GOALS OF PHARMACOTHERAPY:

- Achieve and maintain remission
- Improve quality of life
- Prevent progression of the disease

ONSET OF ACTION:

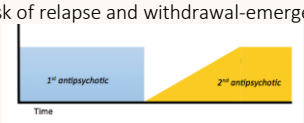
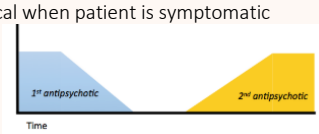
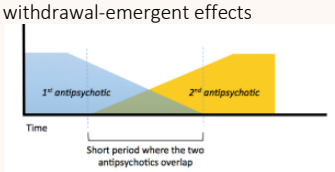
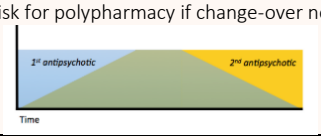
WEEK 1	• Distinct onset within first week
WEEK 1-2	• Almost 22% improvement in first 2 weeks • Clinical observation is vital during this period • If pt does not show 20% sx reduction score in first 2 weeks, then low chance of response on that drug/dose in the future
WEEK 2-3	• If no response, treatment should be changed (switch drug or increase dose)
WEEK 3-4	• Only 9% improvement in weeks 3 or 4
WEEK 6-8	• It is recommended to wait 6-8 weeks to evaluate treatment response

DECISION TO SWITCH ANTIPSYCHOTIC:

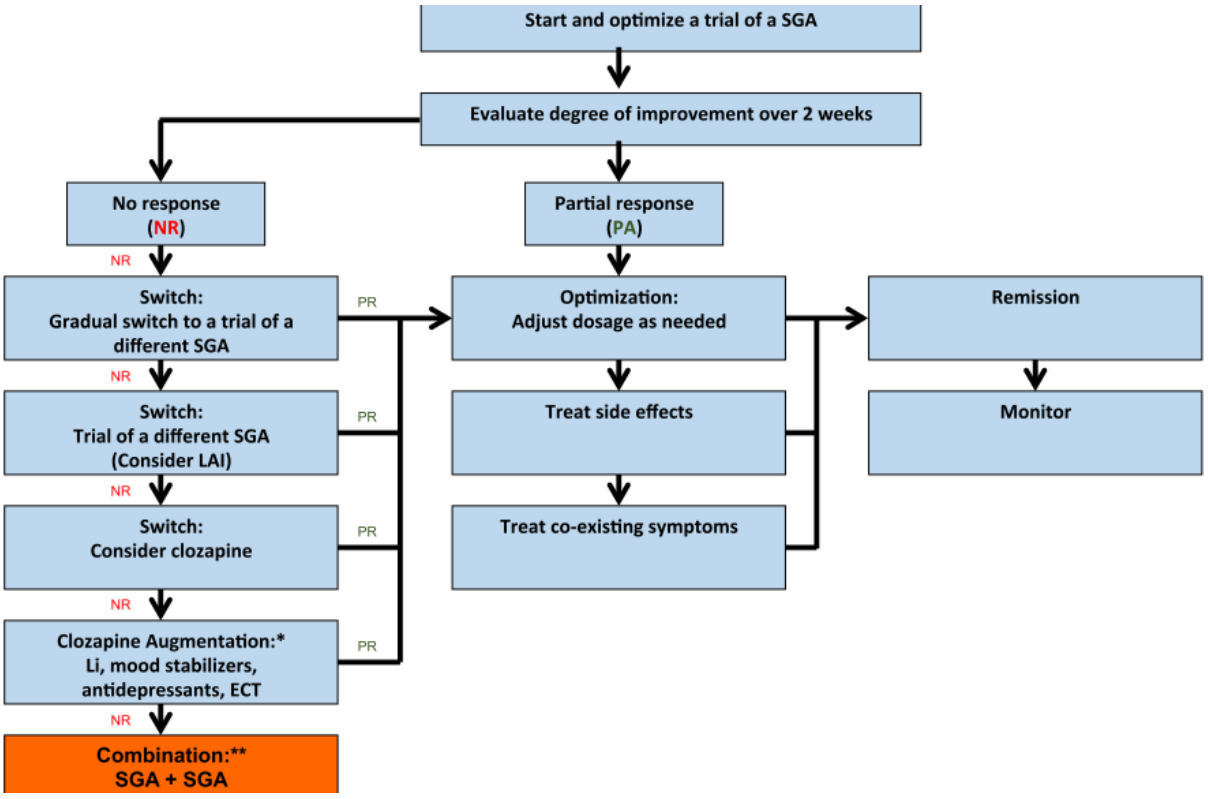
Sx	• Persistent positive symptoms that are more than mild in intensity
	• Persistent negative symptoms
	  ○ Assess and treat any causes of secondary negative symptoms (ex// depression, medication-related SEs like sedation)
	  ○ Remaining sx can be considered primary negative symptoms

