SCHIZOPHRENIA SPECTRUM AND PSYCHOTIC DISORDER GUIDELINES 2017

Assessment and Diagnosis

Diagnosis

- Based on clinical features
- 5 key features:
    - Delusions, hallucinations, disorganized thinking, grossly disorganized/abnormal motor behaviour, and negative symptoms
    - Negative symptoms:
        - Affective flattening*, avolition, alogia, anhedonia* (* = core negative sx)
- First rank symptoms of schizophrenia: "ABCD" (auditory hall, broadcasting thought, control, delusional perception)
    - Auditory hallucinations, thought withdrawal/insertion/interruption, thought broadcasting, somatic hallucinations, delusional perception, feelings/actions controlled by external agents
- Most reliable:
    - Structured clinical interview, info from multiple information and review of medical records (= *best estimate diagnostic method*)
    - Examples: SCID (structured interview for DSM), Schedule for Affective Disorders and SCZ for School-Age children

Levels of Evidence

- 1: Meta-analysis, systematic reviews of RCTs, RCTs
    - 1++ = high quality, very low risk of bias
    - 1+ = well-conducted, low risk of bias
    - 1 = high risk of bias
- 2: Systematic reviews of case-control or cohort studies, case-control or cohort studies
    - 2++ = high quality, low risk of confounding or bias, high probability of causal relationship
    - 2+ = well-conducted, low risk of founding or bias, moderate probability of causal relationship
    - 2 = high risk of bias, significant risk that relationship not causal
- 3: Non-analytic studies (case reports, case series)
- 4: Expert opinion

Grades of Recommendation

- A: At least one 1++ directly applicable to target population
    - OR body of 1+ studies directly applicable to target population, demonstrating overall consistency of results
- B: Body of evidence of 2++ studies directly applicable to target population, demonstrating overall consistency of results
    - OR extrapolated evidence from 1++ or 1+ studies
- C: Body of evidence of 2+ studies OR extrapolated evidence from 2++ studies
- D: Evidence level 3 or 4 OR extrapolated evidence from 2+ studies
- Good practice point: Recommended best practice based on clinical experience of guideline's development group

Strength of recommendation

- Describes the level of confidence that potential benefits of an intervention overweigh potential harms
- Informed by evidence
- Rating is a consensus judgement of the authors
- Recommendation = confidence that benefits outweigh harms
- Suggestion = uncertainty

RECOMMENDATIONS

1: Assessment and care planning - level C

- *Initial comprehensive multidisciplinary assessment, including:
    - Full MSE, risk of suicide and aggression, psychiatric history, past treatments, substance use, psychosocial develop and neurodevelopmental problems, current occupational/educational functioning and social/sexual/housing/financial status, current and history of health problems
    - Include info from family and health records

2: Assessment of first episode of psychosis - good practice point

- *See new patient within 2 weeks (for scheduled, non-urgent referral)
- *Include recommendation 1 and family history
- *Focus on:
    - Longitudinal assessment (onset, timing, course of onset of first symptoms)
    - Relationship to substance use
    - Developmental history - prognostic value for degree of recovery
    - Duration of untreated psychosis (**DUP**) - prognostic value, significant predictor of outcomes
    - Include family members/caregivers with consent of competent patient

3: Neuropsychological assessment - good practice point

- *Suggested for first episode psychosis and those with poor response to treatment
- *Important for documenting cognitive deficits, and treatment/academic planning
- Robust predictor of function and possible target for interventions
- I.e. MATRICS consensus cognitive battery (approved by FDA and NIMH) - done by any trained mental health professional, and optimally interpreted by neuropsychologist

4: Brain imaging - good practice point

- *CT or MRI based on history, neuro exam or neuropsych testing results
    - **Indicated if** signs/symptoms of intracranial pathology, focal CNS findings, seizures, autoimmune encephalitis, later age of symptom onset, rapid progression of memory deficits over < 3 months
- *Consider on case-by-base basis for first episode psychosis
- Routine imaging cannot be justified because findings do not alter treatment, and risk of radiation and delayed treatment

5: Genetic testing - good practice point

- *Consider genetic testing based on history and physical exam, especially for first episode psychosis
- *Identification of CNVs (especially 22q11) may help diagnose rare conditions and inform genetic counselling
- Patient with SCZ have increased genomic CNVs
    - I.e. Of those with 22q11.2 deletion → 25% develop SCZ

6: Ongoing assessment of positive and negative symptoms - good practice point

- *Assess +/- symptoms **at least q3 months** in **stable** patient
- *If +/- symptoms present, **rate the severity** using a quantitative measure
- *Following a change in treatment, reassess the severity/change of key + symptoms at regular intervals
- *Distinguish negative symptoms of SCZ vs. those of other psychiatric/medical conditions
- Examples of scales:
    - DSM-5 includes 8-item scale (+, - , depressive sx) - *clinician-rated assessments of dimensions of psychosis severity*
    - Positive and Negative Syndrome Scale (PANSS)
    - Brief Psychiatric Rating Scale (BPRS)
    - Calgary Depression Scale for SCZ; assess depression independent of negative symptoms
    - Scale use limited by training to utilize them reliably

7: Ongoing assessment of suicide risk - good practice point

- *Essential part of initial assessment, and active reassessment should be performed for those at risk or respond to screening Q about depression and suicidal thinking
- *Includes:
    - Current suicidal ideas, plans, intent including active or passive thoughts
    - Delusions or hallucinations with content related to suicide or risk of harm
    - Hopelessness, impulsivity, access to suicide methods

    - Reasons for living
- Lifetime risk of suicide = 5%
- **Risk factors** = depressive disorders, past suicide attempts, substance use, agitation/restlessness, fear of mental disintegration, poor treatment adherence, recent loss, command AH
- Assessments:
    - Suicide Risk Assessment Guide
    - Columbia Suicide Severity Rating Scale

