Polypharmacy, Antipsychotics in Children and Adolescents

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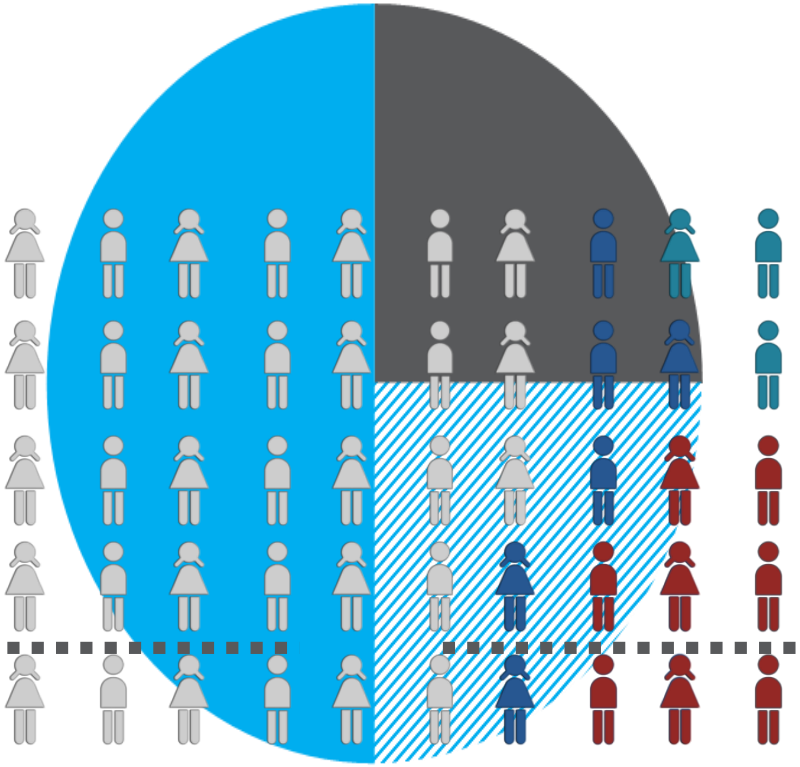
Objectives

- Define and recognize polypharmacy in behavioral health management of children and adolescents.
- Conceptualize common reasons and risk factors leading to polypharmacy of psychotropic medications.
- Identify FDA approved antipsychotic medications and their indications for use in youth.
- Integrate monitoring guidelines for antipsychotic medications in children and adolescents.
- Apply strategies for simplification of medication regimens using case examples.

Thank you pediatrics colleagues !

