity, DLD, diabetes

Arrhythmias & Antipsychotics

- Serious SE of APs → **arrhythmias, sudden cardiac death**
  - **Torsades de pointes** → malignant ventricular arrhythmia
    - Assoc with **syncope + sudden death**
    - Assoc with **prolonged QTc** (occurs with APs, other meds)
  - **Sudden cardiac death (SCD)**
    - FGA, SGA → **2x risk** (vs non-users)
      - No difference between FGA vs SGA
    - **Dose-dependent increase in SCDs**
      - Caution around drug interactions

QTc prolongation

- APs **ASSOC with** risk of QTc prolongation
  - Ziprasidone, risperidone, olanzapine, quetiapine, iloperidone
  - Haloperidol, amisulpride, sertindole

- APs **NOT assoc** with sig QTc prolongation
  - Lurasidone, aripiprazole, paliperidone, asenapine

- Risk factors
  - **Female, CYP3A4 drugs** → incr risk
  - **Drug interactions** → can have additive effects
    - Antibiotics, grapefruit juice → inhibit 3A4 (may incr levels of APs)
    - Care with **PRNs**, during **crossover titrations**
  - **Age** → decr clearance, incr plasma levels
  - **1% of inpatients**

Arrhythmias & Antipsychotics

- [11] ECG before initiating/changing certain APs if
  - Specified in monograph
  - Physical exam → specific CV risk (eg. incr BP)
  - Personal hx of CVD
  - Family hx of QT prolongation

- Health Canada → stop if **QTc >500 ms** **or** **incr >60 ms**
  - Normal QTc = men <450 ms, women <460 ms

EPS & Antipsychotics

- Acute dystonia
  - Within days of starting/increasing dose
  - **Cranial, neck, trunk muscles** preferentially affected
  - Typical → retrocollis, trunk extension, deviation of eyes, forced jaw opening, tongue protrusion

- Acute akathisia → **ARIPIPRAZOLE (OR 1.78)**
  - Excessive restlessness, need to move → **relieved by movement**
  - Inner tension → shaking/rocking legs + trunk, pacing, rubbing face, vocalising (to relieve discomfort)

- Neuroleptic-induced parkinsonism
  - May be **indistinguishable** from idiopathic Parkinson disease
  - Tremor, rigidity, slowness of movement, shuffling gait
  - May be **unilateral or asymmetric**

EPS & Antipsychotics

- Tardive dyskinesia → yearly incidence = **4% for FGAs**
  - Repetitive **choreiform** movement → **mouth, lips, tongue**
    - May also affect fingers, toes, respiratory dyskinesias
  - Resembles **chewing, sucking, lip pursing**

- Tardive dystonia (subtype of tardive dyskinesia)
  - Sustained, slow, involuntary movements
  - Posture affecting **limbs, trunk, neck, face**
  - Generalized form → retrocollis, lower facial grimacing, opisthotonic trunk extension, hyperpronation of arms
  - Focal forms → blepharospasm, cervical dystonia

- Tardive akathisia (persistent akathisia, similar sx)
  - Present for **≥1 month** with **constant AP dose**

EPS & Antipsychotics

- EPS exam
  - **Observation of spontaneous movement**
    - Hyperkinetic movements (akathisia), dyskinesia, tremor
    - Poverty of movement → parkinsonism
  - **Assessment of tone**
    - Cogwheel rigidity, hold in posture
    - Moved through range of motion → postural + kinetic tremor
  - **Performance of repetitive tasks (look for bradykinesia)**
    - Pronation-supination of arms, opening-closing of hands
    - Foot tapping

EPS & Antipsychotics

- Validated rating scales
  - **EPS Rating Scale** → 4 subscales, 4 clinical global impression scales
    - Parkinsonism, akathisia, dystonia, tardive dyskinesias
    - High interrater reliability
  - **AIMS** → tardive dyskinesia
  - **Simpson Angus Scale (SAS)** → antipsychotic-induced parkinsonism
  - **Barnes Akathisia Scale** → akathisia

EPS & Antipsychotics

Class	Antipsychotic	Odd Ratio for EPS
FGA	**Haloperidol**	4.76
	Chlorpromazine	2.65
SGA	**Lurasidone**	2.46
	Risperidone	2.09
	Paliperidone	1.81
	Ziprasidone	1.61
SGA	Olanzapine	~placebo
	Quetiapine	~placebo
	Aripiprazole	~placebo
	Asenapine	~placebo
SGA	**Clozapine**	0.30 (LOWER)

EPS & Antipsychotics

- [12] Inform risk of EPS, encourage pt to report sx
  - HCP should be vigilant for EPS, use validated scale

- [13] If EPS is a concern → consider SGA
  - **Olanzapine, quetiapine, clozapine, asenapine**
    - Clozapine risk LOWER than placebo (OR 0.3)
  - OR low-potency FGA

- [14] If tardive dyskinesia is a concern → consider SGA