8: Ongoing assessment of risk of aggression - good practice point

- *Important part of initial assessment, especially in those at risk or respond to screening Q about aggression
- *Includes:
    - Current aggressive or psychotic ideas (including physical/sexual aggression or homicide)
    - Impulsivity and anger management issues
    - Access to firearms or weapons
    - Specific individuals/groups toward whom homicidal/aggressive ideas or behaviours have been directed to (current and past)
- Psychosis associated with violence and homicide, with excessive risk associated with comorbid substance use
    - Higher risk in less developed countries, psychotic symptoms, high psychopathology scores
- Antipsychotic treatment decreases risk in patients with SCZ

9: Ongoing assessment of substance use - NICE - strong

- *Regular assessment of substance use includes:
    - Particular substances used, quantity/frequency/pattern, duration of current level of use, impact on medication adherence, route, level of dependence, readiness to change
    - Urine toxicology <u>not routine</u> - use in acute situations when indicated or for treatment planning
- Treatment should be integrated
- Screening tools: NIDA-modified ASSIST

10: Involvement of patient in treatment decision making - good practice point

- *Discuss during IA - differential diagnosis, risks of untreated illness, treatment options (including benefits and risks)
- *Discuss during ongoing treatment - same as above, plus relapse prevention
- *Shared decision making = active involvement of both parties
    - Definition = 2+ participants, share info, build a consensus and reach agreement

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PHARMACOTHERAPY OF SCHIZOPHRENIA IN ADULTS

<u>First episode schizophrenia</u>

- *1: **Use of AP**: Antipsychotic medication recommended (NICE - strong)
    - Acute AP use in early SCZ - data too limited to assess outcomes
    - Higher relapse rate if AP discontinued after treatment in first-episode psychosis
    - Modest association between shorter duration of untreated psychosis and improved outcomes
- *2. **AP choice**: made by patient and MD, taking into account carer when appropriate. Provide info and discuss benefits/side effects of each drug (NICE - strong)
    - Response rates and side effects more pronounced in first-episode patients (AP naive)
    - Recent meta-analysis: SGAs superior to FGAs re: all-cause d/c rates (nnt = 12)
        - One meta-analysis: no differences between classes re: efficacy or d/c rate
    - **Decision based on side effect profile** of the individual AP
- ***3. Acute AP treatment:** Continue AP for <u>at least 2 weeks</u> unless there are significant tolerability issues (SIGN - D)
    - *Monitor dose and response in early phase of prescribing

    - *If poor response, assess adherence and substance use before deeming lack of response
    - *If **no response after 4 weeks (despite optimization) - consider CHANGE in AP**
    - *If partial response, reassess after 8 weeks, unless significant adverse events
    - Objective in acute treatment = adequate clinical trial (4 - 6 weeks)
    - Consider different formulations, i.e. earlier use of LAI
- ***4. AP dose and trial duration:** Target lower end of effective dose range, titrate according to efficacy and tolerability (D)
    - Adequate clinical trial = initial titration phase over weeks, then ~6 weeks at adequate therapeutic dose
    - Much of the AP effect evident in first weeks of treatment
- ***5: AP continuation**: following resolution of positive symptoms, maintenance treatment for at least 18 months (D)
    - Older studies suggest 1-20% have only a single episode of psychosis
    - Relapse rates are high due to AP discontinuation - 82% risk of first relapse in 5 year F/U of first-episode patients who responded to treatment (5x greater if NOT taking medications)

Acute exacerbation

- *Following an increase or change of AP meds in response to acute exacerbation, continue medication for at least 4 weeks unless significant tolerability issues
- *If partial response after 4 week review, reassess medication after 8 weeks unless significant adverse effects (D)

Relapse prevention and maintenance

- ***1. AP dose:** After acute episode, offer maintenance treatment with AP at low or moderate regular dosing of ~300-400 mg CPZ or 4-6 mg risperidone equivalents daily (B)
    - Biphasic relationship between dose and efficacy - no benefit with doses > 375mg CPZ
    - Shift to target lower doses with less aggressive titration - optimal AP dose = maintenance dose
    - Only empiric strategy for dose equivalents is **D2 occupancy (***aim for 65%***)**
- ***2. Duration of treatment:** After resolution of positive symptoms of acute episode, offer maintenance treatment and AP meds for **2 and possibly 5 years or longer** (A)
    - AP treatment → lower hospitalization rates, improved QoL
    - Benefit of SGA vs FGA either not identified or modest
    - Several years of stabilization do not confer immunity to relapse
- ***3. AP delivery:** Option of PO or depot AP in line with patient preference (GPP)
    - LAI superior to PO agents in reducing relapse rates in early SCZ and better symptom control

Treatment-resistant SCZ

- ***1: Clozapine:** Offer to patients with TRS (A) and **2.** Consider for patients who have not responded to 2 APs (B)
    - 25-30% of patients with SCZ have TRS; response rate 30-60% with clozapine; only recommended tx for TRS
    - No consistent evidence for high doses, switched, or combined AP
    - Definition of tx-resistance varies, esp re: the amount of improvement allowed on a non-CLZ treatment
        - Maximum allowable treatment response = relative change in scales (i.e. 20+% decrease in PANSS)

Clozapine-resistant SCZ

- ***1. An adequate AP trial:**
    - For PO meds - 6+ weeks of treatment at midpoint or greater of therapeutic dose range
    - For LAI meds - 6+ weeks of treatment following reaching steady state
    - For CLZ - **8-12+ weeks** at dose of 400+mg/day (obtaining trough 350+ ng/mL or 1100 nM/L for OD dosing and 250+ ng/mL for divided dosing)
    - Documentation of adherence, with **AP plasma levels on at least 1 occasion** (if available)
    - **AP TRS:** Persistence of 2+ positive symptoms with at least a moderate level of severity, or 1 severe positive symptom, following 2+ adequate trials with different AP drugs
    - **Specifier of CLZ-resistant SCZ: i**f above criteria met after adequate trial of CLZ
- *2. TRS is associated with ongoing disability