SEs	• Threshold should be low for deciding to switch due to side effects • Patient on multiple medications for SEs • Some SEs can be treated with adjunctive meds • Some SEs decrease with time (sedation, postural hypotension) ○ If patient is benefitting from medication you may decide to wait for 4-6 weeks

SWITCHING ANTIPSYCHOTICS: SwitchRx

Stop/Start	• Abruptly discontinue the first drug • Start second drug at usual initial dose • Often used when patient has serious ADRs to first drug • Increased risk of relapse and withdrawal-emergent reactions 
Washout/ Start	• Withdraw first drug gradually • Begin second drug after suitable washout period • May minimize withdraw-emergent reactions • Not practical when patient is symptomatic 
Cross Taper	• Taper dose of the first medication while simultaneously increasing the dose of the second drug • Duration of cross-titration is usually between 1-4 weeks • Most well-accepted strategy • Minimizes withdrawal-emergent effects 
Delayed Withdrawal	• Establish patient on a therapeutic dose of the second drug before reducing the dose of the first drug • Preferred when relapse is a significant concern • Increased risk for polypharmacy if change-over not complete 

TREATMENT GUIDELINE:



TREATMENT OF SIDE EFFECTS:

ACUTE DYSTONIA:

- Involuntary contraction of muscles causing uncontrollable repetitive or twisting movements of affected body part
- May involve neck, eyes, jaw, tongue, and back
- Can be painful and very frightening

PREVALENCE ≈ 10%
- More common in young males
- Neuroleptic naïve
- High-potency antipsychotics

CLINICAL PEARLS:
- Can occur within hours of starting antipsychotics (minutes if given by IV or IM)
- Patient may not be able to swallow
  - Response to IV in ~ 5 mins
  - Response to IM in ~ 20 mins

TREATMENT:
- Benztropine 2 mg PO/IM/IV STAT, then 1-2 mg bid x 2 days
- Diphenhydramine 25-50 mg PO/IV STAT

AKATHISIA:

- Movement disorder characterized by an inner restlessness and a strong need to be in constant motion

PREVALENCE ≈ 25%
- Less with SGA: ariprazole > risperidone > olanzaprine > quetiapine > clozapine

CLINCAL PEARLS:
- Acute akathisia occurs within hours to weeks of starting an antipsychotic or increasing the dose
- May be misinterpreted as psychotic agitation
- Beta-blockers and BZD can be used in combination
  - However, may be preferable to try another antipsychotic

TREATMENT:
- Reduce dose of antipsychotic
- Propranolol 10 mg qid (range 20-160 mg/day)
- Mirtazapine 15 mg hs
- Benzodiazepines (poor evidence)

INSOMNIA:

CLINICAL PEARLS:
- Insomnia as acute symptom of psychosis vs. chronic difficulty in falling asleep
- Prn treatments for insomnia should be time-limited

TREATMENT:
- Benzodiazepine, zopiclone or trazodone prn
- If partial or non-response, use another

