MÉDICAMENTS DE L'OBÉSITÉ: INTÉRÊT CHEZ LES PATIENTS PRÉSENTANT UNE PATHOLOGIE PSYCHIATRIQUE

OBÉSITÉ ET PSYCHIATRIE

INTRODUCTION

- Patients atteints d'une pathologie mentale sévère: espérance de vie réduite de 15ans(vs pop. Générale)
- Causes principales: maladie cardio métaboliques et obésité

Walker et al. 2015, Correll et al. 2017, Laursen et al. 2018

OBÉSITÉ ET PSYCHIATRIE

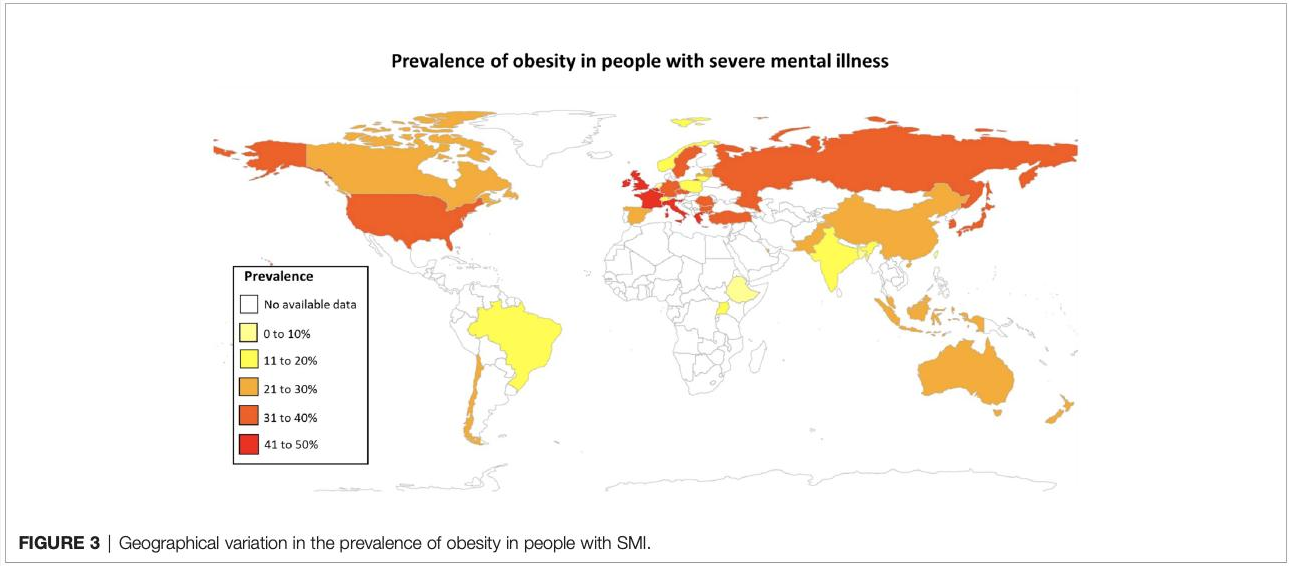


FIGURE 3 | Geographical variation in the prevalence of obesity in people with SMI.