    - Assessing adherence is essential to identifying tx-resistance - trial of LAI is the best adherence test
- *3. Treatment options: No recommendation.
    - No single intervention robust and effective; **maybe add another AP or use ECT**

Specific symptom domains

- ***1. Aggression and hostility:** medication choice based on patient preference, past experience of AP treatment, adverse effect profile, and concurrent medical history
    - *For patients with TRS + aggression/hostility = trial of clozapine (D)
    - Reviews support **CLZ as preferred agent** for psychosis + aggression
- ***2. Comorbid depressive symptoms:** treat based on **depression guidelines** (if meet depressive d/o criteria), including use of antidepressants (GPP)
    - Depression is common in all stages of SCZ, frequently occur prior to onset of psychotic symptoms, first-episode SCZ, and chronic SCZ

PSYCHOSOCIAL TREATMENT OF SCHIZOPHRENIA IN ADULTS

General principles:

1. Optimal management = integrate medical and psychosocial interventions
2. Psychosocial interventions address many aspects of recovery - reduction of acute sx to improve function
3. Therapeutic alliance improves engagement and adherence
4. Encourage realistically hopeful attitude in patients and families
5. Interventions should be undertaken within recovery framework, with goal of QoL
6. Clinical team, patient and family should develop shared goals for treatment and recovery; progress should be monitored and evaluated
7. Delivery of psychosocial interventions require specific skills - train staff
8. Support patients to develop effective self-management skills to improve sx, fn, and QoL
9. Recognize and address comorbidities with psychosocial interventions
10. Consider patient and family preferences in treatment goals and methods

Family Intervention

- *1. Offer FI to all patients (who are in close contact with or live with family); **prioritize** if persistent sx or high risk of relapse
    - *10 sessions over 3 months = minimum effective dose
    - *FI = communication skills + problem solving + psychoeducation
    - NICE/SIGN: strong evidence for FI, including support, education, problem solving, communication, crisis management and relapse prevention
    - RCTs show FI reduces symptoms, distress and hospitalization, **improves functioning and knowledge**

Supported Employment Programs

- *2. Offer supported employment programs to those who wish to find or return to work (strong)
    - *Consider other occupational/education activities/prevocational training for those unable to/unsuccessful re: employment
- *3. Mental health services should work with stakeholders to enable those with psychosis and SCZ to stay in work/education/volunteering activities (strong)
    - Employment interventions should include job development, job search, job supports and integration of vocational and mental health services

CBT

- *4. CBT for psychosis should be offered to all whose symptoms have not adequately responded to AP meds and are experiencing persisting sx, including anxiety or depression (A)
    - *Can be started during initial, acute, or recovery phase including inpatient settings

- *5. CBT should be delivered by trained therapists, using effective protocols, in collaborative manner (strong)
    - *Minimum 16 sessions
    - Benefits - reduce sx severity, hospitalization, relapse, level of depression
    - Unclear evidence re: individual vs. group CBT

Cognitive Remediation

- ***6.** Consider for those with persisting problems associated with cognitive difficulties (B)
    - May improve cognitive domains at end of treatment, maintained at F/U; more impact if offered at same time as other psychosocial interventions

Social Skills Training

- ***7.** Should be available for patients having difficulty or experiencing stress/anxiety related to social interaction (B)
    - Includes instructions about social behaviour, modeling, role-play, rehearsal, feedback, and homework
    - Some evidence for **social function and negative s**x; little evidence for + sx, hospitalization or relapse

Life Skills Training

- *8. Should be available for those having difficulty with self-care related to housekeeping, transport, financial management, etc. (low)
    - Target deficits using assessment, feedback and structured homework
    - Little research and evidence is not strong

Patient Education

- *9. Appropriate education about nature, treatment and recovery from SCZ should be integral part of treatment
    - *Education interventions themselves **do not have robust effects** on treatment outcomes (low)

COEXISTING SUBSTANCE USE DISORDERS

- Regular cannabis use in adolescence increases risk of psychosis even after 1 year of abstinence
- **Psychotic symptoms do not increase risk of cannabis use**
- Cannabis users develop **psychosis 2.7 years earlier**
- Substance use affects course of illness → more + sx, rate of tx non-adherence, higher relapse rate, more depression, more service utilization
    - Impact on neurocognitive symptoms of psychosis less clear
- Indicators of underlying psychotic disorder:
    - Persistence of psychotic sx with abstinence
    - Sx out of keeping with type/amount of substance used
    - Family hx of SCZ
    - Typical + symptoms of SCZ and/or presence of negative/cognitive sx

- **1.** Engage the patient, build a good relationship, be direct in communications, use motivational approach (strong)
    - Remember: stigma associated with psychosis and substance use, people will try to conceal conditions, many fear detainment, forced medication, children going into care, and that they are ‘mad’
- **2.** Ensure confidentiality and privacy, avoid clinical jargon, provide interpreter PRN, preserve continuity of care and minimize change of key workers (strong)
- **3.** HCP should be competent to engage, assess and negotiate with patients from diverse cultural/ethnic backgrounds (strong)
- **4.** Work with minority/ethnic organizations to support, engage patients, and offer information/training on how to recognize psychosis with co-existing substance use and access treatment (strong)

