CARDI·OH

Ohio Cardiovascular and Diabetes Health Collaborative

SCHOOL OF MEDICINE
CASE WESTERN RESERVE UNIVERSITY

In partnership with:

THE OHIO STATE UNIVERSITY WEXNER MEDICAL CENTER

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OHIO Heritage College of Osteopathic Medicine

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Project ECHO®

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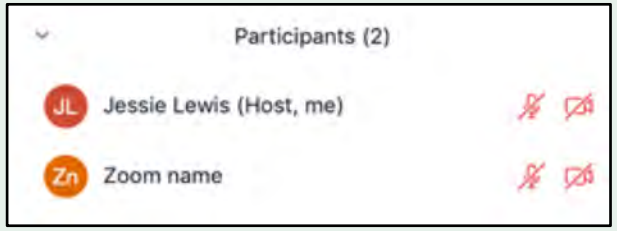
Cardi-OH ECHO Tackling Type 2 Diabetes

Thursday, March 25, 2021

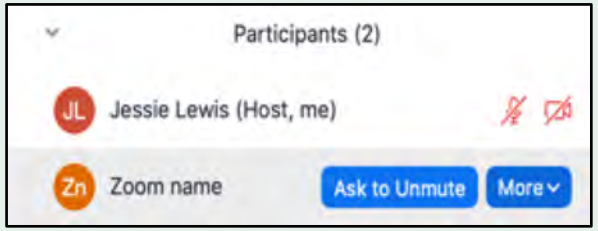
Reminders

- Enter your name and practice name into the Chat to record your attendance
- Rename yourself in the Participant List with your full name and practice name

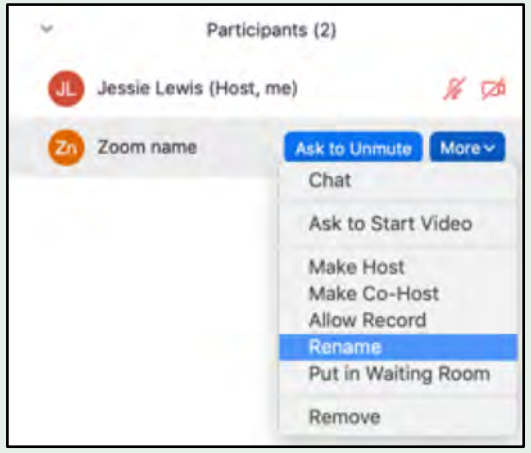
1. Hover over your name



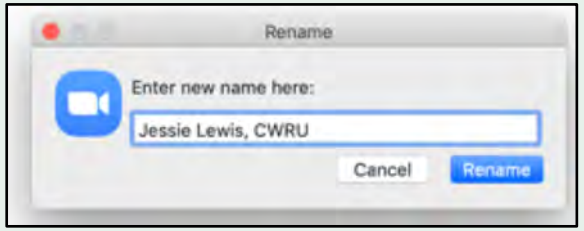
2. Select More



3. Select Rename



4. Type name and practice



- Mute your microphone unless speaking
- Comment or ask questions in the Chat at any time

Cardi-OH ECHO Hub Team

LEAD

Goutham Rao, MD
Case Western Reserve University

FACILITATOR

Kathleen Dungan, MD, MPH
The Ohio State University

DIDACTIC PRESENTER

Trygve Dolber, MD
Case Western Reserve University

CASE PRESENTER

Lisa Kellar, MD
Wright State Family Medicine

Structure of ECHO Clinics

Duration	Item
5 minutes	Announcements and introductions
25 minutes	Didactic presentation, followed by Q&A
25 minutes	Case study presentation and discussion
5 minutes	Wrap-up/Post-Clinic Survey completion

Disclosure Statements

- The following planners, speakers, moderators, and/or panelists of the CME activity have financial relationships with commercial interests to disclose:
  - Kathleen Dungan, MD, MPH receives consulting fees from Eli Lilly and Tolerion, institutional research fees from Eli Lilly, Novo Nordisk, and Sanofi Aventis, and presentation honoraria from Nova Biomedical, Integritas, and Uptodate.
  - Adam T. Perzynski, PhD reports being co-owner of Global Health Metrics LLC, a Cleveland-based software company and royalty agreements for book authorship with Springer Nature publishing and Taylor Francis publishing.
  - Christopher A. Taylor, PhD, RDN, LD, FAND reports grant funding for his role as a researcher and presenter for Abbott Nutrition and grant funding for research studies with both the National Cattleman's Beef Association and the American Dairy Association.
  - Jackson T. Wright, Jr., MD, PhD reports research support from the NIH and Ohio Department of Medicaid and consulting with NIH, AHA, and ACC.
  - These financial relationships are outside the presented work.
- All other planners, speakers, moderators, and/or panelists of the CME activity have no financial relationships with commercial interests to disclose.

