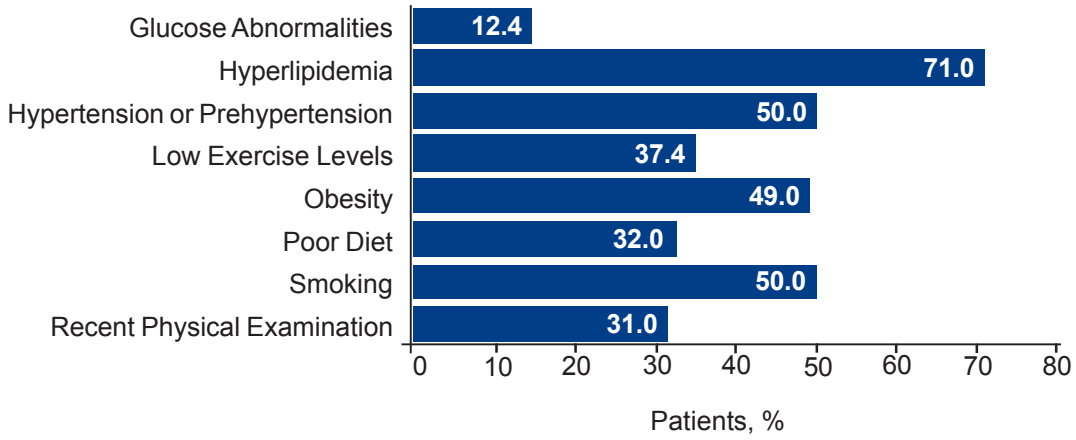
BACKGROUND

MIAMI: MIRECC Initiative on Antipsychotic Management Improvement

Comorbidity and Mortality in Patients with Serious Mental Illness



50% increased risk of death from medical causes in schizophrenia (20% shorter lifespan; die approximately 10 years younger)

Obesity in Patients with Schizophrenia

Prevalence of overweight patients with schizophrenia (BMI ≥25) is 42%.

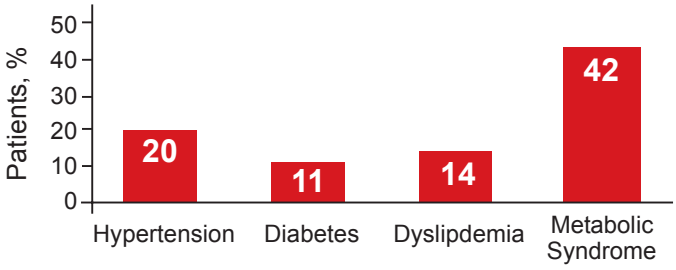
Obesity → **Diabetes mellitus**, **Coronary artery disease**, **Hypertension**, **Gallbladder disease**, **Osteoarthritis**, **Several types of tumors** → **Disability**, **Premature death**

The Metabolic Syndrome

Risk Factor	Defining Factor
BMI	≥ 30
Waist circumference	
Men	Waist > 40 in
Women	Waist > 35 in
Triglycerides	≥ 150 mg/dL
HDL-C	
Men	< 40 mg/dL
Women	< 50 mg/dL
Blood pressure	≥ 130 / 85 mm Hg
Fasting glucose	≥ 110 mg/dL

Metabolic Syndrome in Patients with Schizophrenia

- Metabolic syndrome is a constellation of abnormal physiologic conditions characterized by:
  - Increased body weight
  - Glucose intolerance
  - Dyslipidemia
  - Hypertension



- High prevalence in patients who receive SGAs (varies by antipsychotic agent)
- Antipsychotic polypharmacy has been associated with higher rates of metabolic syndrome