- **5.** Offer info about nature and treatment of psychosis and substance use; offer info about risks associated with substance use and negative impact on experience and management of psychosis (strong)
- **6.** Encourage families/carers/SOs to be involved in treatment; offer family intervention (strong)
- **7.** Offer families/carers an assessment of their physical/social/mental health needs; develop care plan (strong)
- **8.** Offer families info about nature and treatment of psychosis and substance use (strong)
- **9.** Do not exclude patients from MH care due to coexisting substance use disorder
- **10.** Do not exclude patients from SUS due to coexisting psychosis
- **11.** Treatment for both psychosis and SUDs should be provided by HCPs in MH care (strong)
    - Integrated care has best treatment outcomes
- **12.** HCPs should routinely ask patients with psychosis about substance use, including particular substance, quantity/frequency/pattern, route, and duration of current use (strong)
- **13.** HCPs should routinely assess patients with SUDs for psychosis (strong)
- **14.** Patients should be offered comprehensive, multidisciplinary assessment, including:
    - Personal hx, mental/physical/sexual health, social/family/economic situation, accommodation, current and past substance use and impact on health/treatment, forensic hx, personal strengths/weaknesses and readiness to change
- **15.** Review changes in substance use (patterns, mental/physical state, treatment) - share summary with patient and record into care plan (strong)
- **16.** If patients are parents/care for children, ensure child's needs are assessed (strong)
- **17.** If serious issues identified, develop child protection plan (strong)
- **18.** If patient is responsible for vulnerable adult, ensure home situation is risk assessed and that safe-guarding procedures are in place for the vulnerable adult (strong)
- **19.** Ensure needs of young carers or dependent adults of patient are assessed; initiate safeguarding procedures where appropriate (strong)
- **20. Monitor physical health at least once a year**, more frequently if patient has a significant physical illness (strong)
    - Those with SCZ die 20 years earlier (cardiovascular factors)
    - Cigarette smoking = leading preventable cause of premature death/disease in Canada
- **21**. Offer help to stop smoking; be aware of impact on drugs (strong)
- **22.** Consider NRT (psychosis or SCZ), bupropion (SCZ), varenicline (psychosis or SCZ). Warn people about increased risk of adverse neuropsychiatric sx and **monitor them regularly, particular in the first 2-3 weeks** (strong).
    - Ideally smoking cessation should occur when patients psychiatrically stable and motivated to quit
    - If pre- or contemplative: use brief MI and re-evaluate stage of change
    - If preparing or action: psychosocial counselling and pharmacological interventions
    - NRT = well-tolerated, but evidence for benefit in SCZ **limited**
    - Bupropion = **most evidence for benefit**, but patients should be warned about potential neuropsych sx and monitor for them, including sleep impair, SI, and re-emergence of psychotic sx
    - Varenicline = greatest evidence for those with SCZ, however only one RCT and thus it is recommended **SECOND to bupropion**
        - Limited evidence of increased risk of neuropsych sx - warn about risk and monitor
- **23.** Offer info about local family or carer support groups and help families access these (strong)
- **24.** HCPs should seek effective support, i.e. case conference, team setting, staff support (strong)
- **25.** PCP should refer patients to MH services for assessment and management (strong)
- **26.** HCPs should ensure they are competent to recognize and treat patients with psychosis and SUS (strong)
- **27.** HCPs should consider having supervision, advice, consultation and additional training from specialists in SUS (strong)
- **28.** Consider specialist advice/joint working arrangement if:
    - Severe SUD, multiple SUDs of moderate + severity, IV use, serious social disruption (strong)
- **29.** Coordinate delivery of care and transfer between services to maintain engagement and ongoing care (strong)

General Treatment

- **30.** Offer evidence-based tx for both psychosis and coexisting substance use (strong)

- **31.** Ensure informed consent for treatment; if doubt assess mental capacity (strong)

Pharmacological Treatment

- **32.** AP = maintain for patients with psychotic disorder, whether or not they have coexisting SUD
    - **No differential benefit for one AP over another**
    - Use of SGA > FGA preferred due to greater tolerability and lower risk of EPS, in patients with SUD (low)
        - Some evidence to suggest SGA LAI > FGA LAI (no evidence for SGA LAI vs. PO)
        - Benefit of SGA greater for those who d/c illicit substance use compared to those who continue (CATIE)
        - Some literature suggests Clozapine for those with SCZ and SUD
            - Not a recommendation - limited evidence
    - If potential substance-induced psychosis that does NOT resolve rapidly with abstinence - follow guidelines for first-episode psychosis
    - For patient with AUD withOUT psychiatric disorder, **Naltrexone** and Acamprosate have best evidence
        - For those with SCZ, **some evidence for Naltrexone, limited evidence for Disulfiram, and no evidence for Acamprosate**
    - For patient with cocaine UD and SCZ, limited evidence for **desipramine and imipramine**
        - **NOT recommended** due to SI and lack of indication for cocaine UD alone
    - No data for cannabis UD
        - NEGATIVE data for mirtazapine, bupropion, nabilone and dronabinol
        - For adolescent cannabis users with psychosis, possible benefit of PO **N-acetylcysteine with contingency management** (no data for SCZ and CUD)

Psychosocial Treatment

- **33.** Do not exclude patients from contingency management program due to psychosis (strong)
    - Some efficacy for CM, CBT/RP, MI, combo CBT + MI, brief interventions, FI and ACT → use if available (low to moderate)
    - Focus should be: retention in treatment, gradual change in substance use over time, improved physical/mental health and improved function
    - Evaluate stage of change for each substance, and match intervention to stage
    - Coordinate F/U care for patients referred to residential/inpatient/day treatment
    - Optimal treatment duration uncertain, though staying longer = better outcomes

Substance Use Treatment

- **34.** HCPs in SUS should be competent in recognizing signs and sx of psychosis, and undertaking a MH needs and risk assessment to determine how/when to refer to MH services (strong)
- 35. Patients attending substance use treatment services should be offered comprehensive, multidisciplinary MH assessment in addition to substance use assessment (strong)
- 36. Collaboration between substance use and psychosis treatment services should occur - joint meeting, advice/consultation/training, and development of treatment protocol for these patients (strong)

