

# Metformin in Antipsychotic Induced Weight Gain (AIWG)

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## Disclosure Statement

- Trixy Angelie Pilando Ibis has no relevant financial relationship(s) with ineligible companies to disclose.
- The views represented in this presentation are my own and do not represent the VA or the United States Government.

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## Learning Objectives

- Describe antipsychotic-induced weight gain and highlight the potential risks associated with these medications
- Discuss the therapeutic role and effectiveness of metformin as an off-label option to prevent and treat antipsychotic-induced weight gain

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## Metformin for Prevention

Recommendation	Strength of Recommendation for Intervention	Certainty of Evidence
Co-commence metformin with <b>high-risk antipsychotics</b> (olanzapine or clozapine).	Strong	Low
Co-commence metformin with <b>medium-risk antipsychotics</b> (quetiapine, paliperidone, or risperidone) in the presence of <b>one or more cardiometabolic risk factors</b> or in people aged <b>10-25 years</b> .	Strong	Low
Commence metformin with <b>any antipsychotic</b> if <b>&gt;3% increase in baseline body weight</b> is observed during the first year of treatment.	Strong	Low

Gidycz, Aulis et al. "Metformin for the Prevention of Antipsychotic-induced Weight Gain: Guideline Development and Guidance Statement." *Psychopharmacology Bulletin* vol. 54, 2 (2018): 11-19. DOI: 10.1080/00987717.2018.1487040

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## Metformin in the management of antipsychotic-induced weight gain in adults with psychosis: development of the first evidence-based guideline using GRADE methodology



Fitzgerald, Ryan et al. "Metformin in the management of antipsychotic-induced weight gain in adults with psychosis: development of the first evidence-based guideline using GRADE methodology." *Psychopharmacology Bulletin* vol. 54, 2 (2018): 11-23. DOI: 10.1080/00987717.2018.1487040

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## Metformin for Management

**Background:** Prescribing information and place in therapy in the hierarchy of management options is lacking.

**Methods:**

- Key health questions (KHQs)
- Systematic literature review (2008-2020)



Fitzgerald, Ryan et al. "Metformin in the management of antipsychotic-induced weight gain in adults with psychosis: development of the first evidence-based guideline using GRADE methodology." *Psychopharmacology Bulletin* vol. 54, 2 (2018): 11-23. DOI: 10.1080/00987717.2018.1487040

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## Metformin for Management



**Methods:**

- Guideline Development Tools:
  - AGREE II tool
  - AMSTAR assessment
  - Cochrane Risk of Bias 2 tool
  - GRADE methodology

**Results:**

- 11 recommendations and 7 supporting good practices
- Recommendations only apply to *non-diabetic* populations

Figueredo, Is et al. "Metformin in the management of antipsychotic-induced weight gain in adults with psychiatric disorders: a first evidence-based guideline using GRADE methodology." *Cochrane database of systematic reviews* vol. 2023 (2023) 10.1111/coch.54264

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## Metformin for Management

Recommendation	Strength of Recommendation for Intervention	Certainty of Evidence
We recommend the use of metformin to attenuate weight gain induced by <b>any antipsychotic</b> .	Strong	Moderate
We recommend metformin be <b>started at 500 mg twice daily with meals</b> . Metformin dosing should be increased in increments of 500 mg every 1-2 weeks.	Strong	Low
We recommend a <b>target dose of metformin of 2000 mg/day</b> . The target dose, however, should consider individual tolerability and evidence of efficacy.	Strong	Moderate
If metformin is being used as part of an <b>early intervention strategy</b> , we recommend that <b>plateau of weight gain should be the goal of treatment</b> . Reversal of weight gained to date due to antipsychotic treatment may also be feasible.	Strong	Moderate

Figueredo, Is et al. "Metformin in the management of antipsychotic-induced weight gain in adults with psychiatric disorders: a first evidence-based guideline using GRADE methodology." *Cochrane database of systematic reviews* vol. 2023 (2023) 10.1111/coch.54264

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## Guideline Recommendations



Non-pharmacological interventions are *first-line* and to be offered *before* metformin.