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MEDICATION

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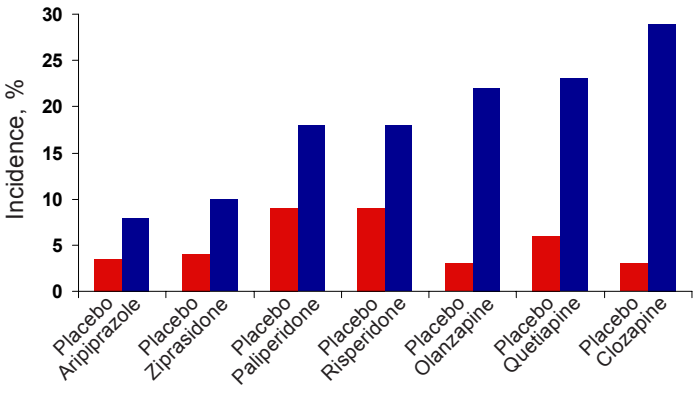
Metabolic Abnormalities with Second-Generation Antipsychotics

Drug	Weight Gain	Risk for Diabetes	Worsening Lipid Profile	Worsening Glucose Profile
Clozapine	+++	+	+	+++
Olanzapine	+++	+	+	+++
Risperidone	++	+/-	+/-	+
Paliperidone	++	+/-	+/-	+
Quetiapine	++	+	+	+
Aripiprazole	+/-	-	-	+/-
Ziprasidone	+/-	-	-	+/-

+ = increase - = no effect +/- = discrepant results

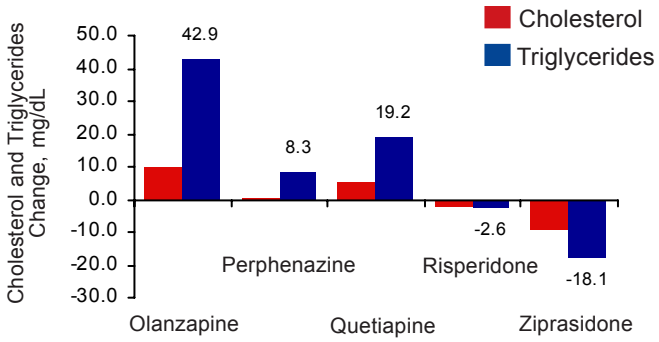
Weight Gain: Second-Generation Antipsychotics Versus Placebo



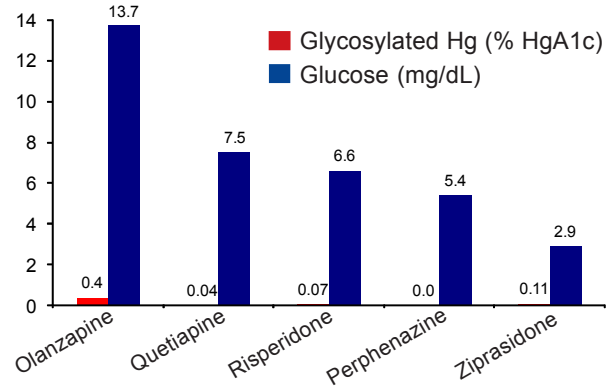
Clinically significant (≥7%) weight gain during antipsychotic treatment

CATIE RESULTS, BY ANTIPSYCHOTIC MEDICATION

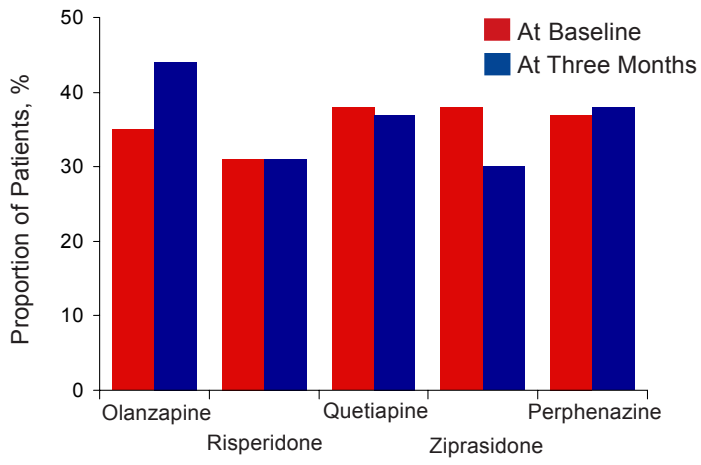
Change in Cholesterol & Triglyceride Levels