Inpatient Mental Health Services

- **37.** Inpatient MH services should have policies to promote environment **free** from cigs, drugs and ETOH (strong)
- **38.** Assess patients for current substance use and evidence of withdrawal symptoms at point of admission (strong)
- **39.** Consider drug testing part of assessment and treatment planning only (strong)
- **40.** Offer NRT to patients who do **not** want to stop smoking (strong)
- **41.** Ensure planned detox from drugs or ETOH is undertaken only if:
    - There is involvement and advice of substance use services, in inpatient setting, and as part of overall treatment plan (strong)
    - Detox alone does **not change treatment outcomes**, however can be part of coordinated treatment plan
- **42.** Do not discharge patients from inpatient MH services solely due to substance use (strong)

- **43**. When patients are discharged, ensure they have:
    - Care coordinator, care plan, and info about risks of overdose (strong)

Summary: SCZ + coexisting SUD common. Limited data for preferential treatment practices (re: specific pharmacotherapy or psychosocial interventions). Integrate psychosis and substance use treatments. Outcome data demonstrate that treatment is beneficial with greater improvements when substance use is stopped.

PHARMACOLOGICAL TREATMENT IN CHILDREN AND YOUTH

- Symptom domains for psychosis can differ depending on age and stage of development
- C&Y interpretation of internal and external experiences influenced by intellect, emotional maturity, developmental stressors, cultural dynamics, family belief systems, etc.
    - Psychotic experience normal for very young children, and occur in 15-20% of adolescents
- Diagnostic accuracy can be improved by using semi-structured interviews for youth:
    - Kiddie Schedule for Affective Disorders and SCZ (KSADS) for School-Age Children
- **Childhood-onset SCZ (<12 years)** rare - 1.6-1.9 in 100k children
    - More severe psychopathology, higher risk of suicide, poorer prognosis

General principles of care

- Training, expertise, and experience with youth and families assists in ID, dx and tx of psychosis
- Assessment of capacity to make tx decisions occurs on ongoing basis (provincial standards)
- Tx decisions made with C&Y and caregiver - foster C&Y's autonomy
- Offer ongoing psychoeducation re: psychosis to patient and family
- Address impact of barriers, such as comorbidity and stigma, can influence tx decisions
- Communicate clearly and ensure that patient and families understand - take into account patient's developmental level, emotional maturity, and cognitive capacity
- Tx should be offered in culturally competent atmosphere
- Continuity of care and consistent therapeutic relationships optimal

First Episodes of Psychosis

Early Identification

1. Refer all C&Y with first presentation of sustained psychosis (4 weeks+) to specialist MH service or EPI (strong)
    a. Evidence: early detection and shorter duration of untreated psychosis → improves executive functioning
2. AP in C&Y with first presentation of sustained psychosis should be done in consultation with psychiatrist who has training in CAP (not in primary care) (strong)

Use of Antipsychotics

3. Offer AP in conjunction with psychological/psychosocial interventions (strong)
    a. **⅓ adults with SCZ have onset <18 years**; AP is as effective as with adults - offer once dx is confirmed
4. Choice of AP and mode of administration should be made jointly with patient and family (strong)
    a. Provide info on benefits and SE: metabolic, extrapyramidal, cardiovascular (QT), hormonal (PRL), etc.
5. Before initiating or changing AP for C&Y with SCZ, **ECG** is suggested if:
    a. Specified in drug product database, physical exam reveals specific CV risk (HTN), personal hx CVD, and family hx of CVD (sudden cardiac death, prolonged QT) (strong)
6. Treatment with AP = explicit individual therapeutic trial; include:
    a. Record the SE that the patient is most/least willing to tolerate
    b. Record the indications, expected benefits/risks, expected time for change in sx, and appearance of SE
    c. Start with dose < lower end of range (if not licenced for C&Y) or at lower end of range (if licenced for C&Y), titrate slowly per drug product database
        i. Justify and record reason if dose is higher

   d. Record rationale for continuing, changing or stopping meds, and the effect of changes
      i. Dosing be targeted to efficacy, avoid abrupt switch to minimize rebound phenomena
   e. Trial at optimal dose for 4-6 weeks (strong)
7. Monitor physical health and effects of AP meds; responsibility established between primary and specialty care (strong)
   a. Treatment resistance = lack of satisfactory improvement despite adequate AP trial for 6-8 weeks
8. Discuss any non-prescribed therapies that patient/family wishes to use, including safety, efficacy, and possible interference with therapeutic effects of prescribed meds/psychological interventions (strong)
   a. Poor engagement directly related to non-adherence, rehospitalization, severity of sx and dropout rates
9. Discuss use of cannabis, ETOH, tobacco and illicit substances, including possible interference with treatment and exacerbation of psychotic sx (strong)
   a. Most associated with poor outcome/relapse: **cannabis use, other comorbidity, and med non-adherence**
   b. Individuals who use regularly use cannabis during adolescence **double the risk of psychotic sx or SCZ dx** in adulthood (possible dose-dependent relationship between use and risk of SCZ)
10. Do not initiate regular combined AP meds, except for short periods (strong)

Early Post-acute Period

11. Review AP meds regularly, including benefits and SE
12. In early period of recovery after acute episode, reflect on episode and impact with C&Y and family, and make plans for recovery/future care (strong)
13. Inform patient/family of high risk of relapse if medication stopped within 1-2 years after acute episode (strong)
14. Gradual taper with regular monitoring for relapse if discontinuing or tapering AP (strong)
15. After d/c or taper, continue monitoring for relapse for 2+ years (strong)
   a. 80% relapse within 5 years if initial remitted episode - usually due to non-adherence
   b. Relapses → reduction in gray matter → reduced response to meds
   c. Intensive psychosocial strategies combined with low-dose AP effective at reducing relapse rates
   d. Weigh long-term exposure to adverse effects of meds and associated functional impair and risk of relapse
   e. Many youth with early psychosis require longlife maintenance AP; no data on length of treatment