Burden of mental illness

50% of all lifetime mental illness start by **age 14**

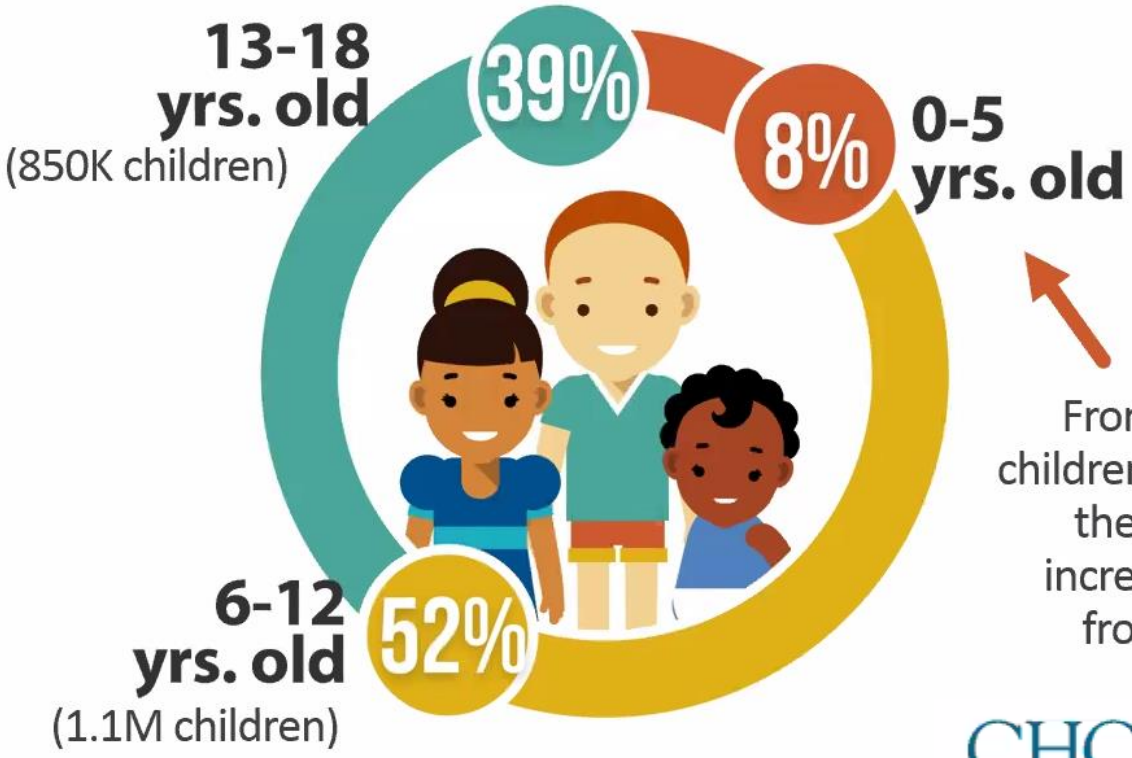


75% of all lifetime mental illness start by **age 24**

Source: National Health & Nutrition Examination Survey , 2010; National Comorbidity Survey Replication-Adolescent Supplement, 2010; NIMH, Mental Illness Exacts Heavy Toll: Beginning in Youth, 2005

Children Receiving Psychotropic Medications by Age

In 2011, **2.1M+ children in Medicaid received psychotropic medications**. The age distribution is as follows:



From 2005 to 2011, children ages 0-5 receiving these medications increased by 130% — from 78K to 179K

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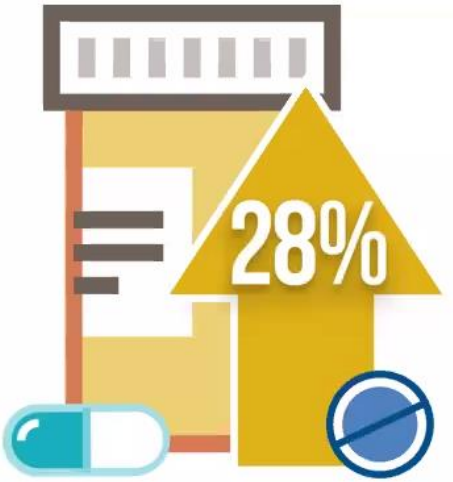
Changes in the Number of Children Receiving Psychotropic Medications

Between 2005 and 2011, the number of **children covered by Medicaid increased by nearly 12%** to 32.4M

During that same period, Medicaid-covered **children receiving psychotropic meds increased by 28%**



And **expenditures for those medications increased by 70%** — a $1B increase, from $1.6B to $2.7B

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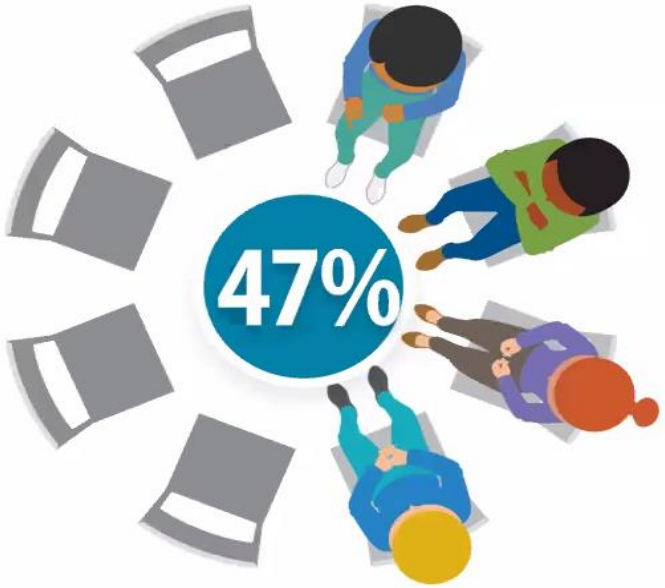
Children Receiving Psychotropic Meds without Behavioral Health Services

Of the 2.1M+ children receiving these medications in 2011, **nearly half (47%) did not receive accompanying behavioral health services**