Special Populations: Patients with Chronic Mental Illness

Trygve Dolber, MD

Departments of Psychiatry and Internal Medicine

Associate Director of Population Behavioral Health

University Hospitals Cleveland Medical Center

Case Western Reserve University School of Medicine

Objectives

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1) Describe the epidemiology and outcomes of diabetes among people with chronic mental illness (CMI)

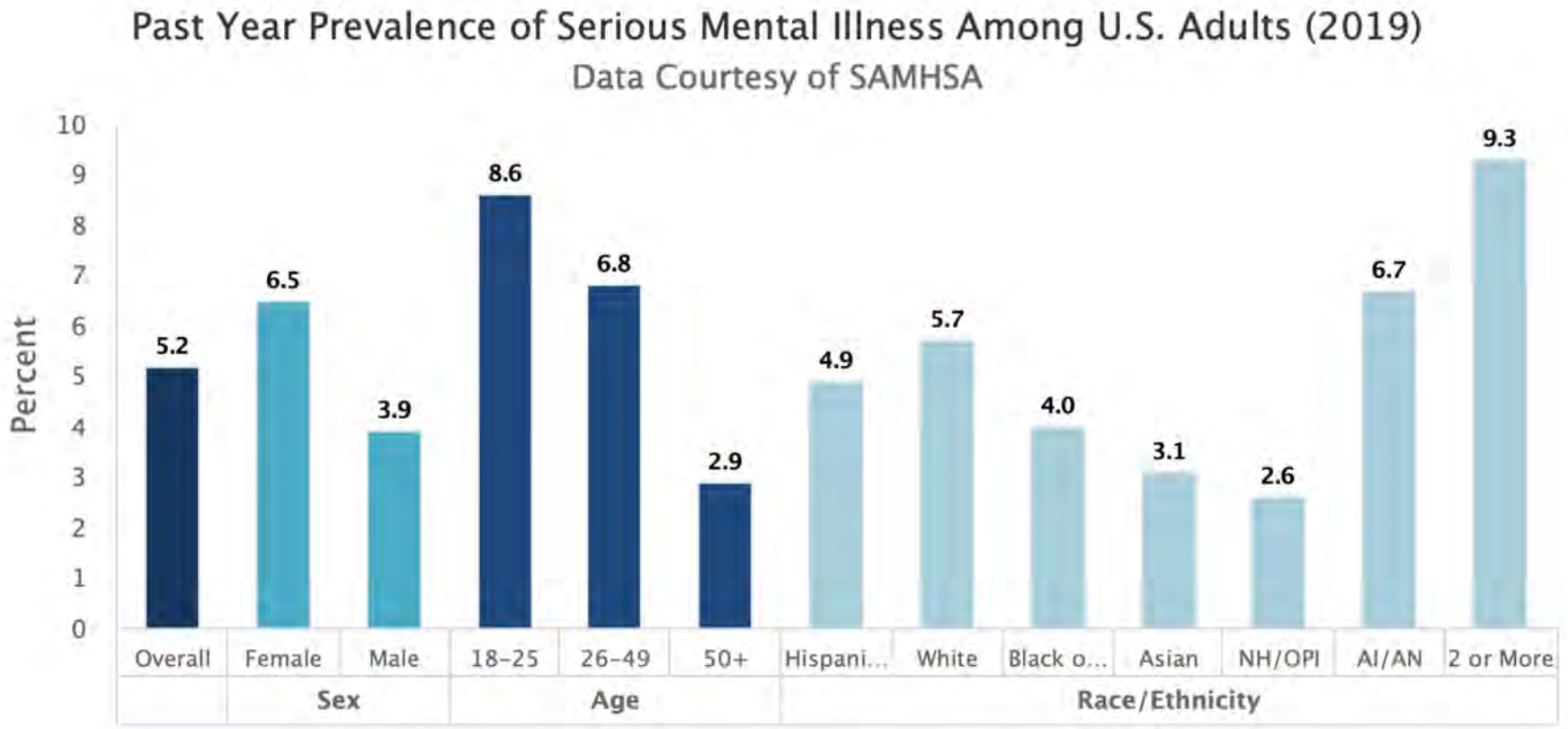
2) Describe the impact of treatments for people with CMI, including atypical antipsychotic medications, on control and outcomes of diabetes

3) List and describe a minimum of 3 strategies to improve control of diabetes among people with CMI

What is CMI?

- Many mental illnesses are chronic (GAD, BPD, AN)
- “CMI” often interchangeable with “SMI”
  - Persistently debilitating psychiatric symptoms
  - Severely impaired functioning
- **Schizophrenia**
- Bipolar Affective Disorder
- Treatment-Resistant Recurrent Depression

CMI Prevalence



Substance Abuse and Mental Health Services Administration. (2020). *Key substance use and mental health indicators in the United States: Results from the 2019 National Survey on Drug Use and Health* (HHS Publication No. PEP20-07-01-001, NSDUH Series H-55). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data/

Medical Comorbidity

- CMIs such as recurrent depression, bipolar disorder and schizophrenia generally complicate general health outcomes
- CMI is often accompanied by additional mental health comorbidities such as substance abuse and PTSD
- CMI inflates costs of medical comorbidities
- CMI life-span reduced by **10-30 years**
- CMI have a **1.2 to 4.9 increase in mortality** compared to age and sex-matched individuals from the general population ***resulting from DM, cardiovascular disease, and stroke***