Subsequent Acute Episodes of Psychosis or SCZ

16. Offer AP with psychological interventions (FI with individual CBT) (strong)
17. Choice of drug based on clinical response and SE associated with current/previous medication (strong)

Hospital Care

18. If hospital care needed, should be in a setting appropriate to their age and developmental level (strong)

Management of Acute Aggression or Agitation

19. HCPs using sedation or restraint should be trained and competent in undertaking these procedures in C&Y (strong)
20. Be cautious when using high-potency AP due to higher risk of acute dystonia in C&Y (strong)
   a. Often IM preferred to avoid physical restraint
   b. Benzo (PO or IM) often used, however risk of paradoxical response
   c. AP preferred if SCZ diagnosis confirmed
   d. Insufficient evidence for antihistamine use
21. Offer patient/family the opportunity to discuss experience, provide clear explanation of decision, and record (strong)

Promoting Recovery and Future Care in Primary Care

22. Clearly establish responsibility for monitoring physical health of C&Y between primary and specialty care
   a. Monitor physical health at least once/year or more if indicated (strong)
   b. Aripiprazole approved for SCZ treatment in youth <18 years
   c. Risk of neurological SE highest with risperidone > OLZ > aripiprazole
   d. Evidence-based monitoring protocols for SGA and FGA strongly encouraged

Interventions for C&Y with Inadequate Treatment Response

23. Offer CLZif inadequate response despite sequential use of adequate doses of 2+ different AP, each for 6-8 weeks (strong)
    a. CLZ superior efficacy for C&Y with TRS
    b. Following initial response, often increased clinical response in the ensuing 6-8 months
    c. Benefits sustained in long-term maintenance studies (up to 2-9 years)
    d. Both psychiatrist and patient/family must commit to increased monitoring requirements

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PSYCHOSOCIAL TREATMENT IN CHILDREN AND YOUTH

1. Clinicians should work with parents/carers and C&Y with SCZ (strong)
2. Offer help/treatment/care in atmosphere of hope and optimism, focusing on recovery (strong)
3. Trusting, supportive, empathetic and non-judgemental relationships essential (strong)
4. Advise parents/carers about their right and access to assessment of their own physical/MH needs (strong)
5. Clinicians need to be trained and skilled in working with families, including legal/ethical considerations (strong)
6. Clinicians should foster C&Y's autonomy/self-management and offer access to peer support (strong)
7. Aim to maintain continuity of individual therapeutic relationships (strong)
8. Ensure patients/families understand confidentiality
9. Discuss how patient wants family involved in care; discussions repeated at intervals (strong)
10. Ensure that information is understood by patient/family - take into account patient's developmental level, emotional maturity and cognitive capacity
11. Work with interpreter if possible, and recommend educational resources for English/French teaching (strong)
12. Clinicians need to gain cultural competence (seek advice/supervision from HCPs with experience) (strong)

Family Intervention

13. Offer to all families during acute phase or later, including inpatient setting (strong)
14. FI should include the patient; at least 10 planned sessions over 3 months to 1 year
    a. Consider family's preference for single-family or multifamily group intervention
    b. Include communication skills, problem solving and psychoeducation (strong)
    c. FI can improve recovery of patient and entire family; can address crisis management and recovery

CBT

15. Offer CBT to assist in promoting recovery for those with **persisting +/- sx and those in remission** (strong)
16. Should be delivered by trained therapist following established protocol, in a collaborative manner
    a. Include teaching patient to monitor thoughts/feelings/behaviours/symptoms, re-evaluate perceptions/beliefs/thoughts that contribute to symptoms, promote ways of coping with sx, self-esteem, stress reduction, and improve functioning
    b. At least 16 sessions (strong)
    c. No RCTs on CBT specifically for C&Y with SCZ
    d. Literature suggest that **group > individual CBT,** however take patient's preferences into account and both formals should be made available if possible

Supported Employment and Education Programs

17. Offer supported employment programs if older than compulsory school age and wish to work (strong)
18. Supported program principles:
    a. Regular/competitive work = goal, zero exclusion, MHT works together with supported employment team, personal job preference considered, offer counselling re: social benefits, rapid job search, job specialist involved, support offered continuously with no time limit (strong)
19. If of compulsory school age, liaise with patient's school/educational authority to ensure ongoing education (strong)

20. Consider supported education programs for C&Y of compulsory school age and wish to complete a degree, obtain training prior to employment, have special education needs or accommodations (B)
21. Supported education programs modeled on/offered along with supported employment; same principles (B)
22. If supported employment/education not available, MH services should work with stakeholders to enable patients to stay at work/school/access employment (strong)
    a. **Employment and education = essential domains of MH recovery**
    b. Supported employment model most effective vocational rehab method for obtaining competitive employment

[Subsequent interventions have less evidence but either common practice, or have promise re: empirical support]

Patient Education

23. Provide patients and family with info re: psychosis/SCZ, including interventions and support groups (strong)
    a. Education does not have significant impact on critical outcomes

Cognitive Remediation

24. Consider CRT for patients who have persistent problems with cognitive difficulties (B)
    a. Not enough empirical evidence to strongly recommend, however can reduce cognitive deficits

Social Skills training

25. Should be available for those having difficulty with stress/anxiety related to social interactions (B)
    a. Includes conversational skills, making friends, assertiveness, instruction about social behaviour, modeling, role-playing, behavioural reversal, feedback and homework → may improve negative symptoms

New developments

- Mindfulness, ACT, compassion-focused therapy, avatar therapy, social cognitive training, and metacognitive training (cognitive biases related to psychosis)