And almost **one-third (30%) are getting more than one** of these medications — **47% for children in foster care**

Antipsychotic medications

- One of the fastest growing class of psychotropic meds

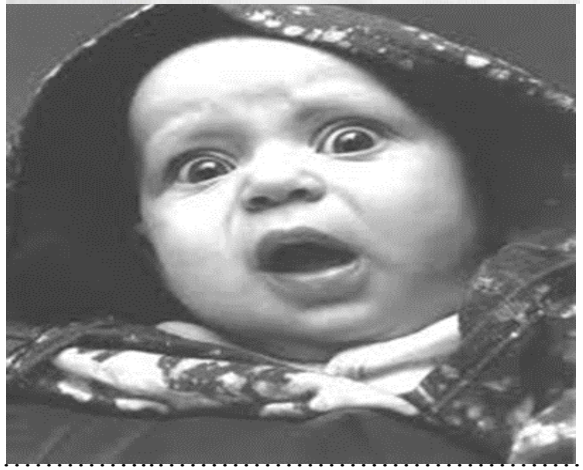
- Male, disruptive behavior disorders, foster care placement and Medicaid enrollment are associated with higher rates of prescription

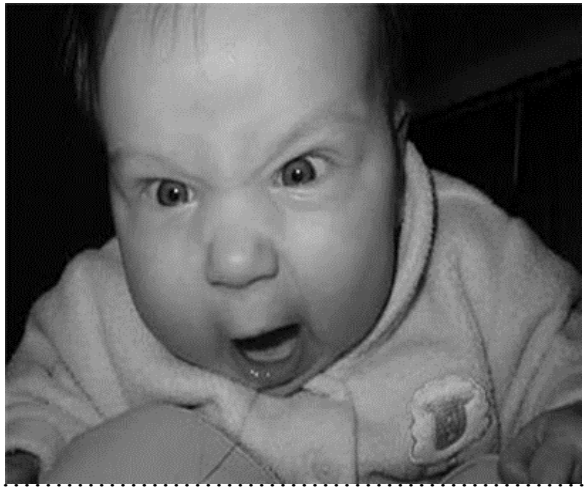
- Only a small percentage of visits associated with antipsychotic Rx are for FDA indicated diagnosis and often associated with polypharmacy

- Significant variation in prescribing patterns (2% Hawaii to 22% Texas) and poor adherence to monitoring guidelines.

- Youth of antipsychotics are at a 50% higher risk of long term metabolic issues including DM2

Pre-test





Polypharmacy

- Most common: ≥2 psychotropic medications in the same class
- For ages 0-5 – any antipsychotic (except risperidone in ASD)
- For ages 6-8: ≥3 psychotropic meds
- For ages 9-17:≥4 psychotropic meds
- For all ages: doses exceeding recommended doses

Polypharmacy is not always irrational…

Type	Example
Multi class	Stimulant + alpha agonist *(ADHD: Concerta + tenex)*
Adjunctive	Antipsychotic + Benztropine (*ASD: Risperidone + Cogentin*)
Augmentation	SSRI + mood stabilizer (*Trichotillomania: Sertraline + Topiramate*)
Same class	*(Anxiety/insomnia: Citalpram + Trazodone)*

But it could be….

Case example:

7 year old child recently came to live with father after changes in custody due to abuse allegations towards mother's boyfriend. Has history of ADHD, 'mood swings', aggression. Dad has the medication list provided by mother.

Medications:

- Concerta 54 mg AM, Ritalin 10 mg at 4 pm
- Periactin 2 mg BID
- Clonidine 0.2 mg bedtime
- Risperidone 0.5 mg TID
- Lamotrigine 25 mg BID
- Colace 50 mg daily
- Melatonin 10 mg bedtime

Avoiding polypharmacy pitfalls

- Obtain accurate medication history and reconciliation including OTC medications
- Ensure adherence to medications
- Link each prescribed medication to the *diagnosis*
- Identify medications for *treating side effects*
- Consider de-prescribing if the drug causing side effects changed or discontinued

Antipsychotic polypharmacy

- More than 2 antipsychotics used in the same patient for extended period of time

- Excess dose that recommended for age

(Does not include cross taper)

Use of Multiple Concurrent Antipsychotics in Children and Adolescents (APC)

- The percentage of children and adolescents 1–17 years of age who were on two or more concurrent antipsychotic medications for *at least 90 consecutive days* during the measurement year.