BENZO BEDTIME PRN DOSE:

Lorazepam 0.5-1 mg	Oxazepam 10-15 mg (max 30)
Temazepam: 15-30 mg	Zopiclone 3.75-7.5
Trazodone 12.5 – 100 mg	

PSEUDO-PARKINSONISM:

- Adverse effect of drugs that cause sx resembling Parkinson's disease, such as tremors, rigidity, mask-like face, slow thinking, and salivation

PREVALENCE ≈ 20%
- More common in elder females and those with pre-existing neurological damage (ex// head injury, stroke)

CLINICAL PEARLS:
- Can occur days to weeks after an antipsychotic is started or after the dose has been increased
- Anticholinergics should be reviewed at least every 3 months
  - Don't prescribe at night since sx are absent during sleep

TREATMENT:
- Reduce dose of antipsychotic
- Change antipsychotic
- Treat with oral anticholinergic
  - Benztropine 1 mg bid (range 2-6 mg/day)
  - Trihexphenidyl 2 mg bid (range 4-12 mg/day)

TARDIVE DYSKINESIA:

- Disorder that involves involuntary movements, most commonly lower face
- Repetitive purposeless movements may include lip smacking or chewing, tongue protrusion, choreiform hand movements, pelvic thrusting

PREVALENCE ≈ 5% per year of antipsychotic exposure
- More common in elderly women, those with affective illness, and those that develop extrapyramidal symptoms (EPS)

CLINICAL PEARLS:
- Occurs in months to years; aproximately 50% are reversible
- Movement worse under stress
  - Stop anticholinergic if prescribed
- Other treatments have included tetrabenazine, clonazepam, amantadine, gingko biloba

TREATMENT:
- Reduce dose of antipsychotic
- Switch to SGA antipsychotic
- Switch to clozapine or quetiapine

NEUROLEPTIC MALIGNANT SYNDROME (NMS):

- Rare, but life-threatening reaction to any antipsychotic agent
- Symptoms include: muscle rigidity, confusion, fluctuating consciousness, diaphoresis, fever, hyperthermia, fluctuating blood pressure, tachycardia

RISK FACTORS:
- Young age
- Neurologic disabilities
- Rapid or parenteral admin of anti-psychotics
- Dehydration
- Male
- Exhaustion
- Agitation

CLINICAL PEARLS:
- Progression of symptoms is a medical emergency requiring supportive medical measures
- NMS has been reported with all antipsychotics

TREATMENT:
- Discontinue antipsychotic
- Bromocriptine + dantrolene
- Amantadine

TREATMENT OF SIDE EFFECTS CONTINUED:

AGITATION ASSOCIATED WITH PSYCHOSIS:

Mild sedation required	• Lorazepam +/- risperidone, olanzapine, or quetiapine PO
Moderate-significant sedation required	• Lorazepam + loxapine or haloperidol PO/IM • Haloperidol + antihistamine (PO/IM) • Olanzapine IM
Sedation required for extended period	• Zuclopenthixol acetate IM

DEPRESSION (NOT IN ACUTE PHASE):

TREATMENT:

- SSRI
- Bupropion SR
- Venlafaxine XR
- Mirtazapine

If partial or non-response, use another

CLINICAL PEARLS:

- Depression and suicide common in schizophrenia
- Some antidepressants can cause akathisia

PERSISTENT SX OF AGGRESSION/HOSTILITY, MOOD LABILITY:

TREATMENT:

- Mood stabilizer (VPA, lithium, carbamazepine)
- If partial or non-response, clozapine

CLINICAL PEARLS:

- Clozapine: an increase risk of seizures at higher dose
- Carbamazepine: strong inducer of CYP3A4 and Pgp
- Clozapine + carbamazepine: ↑risk of bone marrow suppression
- Quetiapine + carbamazepine: quetiapine has a low bioavailability, and carbamazepine will reduce it even further