INDIVIDUALS AT CLINICAL HIGH RISK OF PSYCHOSIS

- 80-90% of patients with SCZ retrospectively report prodromal period
- **3 syndromal subgroups:**
    - Attenuated positive symptom syndrome (APSS) - most common
        - Emergence/worsening of non-psychotic-level disturbances in TC, TF or perceptual abN over the past year
    - Brief intermittent psychotic symptom syndrome (BIPS)
        - 1+ threshold positive sx too brief to meet dx criteria for psychosis
    - Genetic risk and deterioration (GRD)
        - Functional decline + genetic risk (schizotypal PD or 1st degree relative with SCZ spectrum d/o)
- Measures to determine clinical high risk:
    - Comprehensive Assessment of At-Risk Mental States (CAARMS)
    - Structured Interview of Prodromal Syndromes (SIPS) - most common
        - Measures presence of at-risk state for psychosis, sx severity over time, and conversion to psychosis

1. If person is distressed and has a decline in social function, and has APS/symptoms suggestive of possible psychosis OR 1st degree relative with psychosis/schizotypy → refer for comprehensive assessment (strong)
2. Assessment to be done by psychiatrist or trained specialist with experience in at-risk mental states (strong)
    a. Ideally use CAARMS or SIPS; **73% of those at CHR also have comorbid axis I diagnosis** (usually **depression**)
3. **Offer individual CBT, with or without FI** (strong)
4. Offer interventions for the presenting problem (i.e. anxiety, SUDs, personality) (strong)
    a. Comorbid condition **does not increase risk of transition** to psychosis; tx can relieve distress and improve function
5. Offer interventions to prevent development/persistence of functional deficits (D)
    a. Functional and/or cognitive impair often present before and worsen until onset of psychosis - may also predict conversion, thus **carefully assess function and suggest social skills training**
6. Psychological interventions (CBT) and pharmacological interventions are able to prevent/postone first psychotic episode in adult CHR patients (A) → 7 RCTs showed **reduced risk of conversion by 64%**
7. Tx should be monitored by psychiatrist, psychologist or equivalent MHP (D)
8. In adult CHR patients, a staged intervention model should be applied with the least restrictive approach

a. Offer psychological intervention (CBT) → if ineffective then add low-dose SGA
b. Goal of symptomatic stabilization - **long-term AP for prevention NOT recommended (**D)

9. If despite tx patient continues to have sx, impaired function, or is distressed BUT clear dx of psychosis cannot be made, monitor regularly for change in sx/function for **up to 3 years** using assessment tools
    a. Frequency/duration of monitoring based on:
        i. Severity and frequency of sx
        ii. Level of impairment and distress
        iii. Degree of family disruption or concern
    b. If patient wants discharge, offer F/U appt and option to self-refer, and ask GP to continue monitoring (strong)
    c. 2.5 year F/U → 70% did NOT transition (*assume that this is those without tx*)
    d. Also 25-35% develop a diagnosable illness

COMPREHENSIVE COMMUNITY TREATMENT

- Successful tx of SCZ requires organized, recovery-oriented mental health system with coordinated services
    - MHT, forensic services, supportive living, support for care providers, EPI, ACT programs
- Limited evidence that national MH strategy has led to improved service delivery and outcomes
- Core value for MH services = **supporting recovery**
- 5 key recovery processes: **connectedness, hope, identity, meaning, empowerment**
- No published decision aids for for facilitating shared decision making in SCZ

1. ***Comprehensive Care across All Phases*** - mental health services should offer a comprehensive range of interventions (strong)
    a. The planning of treatment services for individuals with schizophrenia can be organized around population-based estimates of prevalence and treatment need
    b. In developed countries such as Canada, services to a defined population should include a range of services - outpatient clinics, CMHTs, inpatient care and community residential care, ACT teams, EPI teams, etc.
    c. Economic modeling suggests that combinations of optimal evidence-based treatments for SCZ are cost-effective
2. ***Full Range of Interventions*** - mental health services should be able to offer the full range of psychological, pharmacological, social, occupational and culturally safe interventions recommended.
    a. Key - be competent, emphasize **engagement** (rather than risk management), provide tx/care in the least restrictive/stigmatizing environment possible, offer diversity-related practices (strong)
3. ***CMHTs serving a defined population*** - mental health services shall be available for all patients with SCZ
    a. CMHTs shall expect to cover **1.5% of the population**
    b. CMHTs must be sufficiently resourced to provide high-intensity support (1 staff: 10 patients) to 10% of patients with SCZ, ACT/medium intensity support (1:20) to another 20%, and ICM to remaining 70%
    c. Majority of patients receive services with 1 member of CMHT as case manager (1:80)
4. ***Service User Experience*** - improve mental health care experience for patients with psychosis/SCZ
    a. Work in partnership, build relationships, foster autonomy
5. ***Communication with patients/carers from diverse backgrounds*** **-** avoid clinical jargon, ensure written info is available in appropriate language/audio format, work with interpreter, offer English-language teaching providers
6. ***Assertive Community Treatment*** - should be provided for patients with serious mental disorders who make high use of inpatient services, have residual psychotic sx and have a history of poor engagement with services
    a. ACT combines team-based and outreach approach, 1:10 staff:patient, and some on call 24/7
    b. **Effective** at **reducing readmission rates, improving housing/occupation fn, QoL, and service satisfaction**
    c. **NO improvement in clinical state or overall costs of care**; most impactful when high rate hospitalization
7. ***Intensive Case Management*** **-** consider for patients likely to disengage from treatment/services
    a. Caseload is NOT shared between clinicians (unlike ACT)
    b. Mixed outcomes - increased hospitalization/cost, increased medication use
8. First-onset Psychosis Models of Care - these individuals should receive tx in an evidence-based coordinated specialty service that is multidisciplinary and includes:

   a. Assertive outreach, family involvement/FI, access to psychological interventions, vocational/educational interventions, and AP meds
      i. Assess quality of care using First Episode Psychosis Fidelity Scale (FEPS-FS)
9. Assess early intervention referrals without delay (or refer to urgent care services)
   a. Untreated psychosis associated with suicide attempts (**occurs in 15-29% of patients**), aggression and violence, and association between duration of untreated psychosis and poor outcome
10. ***Early Intervention*** - should be accessible to all with first episode/presentation regardless of age/duration of illness
    a. Mean age of onset 21.4 (men) and 27.4 (women)
11. ***Crisis resolution and home treatment teams*** - offer as a first-line service to support people with psychosis/SCZ during acute episode if severity/risk to self or others exceeds capacity of EPI/community teams
    a. Definition = any type of crisis-oriented treatment of acute psychiatric episode
12. ***Crisis houses or acute day facilities*** - residential alternatives to acute admission
    a. Consider acute community treatment before admission and to enable timely discharge from IPU
    b. Can consider this in addition to crisis resolution/home treatment depending on patient preference/need
    c. Cochrane review - no differences between home vs. inpatient care
13. ***Hospitalization*** - think about the impact of hospital care on patient/family
    a. If unavoidable, ensure setting is suitable for their age/gender/vulnerability and supports their carers
14. ***Supported employment*** - offer to those who wish to find/return to work
    a. More effective than prevocational training for getting competitive employment
15. Supported housing and long-term residential care - people with SCZ shall live in housing of their choice
    a. Supported housing shall be available (couples independent housing and community-based supports)
    b. Governments need to consider non-institutional residential facilities for those who cannot live independently
16. ***Peer support and self-management*** - PSW are trained, stable, recovered from psychosis and receive support/mentorship from the team
    a. Consider for people with SCZ to improve user experience and QoL
17. ***Return to primary care*** - Offer this option if symptoms have responded to treatment and remain stable
    a. Record in notes and coordinate transfer of responsibilities
18. ***Relapse and re-referral to secondary care*** **-** if patient relapses, PCP should refer to crisis section of care plan
19. ***Transfer between health regions*** - a meeting should be arranged between the services involved, patient should agree to transition plan, and this should be sent to PCP and secondary care providers

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PHYSICAL HEALTH AND DRUG SAFETY

Dosing and polypharmacy

- Ceiling effect due to maximal occupancy of D2 receptors → lack of efficacy of high-dose strategies
- AP polypharmacy may be used in select or tx-refractory situations

1. HCP and patients should work together to find most appropriate med and the lowest effective dose
2. Should NOT be routine use of multiple AP meds; if being considered discuss benefits and harms with patient

Monitoring CV health and metabolic syndrome

- Options for monitoring CV status include liaison with PCP/CV specialty service, undertaking this responsibility in specialized psych service, or a staged handover to primary care

3. Patients with psychosis/SCZ should be offered combined **healthy eating and physical activity program** by MH provider
4. Routinely monitor weight and CV/metabolic indicators of morbidity
5. Suggested monitoring schedule:
   a. Low rates of screening/monitoring due to ambiguity about who is accountable

Test	Baseline	At 1 Month	At 3 Months	Annually
Individual and family history of physical illness	✓			✓
Smoking history	✓		✓	✓
Body mass index/ weight/waist circumference	✓	✓	✓	✓
Blood pressure	✓	As clinically indicated	✓	✓
HbA1C/fasting glucose	✓	As clinically indicated	✓	✓
Random lipids/fasting lipids	✓	As clinically indicated	✓	✓
Prolactin		As clinically indicated		
History and examination for extrapyramidal symptoms	✓	✓	✓	✓

6. Local arrangement for physical health monitoring should be put in place at the time of AP prescribing
7. PCPs should monitor physical health of patients at least annually; should be comprehensive and include CV risk assessment

Prevention and management of metabolic side effects

- AP risk for weight gain: lower (<12%) aripiprazole, asenapine, ziprasidone; intermediate (10-24%) lurasidone, FGAs, paliperidone, perphenazine, quetiapine, risperidone; higher (>24%) CPZ, CLZ, OLZ
- Mechanism of weight gain unknown - possible due to H1-receptor binding, and genetic susceptibility
- Metformin may help with managing weight during AP treatment, and may promote weight loss within 3 months
    - May reduce rate of new-onset diabetes in patients with dysglycemia

8. Lifestyle interventions should be considered for those experiencing weight gain on AP meds
9. Metformin should be considered for those experiencing weight gain on AP meds
10. If there is rapid/excessive weight gain, abnormal lipid levels, or problems with blood glucose, offer interventions relevant to Canadian guidelines

AP meds and arrhythmias

- FGA and SGA have x 2 rate of sudden cardiac death, dose-dependent
- No significant QTc increase with lurasidone, aripiprazole, paliperidone, and asenapine
- Health Canada suggests drug d/c for QTc >500ms or increase of >60ms from baseline

11. ECG before AP med suggested if:
    a. Specified in summary of product characteristics, physical exam identified specific CV risk (i.e. HTN), personal hx of CVD, or family hx of QT prolongation

Extrapyramidal side effects

- Include dystonia, akathisia, parkinsonism, TD, tardive dystonia, tardive akathisia
    - Tardive dystonia - subtype of TD; sustained, slow, involuntary movements/postures affecting limbs, trunk, neck or face (i.e. retrocollis, facial grimacing, opisthotonus, blepharospasm, cervical dystonia)
    - Tardive akathisia - persistent form x >1 month when patient on a constant dose of AP
- Assess with **EPS Rating Scale** (for all sx), AIMS (for TD), Simpson Angus Scale (parkinsonism), Barnes Akathisia Scale

12. Inform patients of risk of EPS and encourage sx reporting. HCP should be vigilant of EPS; use scale at least annually
13. If EPS are of particular concern, then SGAs (especially OLZ, QTP, CLZ, asenapine) or low-potency FGAs should be considered
14. IF TD a specific concern, consider SGA