Antipsychotics: Preview

First Generation Antipsychotics (FGA)	Second Generation Antipsychotics (SGA)
• Chlorpromazine • Fluphenazine • Haloperidol • Loxapine • Perphenazine • Pimozide • Thioridazine • Thiothixene • Trifluoperazine	• Aripiprazole • Asenapine • Brexpiprazole • Clozapine • Iloperidone • Lurasidone • Olanzapine • Paliperidone • Quetiapine • Risperidone • Ziprasidone

FGA: approved indications

	Schizophrenia	Tourette's	Severe Behavioral Problems
Chlorpromanzine			6 mo - 12 yrs
Haloperidol		≥ 3 yrs	"children"
Perphenazine	≥ 12 yrs		
Pimozide		≥ 12 yrs	
Thiothixene	≥ 12 yrs		
Trifluoperazine	≥ 12 yrs		

SGA: approved indications

	Schizo	BPD, Mania	BPD, Mixed	BPD, Maint	ASD, Agitation
Aripiprazole	13-17 yrs	10-17 yrs	10-17 yrs		6-17 yrs
Asenapine		10-17 yrs	10-17 yrs		
Lurasidone	13-17 yrs				
Olanzapine	13-17 yrs	13-17 yrs	13-17 yrs		
Paliperidone	12-17 yrs				
Quetiapine	13-17 yrs	10-17 yrs		10-17 yrs	
Risperidone	≥ 13 yrs	≥ 10 yrs		≥ 10 yrs	≥ 5 yrs

SGA: Side effects to look for…

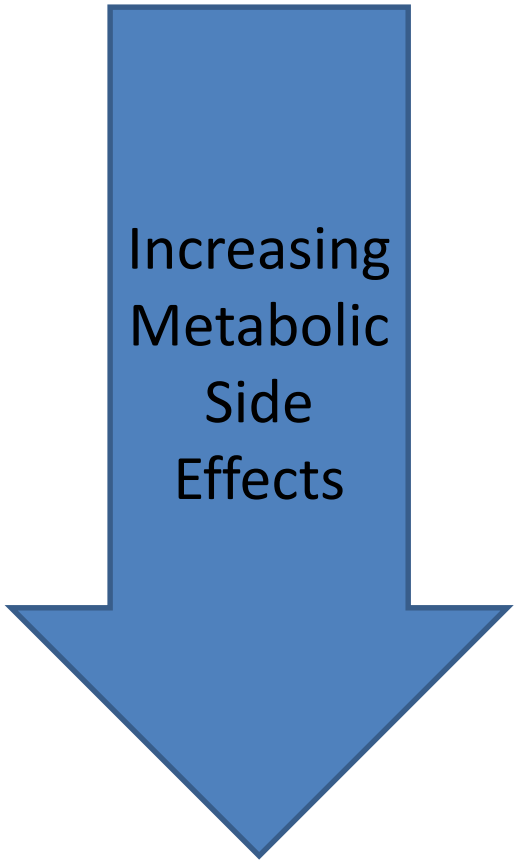
- Sedation
- Stomach upset
- Nausea
- Constipation
- Prolactin elevation
  - Risperidone
  - Paliperidone
- Cardiovascular
  - QTc prolongation
- Extrapyramidal Symptoms (EPS)
  - Dystonic Reaction
  - Akathisia
  - Tardive Dyskinesia
- Metabolic Effects
  - Weight gain
  - Lipid abnormalities
  - Glucose intolerance

SGA: nuts and bolts

Drug name	Dosage form	Starting dose	Specific comment
Risperidone	0.25, 0.5,1– 4 mg 1mg/ml - liquid	0.25 mg HS	EPS ++ Prolactin increase risk Lowers sz threshold
Aripiprazole	2,5,10,15,30 mg 1mg/ml - liquid	2 mg daily	Long half life Black box - suicide Impulsivity, gambling
Olanzapine	2.5, 5, 7.5, 10, 15, 20 mg	2.5 mg HS	Weight gain highest Dyslipidemia risk
Quetiapine	25, 50, 100, 200, 300, 400 mg	25 mg BID	Sedation, orthostasis Large pills to swallow QTc prolongation risk
Ziprasidone** (off label)	20, 40, 60, 80 mg	20 mg HS	Nausea Take with food (500 calories) for absorption EKG at baseline for QTc