Colton CW, Manderscheid RW. Preventing Chronic Disease 3: A42: 2006
Whiteman, K. L et al. *Psychiatric Services* *67*(11), 1213–1225.2016
Walker, E. R. et al *JAMA psychiatry*, *72*(4), 334–341. 2015

Increased Medical Burden

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Modifiable Risk Factors	Estimated Prevalence and Relative Risk (RR)	
	Schizophrenia	Bipolar Disorder
Obesity[1-5]	45–55%, 1.5–2 × RR	21–49%, 1–2 × RR
Smoking[4-8]	50–80%, 2–3 × RR	54–68%, 2–3 × RR
Diabetes[2, 8-11]	10–15%, 2 × RR	8–17%, 2 × RR
Hypertension[2-4, 7-9, 11]	19–58%, 2–3 × RR	35–39%, 2 × RR
Dyslipidemia[2, 4, 11-13]	25%, ≤ 5 × RR	23%, ≤ 5 × RR

1. Allison D, et al. *J Clin Psychiatry.* 1999;60(4):215-220;
2. Fagiolini A, et al. *Bipolar Disord.* 2005;7(5):424-430;
3. McElroy S, et al. *J Clin Psychiatry.* 2002;63(3):207-213;
4. Hennekens C, et al. *Am Heart J.* 2005;150(6):1115-1121;
5. Davidson S, et al. *Aust N Z J Psychiatry.* 2001;35(2):196-202;
6. Ucok A, et al. *Psychiatry Clin Neurosci.* 2004;58(4):434-437;
7. Herran A, et al. *Schizophr Res.* 2000;41(2):373-381;
8. Goff D, et al. *Schizophr Res.* 2005;80(1):45-53;
9. Dixon L, et al. *J Nerv Ment Dis.* 1999;87(8):496-502;
10. Cassidy F, et al. *Am J Psychiatry.* 1999;156(9):1417-1420;
11. Kilbourne A. *Bipolar Disord.* 2004;6(5):368-373;
12. Allebeck P. *Schizophr Bull.* 1989;15(1):81-89;
13. Koro C, et al. *Arch Gen Psychiatry.* 2002;59(11):1021-1026

Diabetes in CMI

- Risk of DM 1.2-2.6x higher in depression of any type
- Prevalence of DM 4-5x higher in CMI
- Age of onset of DM 10-20 years earlier in CMI
- Why?
  - Increased prevalence of well-established DM risk factors
  - Disease-specific risks
  - Treatment-specific risks
- Risk determinations may be different from the general population…

Barnett AH, et al, J Psychopharmacol. 2007
Carnethon MR, et al, Am J Epidemiol. 2003
De Hert M, et al, Eur Psychiatry. 2009
McEvoy JP, et al Schizophr Res. 80(1):19-32.2005
Whiteman, K. L et al. *Psychiatric Services* *67*(11), 1213–1225.2016

Schizophrenia-Specific DM Risk

- **Genetic susceptibility**
  - Higher occurrence of DM in family members of people with schizophrenia
  - Abnormal glucose metabolism
  - Common mechanism proposed for cognitive deficit and glucose metabolism
- **Neuroendocrine pathways**
  - Hypothalamic axis dysregulation and elevated cortisol in schizophrenia
  - Nutritional deficiencies proposed as common pathway for both diseases
- **Antipsychotic medications**
  - Effect on hypothalamic regulation, dopaminergic, serotonergic, and histaminergic receptors
  - Other proposed mechanisms: action on pancreatic muscarinic receptor and leptin resistance
- **Environmental/additional comorbidity**
  - Diet and lack of access to quality foods
  - Inadequate physical activity due to symptoms and social isolation

Anamalie. Int J Endocrinology. Volume 2015 |Article ID 969182 | https://doi.org/10.1155/2015/969182

Assessing Medical Risk in CMI

- Composite, CVD/general medical burden measures such as the Framingham Risk Score may not optimally assess risk in CMI
- One review found Framingham not associated with any changes within multicomponent intervention models in adults with CMI
- May relate to the fact that the Framingham Heart Study risk scores were determined with a sample that excluded adults with CMI
- Risk prediction models that include bio-behavioral variables yielded better predictive models than the Framingham Risk Score for adults with CMI:
  - Social deprivation
  - Psychiatric diagnosis
  - Prescriptions for antidepressants/antipsychotics
  - Alcohol use
- BOTTOM LINE: "Standard" diabetes interventions and/or a focus entirely on biological variables may fail to account for key factors that contribute to medical complications among those with CMI. This has important clinical care implications.