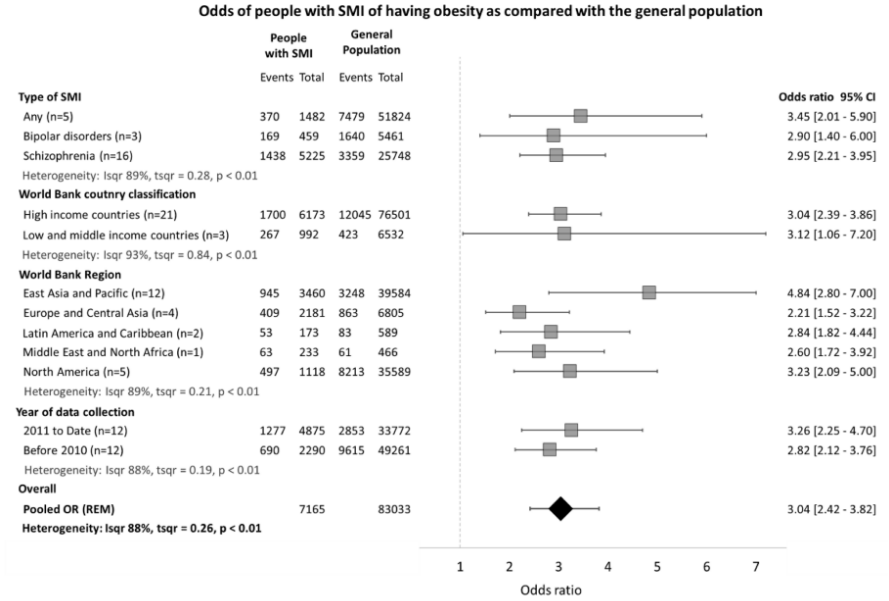
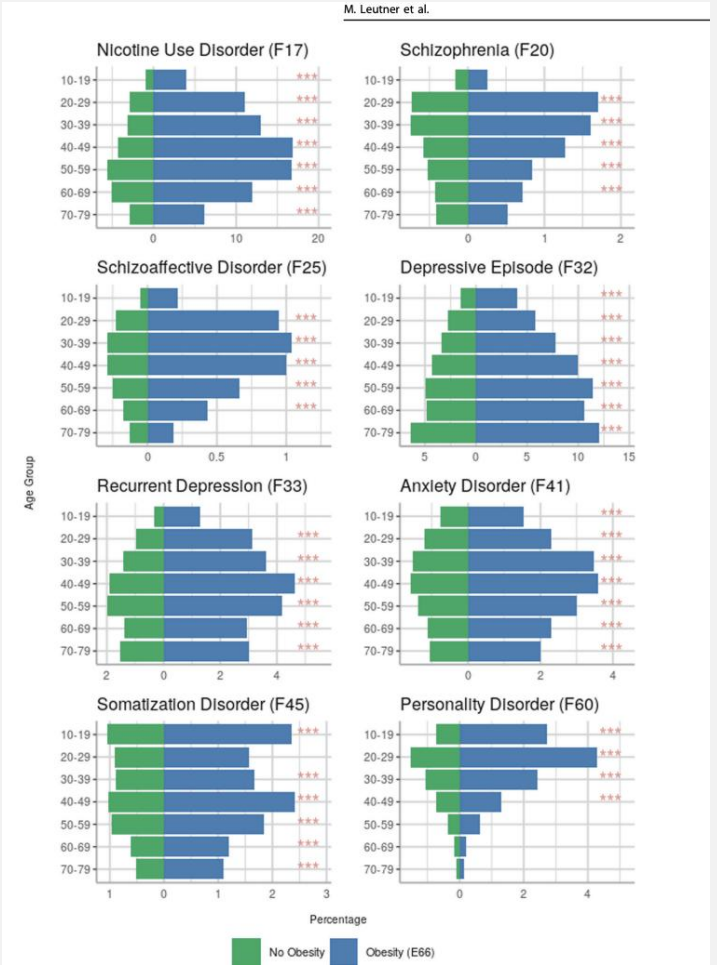


FIGURE 5 | Odds of people with SMI of having obesity as compared to the general population.