- Children and adolescents appear to be more susceptible to a number of side effects caused by antipsychotic medications
  - Sedation, withdrawal dyskinesia, endocrine abnormalities, age-inappropriate weight gain
- Safety and tolerability data are still sparse fewer long-term safety studies exist to evaluate the risks/benefits

- Aripiprazole
- Lurasidone
- Asenapine
- Risperidone
- Paliperidone
- Quetiapine
- Olanzapine



ADA Monitoring protocol for patients on SGAs*

	Baseline	4 weeks	8 weeks	12 weeks	Quarterly	Annually	Every 5 years
Personal/family history	X					X	
Weight (BMI)	X	X	X	X	X		
Waist circumference	X					X	
Blood pressure	X			X		X	
Fasting plasma glucose	X			X		X	
Fasting lipid profile	X			X		X	X

***More frequent assessments may be warranted based on clinical status**

De-prescribing

What is it NOT

- Indication that prescribing provider is doing it wrong
- Need to take children off of individual medications (rather than cumulative risk from multiple drugs)
- Denial of effective treatment for eligible patient
- Abrupt discontinuation without monitoring, consent from patient and collaboration with other providers

De-prescribing

What it IS:

- Part of good prescribing continuum - backing off when doses are too high, or stopping medications that are *no longer needed.*

- *Systematic*, patient centered process of identifying and discontinuing medications where existing or potential harms (current and future) outweigh the risks

- In the context of individual patient's status, goals and preferences

De-prescribing principles

- Review of *diagnosis and rationale* for med regimen
- *Side effects* from medications mistaken as target symptom?
- Establish *stability* of symptoms (remission, no regression) for specified period of time
- Consider *tapering* the medication that:
  - have greatest risk of side effects
  - least evidence of efficacy
  - supratherapeutic dose without justification
  - subtherapeutic dose with limited effectiveness
- Taper one medication at a time

De-prescribing principles

- Intensive therapy and psychosocial supports
- Close monitoring of recurrence or worsening of symptoms
- Some dysregulation and defiance is expected

- If symptoms recur and impair functioning:
- Restart the last tapered medication or increase the dose to the last effective dose
- Consider alternative medication

Revisiting 7 y/o Joe….

Medications:

- Concerta 54 mg AM, Ritalin 10 mg at 4 pm (*given at 6 pm by mom*)
- Periactin 2 mg BID
- Clonidine 0.2 mg bedtime
- Risperidone 0.5 mg TID
- Lamotrigine 25 mg BID
- Colace 50 mg daily
- Melatonin 10 mg bedtime

- ADHD: Concerta, Ritalin
- Mood: Risperidone, Lamotrigine
- Side effects: Periactin, Clonidine, Colace
- Primary/sleep: Melatonin

Revisiting 7 y/o Joe

DDx
- ADHD, anxiety related to trauma, possible PTSD
- Referral for trauma informed cognitive behavioral therapy

T0
- 1.- Reduced Concerta to 36 mg, moved Ritalin 10 mg from 6 pm to 2 pm
- 2- Stopped Clonidine, Reduced melatonin to 3 mg + sleep hygiene
- 3- Periactin reduced to AM

T1
- 1. Weaned off Lamotrigine
- 2. Tapered Risperidone to 0.5 mg in BID over 2 weeks
- 3. Started Sertraline 12.5 mg and titrated to 25 mg daily

T2
- 1. Decreased Risperidone to 0.5 mg in PM due to continued irritability, aggression.
- 2. Stopped melatonin, stopped Colace

T3
- ADHD – Concerta 36 mg AM, Ritalin 5 mg 2 pm (plan to reassess and d/c trial during holidays)
- PTSD – Zoloft 25 mg AM, Risperidone 0.5 mg PM (plan to d/c Risperidone in future)