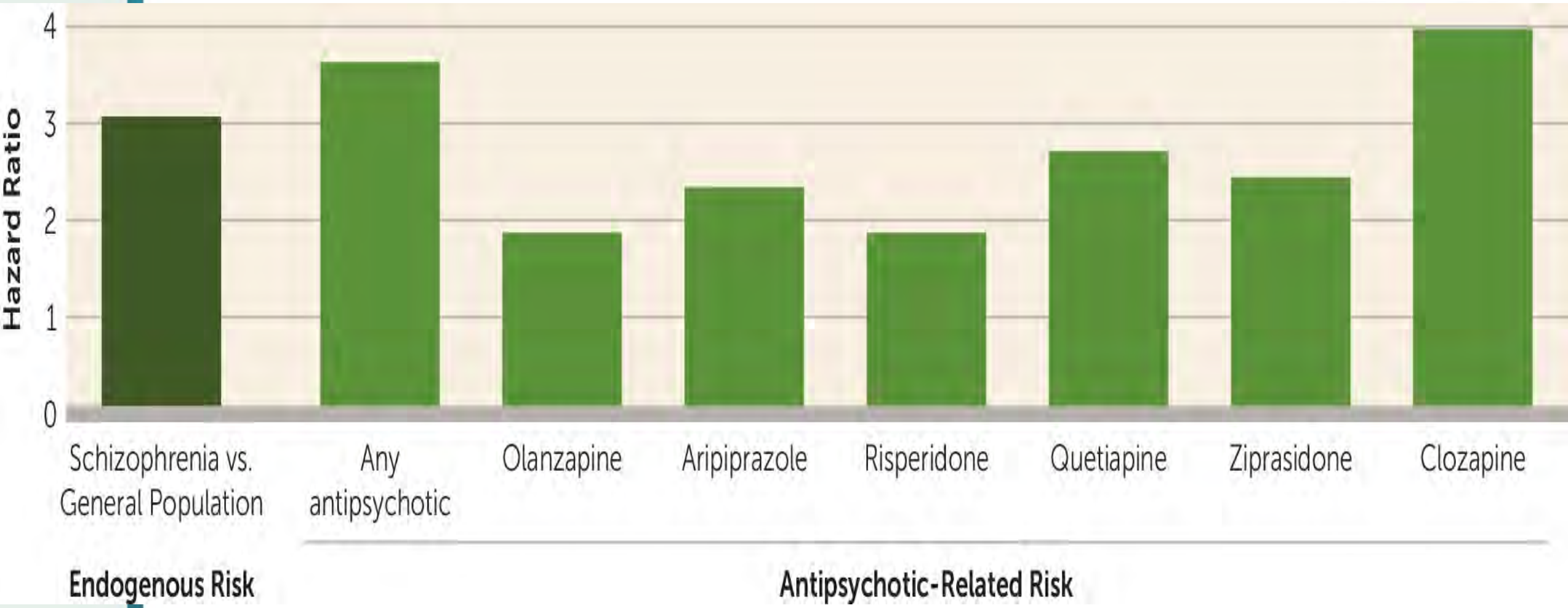
AHRQ: effectivehealthcare.ahrq.gov/ehc/products/377/1464/mental-illness-cardio-risk-executive-130422.pdf.
D'Agostino RB, et al, Circulation. 2008
Osborn DP, et al, JAMA Psychiatry. 72(2):143-51.2015

Antipsychotics and DM Risk

- **About 12%** of people receiving antipsychotic drugs have DM
- Meta-analyses suggest the prevalence of DM is not appreciably increased in drug-naïve, first-episode CMI patients
- Many (but not all) studies suggest second-generation antipsychotics (SGAs) have greater diabetogenic potential vs. first-generation antipsychotics (FGAs)
- Metabolic abnormalities accumulate rapidly after the initiation of treatment .
- Antipsychotics **may induce DM independent of adiposity**, contributing to DM both indirectly, by inducing weight gain, and directly, by promoting insulin resistance
- Children and youth exposed to antipsychotics have a 3-fold increased risk of DM (***young patients with normal BMI are at risk***)

Chesney E, et al World Psychiatry. 2014 Jun; 13(2):153-60.
Mitchell AJ, et al,Schizophr Bull. 2013 Mar; 39(2):295-305
Correll, C. U., et al, *World Psychiatry*, *14*(2), 119–136. 2015

Antipsychotics and DM Risk



Andreasson, Am J Psychiatry2017https://doi.org/10.1176/appi.ajp.2017.17040409
Rajkumar AP, Horsdal HT, Wimberley T, et al.: Endogenous and antipsychotic-related risks for diabetes mellitus in young people with schizophrenia: a Danish population-based cohort study. Am J Psychiatry 2017; 174:686–694

Adverse Effects of Psychotropics

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	Antipsychotics	Antidepressants	Mood stabilizers
Obesity	**0/+ (haloperidol, lurasidone, ziprasidone, aripiprazole) to +++ (clozapine, olanzapine, low potency FGAs)**	**− (bupropion) to + (mirtazapine, paroxetine, TCAs)**	**0 (lamotrigine) to ++ (valproate, lithium)**
Dyslipidemia	+ to ++	0 to + (if weight gain)	− (valproate: cholesterol) to +
Diabetes	**0/+ (haloperidol, lurasidone, ziprasidone, aripiprazole) to +++ (clozapine and olanzapine > low and mid potency FGAs)**	**0 to +**	**0 to ++ (valproate)**
Hypertension	0 to ++	0 to + (venlafaxine)	0