METFORMIN		
Dose	American Association of Psychiatric Pharmacists (AAPP)	British Medical Journal (BMJ)
<i>Initial</i>	IR: 250 mg – 500 mg PO BID ER: 500 mg – 1000 mg PO daily	500 mg PO BID Increased in increments of 500 mg every 1-2 weeks
<i>Target</i>	IR: 750 mg – 2000 mg PO daily in divided doses ER: 1000 mg – 2000 mg PO daily	2000 mg PO daily Consider individual tolerability

American Association of Psychiatric Pharmacists. "Antipsychotic-Induced Weight Gain." AAPP. <https://www.aapp.org/antipsychotic-induced-weight-gain/>  
Figueredo, Is et al. "Metformin in the management of antipsychotic-induced weight gain in adults with psychiatric disorders: a first evidence-based guideline using GRADE methodology." *Cochrane database of systematic reviews* vol. 2023 (2023) 10.1111/coch.54264

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## Non-pharmacological Interventions





Intervention Type	Focus Area	Description
Mindful Eating	Healthier food choices	Practice awareness during meals to choose more nutritious foods and recognize hunger/fullness cues.
Physical Activity	Increased daily movement	Incorporate regular activity, such as walking

American Association of Psychiatric Pharmacists. "Antipsychotic-induced Weight Gain." AAP, <https://www.aap-pp.com/antipsychotic-induced-weight-gain/>  
 Fitzgerald, R. et al. "Metformin in the management of antipsychotic-induced weight gain in adults with psychosis: development of the first evidence-based guideline using GRADE methodology." *International journal of gerontology* vol. 35, 1 (2011): 11-21. doi:10.1016/j.aging.2010.09.005

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## Non-pharmacological Interventions



Intervention Type	Focus Area	Description
Cognitive Therapy	Thoughts, beliefs, and eating behaviors	Explore how thoughts and emotions influence eating patterns and overall well-being.
Behavioral Therapy	Actions, routines, and support systems	Use goal setting, social support, and monitoring of exercise and habits to build lasting change.



American Association of Psychiatric Pharmacists. "Antipsychotic-induced Weight Gain." AAP, <https://www.aap-pp.com/antipsychotic-induced-weight-gain/>  
 Fitzgerald, R. et al. "Metformin in the management of antipsychotic-induced weight gain in adults with psychosis: development of the first evidence-based guideline using GRADE methodology." *International journal of gerontology* vol. 35, 1 (2011): 11-21. doi:10.1016/j.aging.2010.09.005

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## Metformin



**Drug-class:** Biguanide

**Mechanism of Action (MOA):**  
 Reduces hepatic glucose production, decreases intestinal glucose absorption, and enhances insulin sensitivity

**Adverse Drug Reactions (ADR):** GI effects, lactic acidosis, hepatotoxicity, vitamin B12 deficiency

**Weight loss:** ~3%

Cassidy-Gault, Andrea, et al. "Obesity Management in Adults: A Review." *JAMA*, vol. 325, no. 20, 28 Nov. 2021, pp. 2005-2015. doi:10.1001/jama.2021.12147. <https://doi.org/10.1001/jama.2021.12147>  
 Report ID: www.accessdata.fda.gov/drugsatfda\_docs/nda/2011/0201237Orig1s001.pdf

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### Post-Test Question #1



Patient X reports weight gain after initiating risperidone. Which treatment options would you consider?

- a. Metformin
- b. Well-balanced diet and increase in physical activity
- c. CBT
- d. All of the above

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### Post-Test Question #2



What is the target daily dose for metformin (IR and ER)?

- a. 1000 mg
- b. 2000 mg
- c. 500 mg
- d. 3000 mg

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## Thank you!

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 VA Roseburg Health Care System




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