Prescribing Optimization

Behavioral Health

Prescribing Guidelines for Behavioral Health

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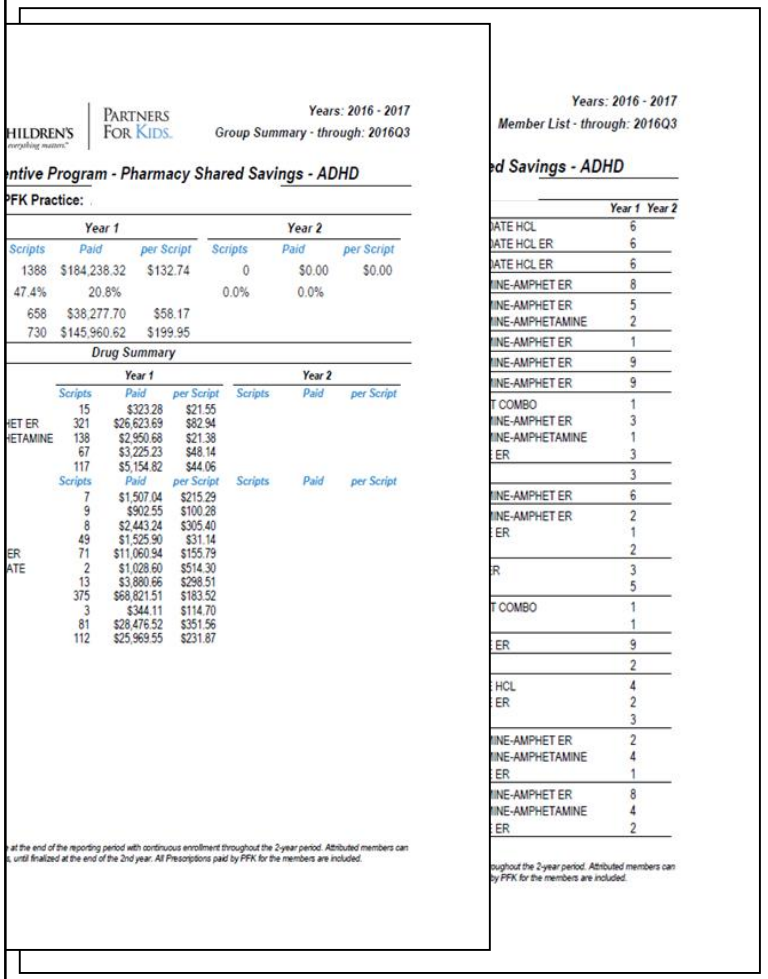

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Years: 2016 - 2017
Group Summary - through: 2016Q3

ntive Program - Pharmacy Shared Savings - ADHD

PFK Practice:

	Year 1			Year 2		
	Scripts	Paid	per Script	Scripts	Paid	per Script
	1388	$184,238.32	$132.74	0	$0.00	$0.00
	47.4%	20.8%		0.0%	0.0%	
	658	$38,277.70	$58.17			
	730	$145,960.62	$199.95			

Drug Summary

	Year 1			Year 2		
	Scripts	Paid	per Script	Scripts	Paid	per Script
	15	$323.28	$21.55			
HET ER	321	$26,623.69	$82.94			
HETAMINE	138	$2,950.68	$21.38			
	67	$3,225.23	$48.14			
	117	$5,154.82	$44.06			
	Scripts	Paid	per Script	Scripts	Paid	per Script
	7	$1,507.04	$215.29			
	9	$902.55	$100.28			
	8	$2,443.24	$305.40			
	49	$1,525.90	$31.14			
ER	71	$11,060.94	$155.79			
ATE	2	$1,028.60	$514.30			
	13	$3,880.66	$298.51			
	375	$68,821.51	$183.52			
	3	$344.11	$114.70			
	81	$28,476.52	$351.56			
	112	$25,969.55	$231.87			

at the end of the reporting period with continuous enrollment throughout the 2-year period. Attributed members can
, until finalized at the end of the 2nd year. All Prescriptions paid by PFK for the members are included.

Years: 2016 - 2017
Member List - through: 2016Q3

ed Savings - ADHD

	Year 1	Year 2
IATE HCL	6	
IATE HCL ER	6	
IATE HCL ER	6	
INE-AMPHET ER	8	
INE-AMPHET ER	5	
INE-AMPHETAMINE	2	
INE-AMPHET ER	1	
INE-AMPHET ER	9	
INE-AMPHET ER	9	
T COMBO	1	
INE-AMPHET ER	3	
INE-AMPHETAMINE	1	
ER	3	
	3	
INE-AMPHET ER	6	
INE-AMPHET ER	2	
ER	1	
	2	
R	3	
	5	
T COMBO	1	
	1	
ER	9	
	2	
HCL	4	
ER	2	
	3	
INE-AMPHET ER	2	
INE-AMPHETAMINE	4	
ER	1	
INE-AMPHET ER	8	
INE-AMPHETAMINE	4	
ER	2	

oughout the 2-year period. Attributed members can
by PFK for the members are included.