Mean Glucose Change



Change in Metabolic Syndrome



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MIAMI project

MONITORING

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VA Monitoring Protocol in Patients Receiving Second-Generation Antipsychotics

	Baseline	4 Weeks	8 Weeks	12 Weeks	6 Months	Yearly
Medical history	X					X
Weight (BMI)	X	X	X	X	X	X
Blood pressure	X			X		X
Fasting plasma glucose or HgA1c	X			X		X
Fasting lipids	X			X		X

More frequent assessments should be conducted for those who have gained more than 5% of their body weight (approximately 7.5 pounds for most people).

Body Mass Index Chart

BMI	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39
HEIGHT (Inches) / WEIGHT (Pounds)																					
58”	91	96	100	105	110	115	119	124	129	134	138	143	148	153	158	162	167	172	177	181	186
59”	94	99	104	109	114	119	124	128	133	138	143	148	153	158	163	168	173	178	183	188	193
60”	97	102	107	112	118	123	128	133	138	143	148	153	158	163	168	174	179	184	189	194	199
61”	100	106	111	116	122	127	132	137	143	148	153	158	164	169	174	180	185	190	195	201	206
62”	104	109	115	120	126	131	136	142	147	153	158	164	169	175	180	186	191	196	202	207	213
63”	107	113	118	124	130	135	141	146	152	158	163	169	175	180	186	191	197	203	208	214	220
64”	110	116	122	128	134	140	145	151	157	163	169	174	180	186	192	197	204	209	215	221	227
65”	114	120	126	132	138	144	150	156	162	168	174	180	186	192	198	204	210	216	222	228	234
66”	118	124	130	136	142	148	155	161	167	173	179	186	192	198	204	210	216	223	229	235	241
67”	121	127	134	140	146	153	159	166	172	178	185	191	198	204	211	217	223	230	236	242	249
68”	125	131	138	144	151	158	164	171	177	184	190	197	204	210	216	223	230	236	243	249	256
69”	128	135	142	149	155	162	169	176	182	189	196	203	210	216	223	230	236	243	250	257	263
70”	132	139	146	153	160	167	174	181	188	195	202	209	216	222	229	236	243	250	257	264	271
71”	136	143	150	157	165	172	179	186	193	200	208	215	222	229	236	243	250	257	265	272	279
72”	140	147	154	162	169	177	184	191	199	206	213	221	228	235	242	250	258	265	272	279	287
73”	144	151	159	166	174	182	189	197	204	212	219	227	235	242	250	257	265	272	280	288	295
74”	148	155	163	171	179	186	194	202	210	218	225	233	241	249	256	264	272	280	287	295	303
75”	152	160	168	176	184	192	200	208	216	224	232	240	248	256	264	272	279	287	295	303	311
76”	156	164	172	180	189	197	205	213	221	230	238	246	254	263	271	279	287	295	304	312	320
	HEALTHY WEIGHT						OVERWEIGHT					OBESE									

Source: National Institutes of Health

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INTERVENTION

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Intervention for Overweight Patients on Antipsychotic Medication

- Refer to a weight management program
- Consider switching to medication with less weight gain liability
- Switching SGA should be considered if patient gains ≥ 5% of baseline body weight (approximately 7.5 pounds for most people)
  - Abrupt discontinuation of SGAs should be avoided
  - Discontinuing clozapine should be carefully considered due to the potential for serious psychiatric sequelae
  - For patients with worsening glycemia or dyslipidemia, it is recommended that switching to an FGA or an SGA that has not been associated with significant weight gain or diabetes (i.e., ziprasidone and aripiprazole) should be considered