Afzal et al. 2020

OBÉSITÉ ET PSYCHIATRIE



Leutner et al. 2023

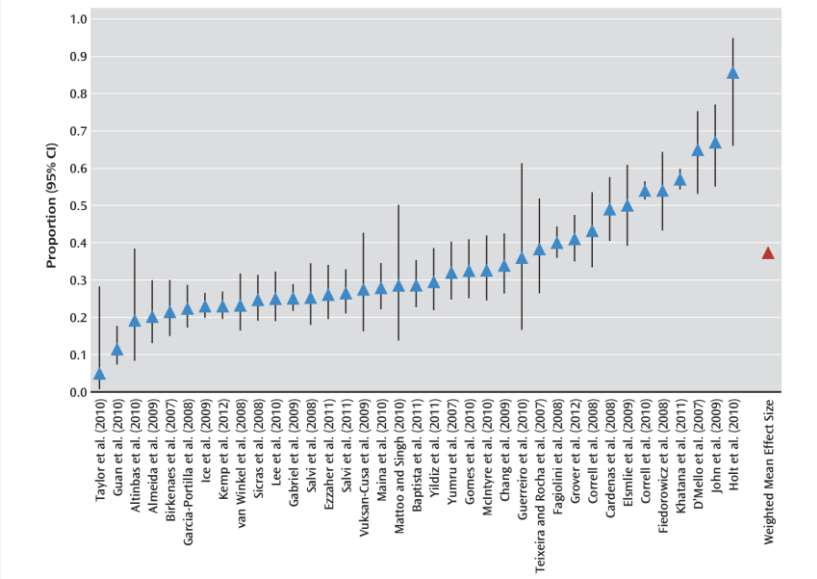
PRÉVALENCE SYNDROME MÉTABOLIQUE

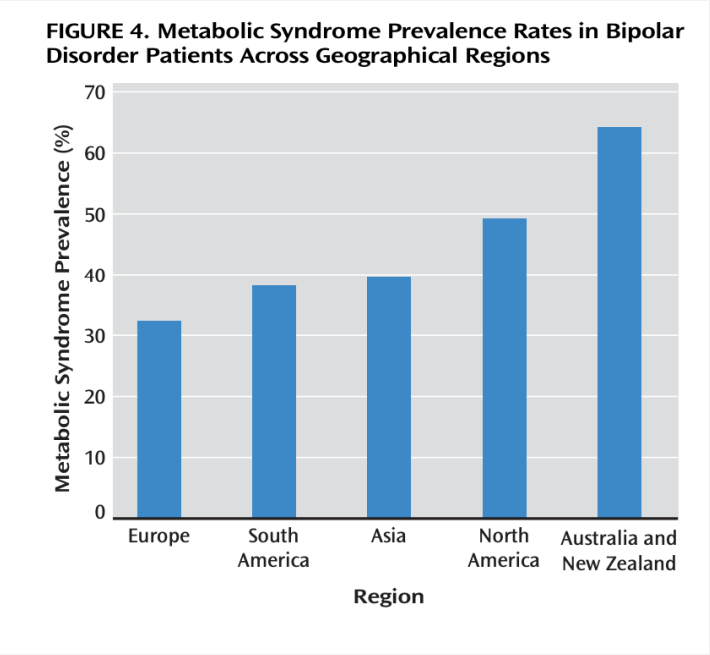
Table 1 Geographical differences in pooled metabolic syndrome (MetS) prevalence

Region	No. studies	Pooled MetS prevalence	Cochran Q
Australia and New Zealand*	6	50.2% (95% CI: 35.3%-65.0%)	73.8, p<0.001
Middle-East	6	35.3% (95% CI: 31.3%-39.5%)	1287.6, p<0.001
North-America	46	32.4% (95% CI: 24.7%-40.8%)	38.0, p<0.001
Europe	81	32.0% (95% CI: 29.4%-34.7%)	1226.4, p<0.001
Asia	50	31.0% (95% CI: 27.7%-34.4%)	691.3, p<0.001
South-America	10	25.8% (95% CI: 20.7%-31.3%)	42.3, p<0.001

Vancampfort et al.2015

SYNDROME MÉTABOLIQUE ET TROUBLE BIPOLAIRE





McIntyre 2010, Vancampfort et al. 2013

SYNDROME MÉTABOLIQUE ET SCHIZOPHRÉNIE

- Environ 37%
- Surpoids et Obésité env. 50%
- Hyperglycémie env. 20%
- HTA en. 40%
- Prévalence diabète type 2: x4 > pop. générale

=> **1er EPA**: Patients naïfs antipsychotiques=>dérégulation métabolique subclinique (homéostasie anormale du glucose et perturbation bilan lipidique).

=> Patients **schizophrènes** :

- leptine + élevée vs témoins
- élévation + marquée lors des décompensations => diminution du métabolisme de base