− = reduction; 0 = likely/generally no effect; + = some effect; ++ = moderate effect; +++ = marked effect, ? = questionable
FGAs – first-generation antipsychotics, SSRIs – selective serotonin reuptake inhibitors, TCAs – tricyclic antidepressants

Adapted from Correll, C. U., et al, *World Psychiatry*, *14*(2), 119–136. 2015

Minimizing Metabolic Liability

- Young, drug–naïve patients are particularly vulnerable to weight gain
- Use SGAs with high metabolic liability conservatively and ***limit off–label use***
- Screening and monitoring per ADA guidelines
- Patients with significant weight gain should be switched to a lower metabolic liability SGA
- Metformin may help young patients with limited exposure to antipsychotic drugs if lifestyle interventions fail and switching the SGA is not an option. However, benefits may be modest.

Hasnain M, Vieweg WV, Hollett B. Postgrad Med. 2012 Jul; 124(4):154-67

Metabolic Monitoring

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Table 1 – Metabolic monitoring parameters based on American Diabetes Association/ American Psychiatric Association consensus guidelines[4]

	Baseline	Week 4	Week 8	Week 12	Every 3 months thereafter	Annually
Medical history[a]	X			X		X
Weight (BMI)	X	X	X	X	X	X
Waist circumference	X			X		X
Blood pressure	X			X		X
Fasting glucose/hemoglobin A_{1c}	X			X		X
Fasting lipids	X			X		X

[a] Personal and family history of obesity, diabetes, hypertension, and cardiovascular disease.

Diabetes Care. 2004;27:596-601.

Chronic Disease Comorbidity Model

- Concordant comorbidity has similar pathogenesis/management (schizophrenia & DM)
- Discordant comorbidity has different pathogenesis/management (seborrheic dermatitis and heart failure)
- Dominant comorbidity (metastatic cancer) overshadows all other illnesses

- Concordant conditions may share underlying pathology such as inflammation. → Target both conditions with one treatment.
- Identifying discordant conditions is essential. → Targeted approaches to comorbidity can improve both CMI and DM.

Piette JD, Kerr EA. Diabetes Care 2006;29:725–731
*Pentakota Diabetes Care **June 2012** vol. 35 no. 6*

Discordant Comorbidities in DM and CMI

- Alcohol cessation
  - > 1/3 of people with DM age 18-25 had past-month binge drinking
  - DM self-care behaviors are inversely correlated with alcohol consumption starting at 1 drink/day
- Depression treatment
  - Depression predisposes to weight gain and is a risk factor for glucose dysregulation
  - Optimal treatment of depression (may involve treatment of anxiety) improves glucose metabolism and makes it easier for patients to manage complex self-management plans

Center for Behavioral Health Statistics and Quality. (2012, March 27). Substance Abuse and Mental Health Services Administration.
Ahmed, A. T., et al Diabetic Medicine, 23(7), 795–802.2006
Hasnain M, Vieweg WV, Hollett B. Postgrad Med. 2012 Jul; 124(4):154-67

Antidepressant Drugs and DM Risk in CMI

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- Antidepressants associated with new-onset DM
  - Meta-analysis OR = 1.50
  - Only observational studies (insufficient for causation)
- Increased DM risk with TCAs and SSRIs (OR = 1.89)
- When treating depression or anxiety, remember paroxetine and mirtazapine are associated with weight gain
- Bupropion may cause modest weight loss
- Other second-generation antidepressants are mostly weight neutral, but individual variations may occur
- *DM risk with antidepressants might be elevated with long-term use of TCA or SSRIs and/or in high-risk patients*
- *Titrate and taper these medications!*

Bhattacharjee S, et al, Diabetes Metab Res Rev. 29(4):273-84.2013
Brown LC, et al, Diabetes Res Clin Pract. 79(1):61-7.2008
Rubin RR, et al Diabetes Care. 2008 Mar; 31(3):420-6.

Enhancing Medical Care with Self-Management/Multi-Component Support

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- Chronic disease self-management (CDSM) is an evidence-based set of practices that are effective in improving the health of people with multiple morbidities.
  - Nutrition and exercise counseling
  - Behavioral modeling
  - Increased disease awareness
- Collectively shows modest positive impact on HbA1c, fasting plasma glucose, BMI and weight
- CDSM approaches are acceptable to those with CMI

Lorig , Ann Behav Med 2003;26(1):1–7. , Chodosh, Ann Intern Med 2005;143:427–38
Gron et al. Primary Care Diabetes 2018DOI:https://doi.org/10.1016/j.pcd.2018.03.008