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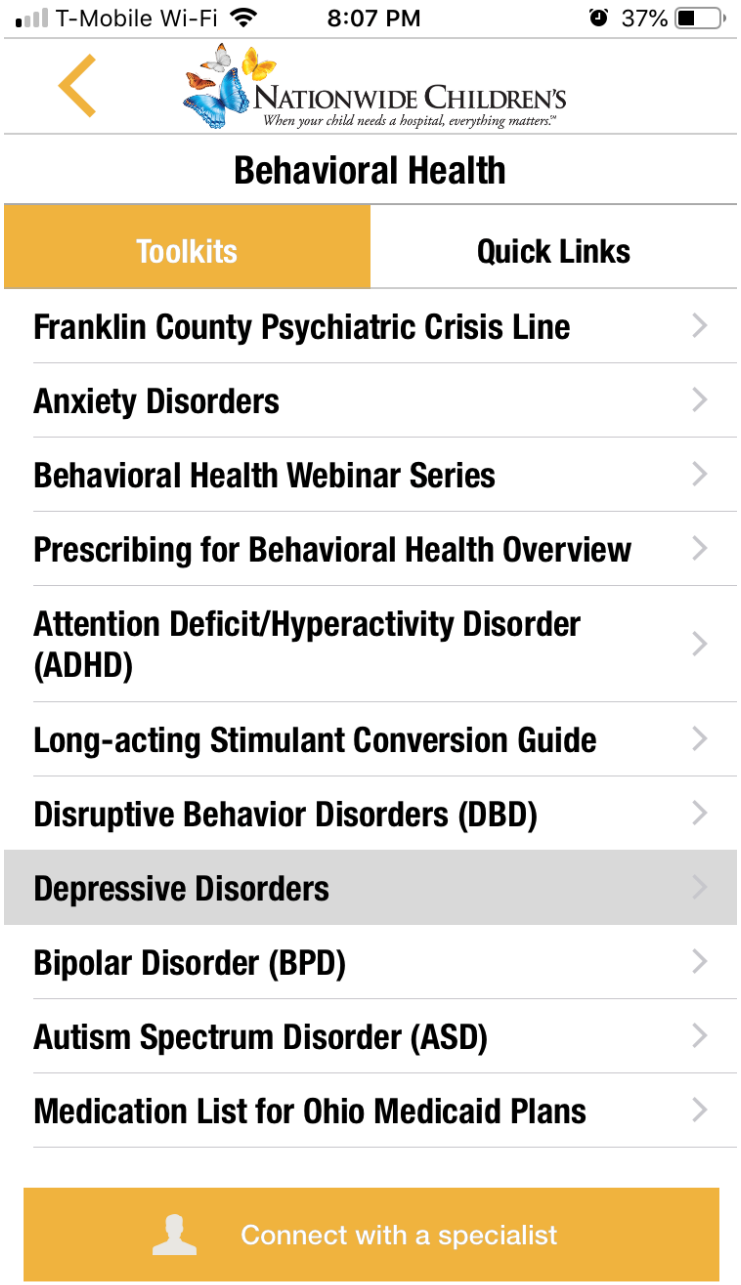
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Long-acting Stimulant Conversion Guide
Disruptive Behavior Disorders (DBD)
Depressive Disorders
Bipolar Disorder (BPD)
Autism Spectrum Disorder (ASD)
Medication List for Ohio Medicaid Plans
Connect with a specialist

Resources

- Partners for Kids: http://partnersforkids.org/wp-content/uploads/2018/08/W33230_PFK-Prescribing-Guidelines-for-Behavioral-Health.pdf

- AACAP: Resources for Primary Care https://www.aacap.org/AACAP/Resources_for_Primary_Care/Home.aspx

- Nationwide Children's Hospital: Physician direct connect

Questions?