Psychosocial Weight Management Programs

- Review of 11 studies targeting weight loss among individuals with schizophrenia-spectrum disorders
- Compared psychosocial weight intervention to control condition
- 10 of the 11 studies found support for modest weight loss
  - Mean weight loss of 5 pounds across all 10 studies
  - Weight loss ranged from 1-7 pounds
- Treatment may include:
  - Psychoeducation regarding diet and exercise
  - Goal setting
  - Self-monitoring of food and physical activity level
  - Caloric restriction
  - Increase in physical activity

Weight Loss Due to Medication Switch: CATIE Study

- Patients who gained more than 7% of their body weight in Phase 1 had their medication switched.
- Switching resulted in greater weight loss for some medications than others.
- Switch to olanzapine: 0% lost greater than 7% of their weight
- Switch to quetiapine: 7% lost greater than 7% of their weight
- Switch to risperdone: 20% lost greater than 7% of their weight
- Switch to ziprasidone: 42% lost greater than 7% of their weight

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HOW TO KNOW WHEN TO REFER TO PRIMARY CARE

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BLOOD PRESSURE

- BP 120-139/80-89: Counsel on diet/exercise, re-evaluate pharmacotherapy, and recheck at next visit
- BP > 130/80: Refer to primary care if patient has any of the following co-occurring diseases:
  - Diabetes
  - Chronic kidney disease
  - Cerebrovascular disease
  - Coronary artery disease
- BP > 140/90: Refer to primary care

Recommendations for Blood Pressure

				Initial Drug Therapy	
BP Classification	SBP MMHG	DBP MMHG	Lifestyle Modification	Without Compelling Indication	With Compelling Indications
Normal	< 120	and < 80	Encourage	No antihypertensive drug indicated.	Drug(s) for compelling indications.
Prehypertension	120-139	or 80-89	Yes		
Stage 1 Hypertension	140-159	or 90-99	Yes	Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination.	Drug(s) for the compelling indications. Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed.
Stage 2 Hypertension	≥ 160	or ≥ 100	Yes	Two-drug combination for most (usually thiazide-type diuretic and ACEI or ARB or BB or CCB).	

BLOOD GLUCOSE

- If fasting glucose is between 110 and 126 mg/dl or is > 126 with HgbA1c < 7%: Counsel on diet/exercise, re-evaluate pharmacotherapy, and recheck blood sugar at a reasonable interval
- If fasting glucose is 126-199 and HgbA1c > 7%: Refer to primary care
- If fasting glucose is > 200 or symptoms of diabetes:Urgent followup with primary care for consult

LIPIDS

- If test reveals an increase in LDL that is clinically significant but still below 160, more frequent monitoring is recommended
- If LDL >160: Refer to primary care
- Treatment/referral decision must consider risk factors in addition to lab values (see table of recommendation for LDL)

Recommendations for LDL

Risk Category *	LDL Goal (mg/dL)	Initiate Therapeutic Lifestyle Changes (mg/dL)	Consider Drug Therapy
High risk: CAD or CAD equivalents** (10-year risk > 20%)	< 100 (aggressive goal: < 70)	≥100	≥130 (100-129: consider drug options)
Moderately high risk: 2+ risk factors (10-year risk 10-20%)	< 130	≥130	≥130
Moderate risk: 2+ risk factors (10-year risk < 10%)	< 130	≥130	≥160
Low risk: 0-1 risk factor	< 160	≥160	≥190 (160-189: LDL-lowering drug optional

*Risk factors: tobacco use, HTN, family history, age (> 45 ♂, > 55 ♀), HDL (< 40 ♂, < 50 ♀)

**CAD equivalents: diabetes, abdominal aortic aneurysm, peripheral or coronary artery disease, carotid artery stenosis

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Educational materials and implementation tools are available at
http://vaww.mirecc.va.gov/miamiproject/

A technical assistance center is available to offer clinical consultation on metabolic effects of antipsychotics, advice about effective implementation strategies, and access to additional educational materials.

Contact us:
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