Meta-analysis of Interventions

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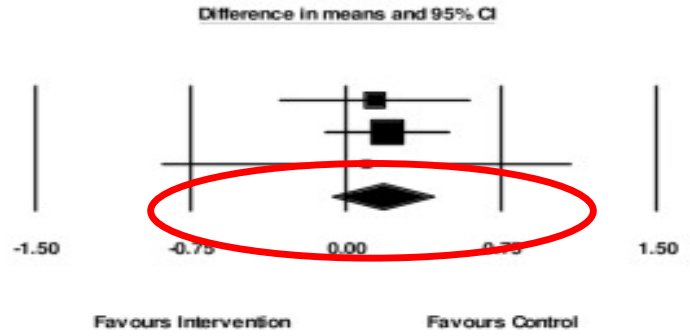
HbA_{1c}

Study name	Subgroup within study	Outcome	Statistics for each study: Difference in means	Standard error	Lower limit	Upper limit	Sample size: Intervention	Control	Relative weight
Forsberg 2008	Behavioural	HbA1c	0.140	0.236	-0.322	0.602	21	12	28.14
Gillhoff 2010	Behavioural	HbA1c	0.200	0.154	-0.102	0.502	26	24	65.73
McKibbin 2006	Behavioural	HbA1c	0.100	0.505	-0.890	1.090	28	29	6.13
			0.177	0.125	-0.068	0.422			

Difference in means = 0.177% (95% confidence interval = -0.068 to 0.422)
Test of significance: Z = 1.415, p = 0.16; Test of heterogeneity: I^2 = 0.00, p = 0.97

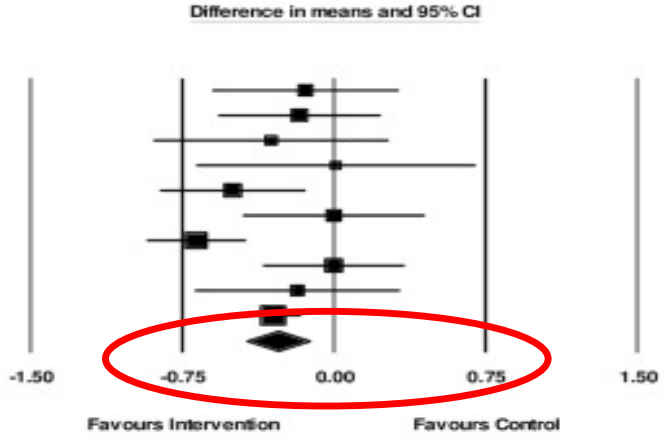


Fasting blood glucose

Study name	Subgroup within study	Outcome	Statistics for each study: Difference in means	Standard error	Lower limit	Upper limit	Sample size: Intervention	Control	Relative weight
Attux 2013	Behavioural	Fasting glucose	-0.140	0.235	-0.601	0.321	60	66	7.82
Cordes 2014	Behavioural	Fasting glucose	-0.170	0.205	-0.572	0.232	13	18	9.37
Daumit 2013	Behavioural	Fasting glucose	-0.310	0.297	-0.891	0.271	96	95	5.56
Forsberg 2008	Behavioural	Fasting glucose	0.010	0.352	-0.681	0.701	23	14	4.21
Green 2015	Behavioural	Fasting glucose	-0.500	0.183	-0.859	-0.141	104	96	10.71
Mauri 2008	Behavioural	Fasting glucose	0.000	0.230	-0.450	0.450	15	18	8.08
Poulin 2007	Behavioural	Fasting glucose	-0.680	0.125	-0.925	-0.435	59	51	15.42
Scheewe 2013	Behavioural	Fasting glucose	0.000	0.179	-0.351	0.351	29	25	11.01
Wu 2007	Behavioural	Fasting glucose	-0.180	0.259	-0.687	0.327	28	25	6.83
Wu 2008A	Behavioural	Fasting glucose	-0.300	0.070	-0.437	-0.163	32	32	20.98
			-0.277	0.079	-0.433	-0.122			

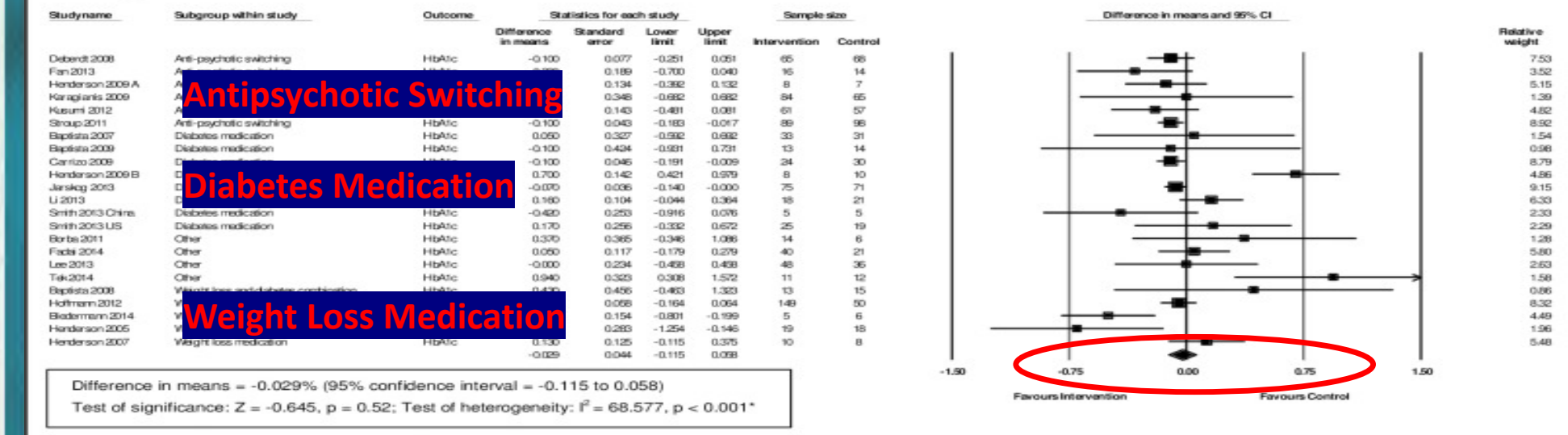
Behavioral

Difference in means = -0.277mmol/L (95% confidence interval = -0.433 to -0.122)
Test of significance: Z = -3.500, p < 0.001*; Test of heterogeneity: I^2 = 46.147, p = 0.05



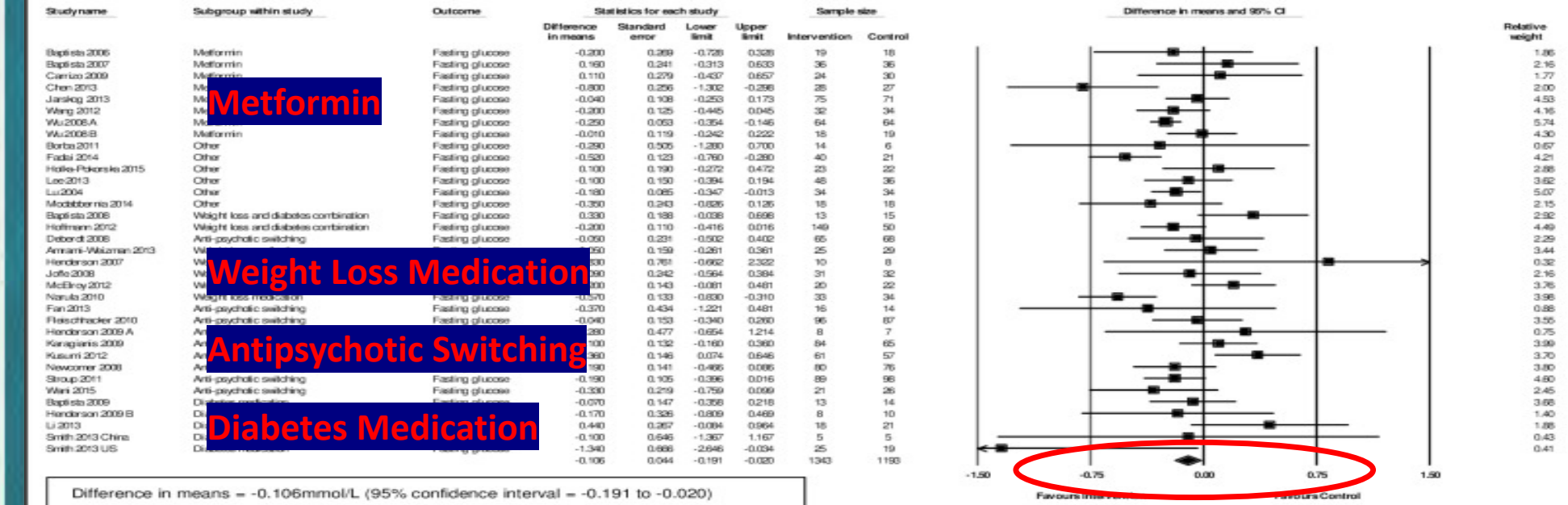
The Effectiveness of Pharmacological and Non-Pharmacological Interventions for Improving Glycaemic Control in Adults with Severe Mental Illness: A Systematic Review and Meta-Analysis. Taylor et al. *PloS one* vol. 12,1 e0168549. 5. 2017

HbA_{1c}



Difference in means = -0.029% (95% confidence interval = -0.115 to 0.058)
Test of significance: Z = -0.645, p = 0.52; Test of heterogeneity: I^2 = 68.577, p < 0.001*

Fasting blood glucose



Difference in means = -0.106mmol/L (95% confidence interval = -0.191 to -0.020)
Test of significance: Z = -2.407, p = 0.02*; Test of heterogeneity: I^2 = 57.352, p < 0.001*

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The Effectiveness of Pharmacological and Non-Pharmacological Interventions for Improving Glycaemic Control in Adults with Severe Mental Illness: A Systematic Review and Meta-Analysis. Taylor et al. *PloS one* vol. 12,1 e0168549. 5. 2017

Supporting Adults with Comorbid DM & CMI

- Standard **diabetes education** needs to accommodate possible cognitive deficits and/or significant mood states that may make knowledge accumulation and retention challenging
- Prescribe psychotropic drugs that minimize metabolic/weight gain propensity
- Optimize outcomes of psychiatric comorbidity (SUD, depression)
- Self-management support that addresses bio-behavioral factors
- Collaborative or integrated care models that include behavioral medicine

Anamalie. Int J Endocrinology. Volume 2015 |Article ID 969182 |
https://doi.org/10.1155/2015/969182
https://store.samhsa.gov/sites/default/files/d7/priv/sma13-4780.pdf

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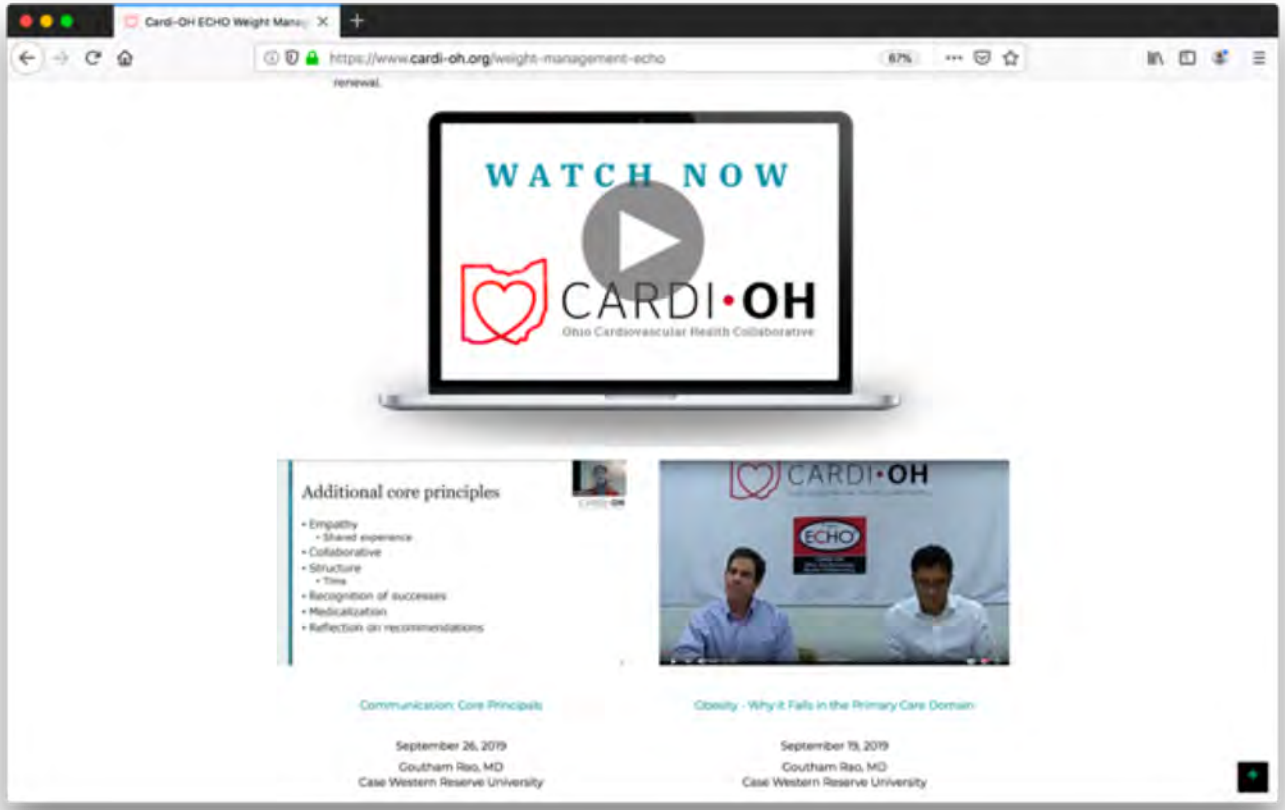
Thank you!

Questions/Discussion

Watch Previous Cardi-OH TeleECHO Clinics

Register on Cardi-OH.org to watch all Tackling Type 2 Diabetes TeleECHO Clinics:

https://www.cardi-oh.org/user/register
https://www.cardi-oh.org/echo/diabetes-spring-2021



Surveys

You will receive 2 surveys today:

1. The Post-Clinic Survey has been emailed to you.
   Please complete this survey **by Friday at 5:00 PM**.
2. “Feedback for Final Clinic” Survey has also been emailed.
   - Gathers input for our final session next week. Also due **by Friday at 5:00 PM**.

CME

- *The MetroHealth System is accredited by the Ohio State Medical Association to provide continuing medical education for physicians.*
- *The MetroHealth System designates this educational activity for a maximum of 1 AMA PRA Category 1 Credit(s)TM. Physicians should only claim credit commensurate with the extent of their participation in the activity.*
- You will receive a survey from the CME office through **MyEvaluations.com** on 4/6/21
  - Register with MyEvaluations.com to begin this process
  - Please complete by Friday, 4/23/21

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Save the date!

Fall 2021 Cardi-OH ECHO

September 16 – December 9, 2021

Thursdays, 8 – 9 AM

Details and registration information to follow!