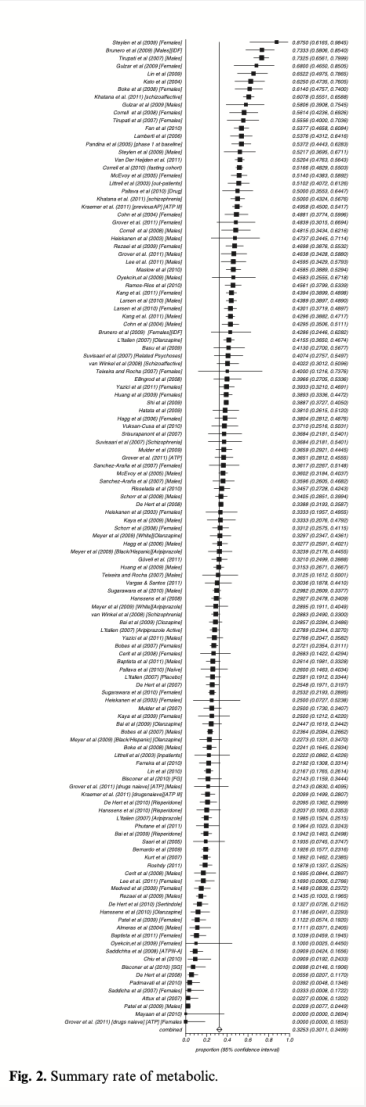


Fig. 2. Summary rate of metabolic.

Vancampfort et al. 2013; Mitchell et al. 2013;Pillinger et al. 2017; Stubbs et al. 2016

SYNDROME MÉTABOLIQUE ET ÉPISODE DÉPRESSIF

Study (first author)	Event rate	Lower limit	Upper limit	Z-Value	p-Value
Kloiber 2010	0.174	0.152	0.199	−18.557	0.000
Carroll 2009	0.206	0.162	0.257	−9.087	0.000
Van Reedt 2010	0.223	0.198	0.250	−16.027	0.000
Goethe 2009	0.234	0.210	0.261	−16.075	0.000
Zeugmann 2010	0.243	0.157	0.356	−4.079	0.000
Goldbacher 2009	0.245	0.183	0.320	−5.947	0.000
Richter 2010	0.250	0.157	0.374	−3.685	0.000
Grimaldi 2009	0.258	0.210	0.313	−7.660	0.000
Ifteni 2009	0.292	0.207	0.395	−3.797	0.000
Blank 2010	0.293	0.257	0.331	−9.681	0.000
Sagud 2013	0.335	0.273	0.403	−4.612	0.000
Aggarwal 2012	0.366	0.278	0.464	−2.653	0.008
Hatt 2011	0.375	0.271	0.492	−2.098	0.036
Kahl 2012	0.413	0.351	0.478	−2.624	0.009
Lehto 2010	0.414	0.305	0.532	−1.427	0.154
Correll 2006	0.434	0.328	0.547	−1.144	0.253
Dutt 2011	0.451	0.377	0.528	−1.247	0.212
Silić 2012	0.455	0.376	0.537	−1.078	0.281
	0.305	0.263	0.351	−7.792	0.000

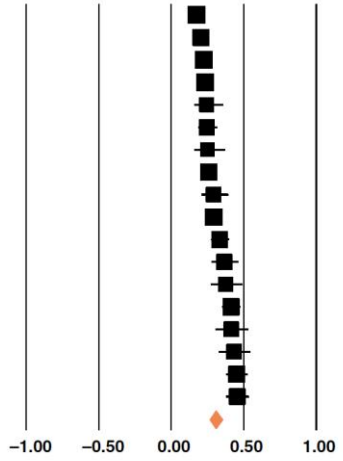


Fig. 3. Summary of metabolic syndrome (MetS) rates in major depressive disorder (MDD). (See Appendix 1 online for study citations.)

Vancampfort et al.2013

FACTEURS

- **Liés aux patients**:
  - Mode de vie: sédentarité, alimentation, TUS etc..
  - Nomadisme médical
  - Vulnérabilité croisée: génétique, inflammatoire, sommeil

FACTEURS

- **Liés aux patients**:
  - Mode de vie: sédentarité, alimentation, TUS etc..
  - Nomadisme médical
  - Vulnérabilité croisée: génétique, inflammatoire, sommeil
- **Liés aux soins:**
  - Accès aux soins réduits
  - Séparation soins psychiatriques / soin non psychiatrique
- **Liés aux traitements:**

ANTIPSYCHOTIQUE ET SYNDROME MÉTABOLIQUE

Table 2 Odds ratios for metabolic syndrome risk for individual antipsychotic medications (if monotherapy and N≥5)

Medication	Antipsychotic-naive	Amisulpride	Aripiprazole	Clozapine	Olanzapine	Quetiapine	Risperidone
Amisulpride	3.86*** (↑) (2.54-5.84) N = 15; n = 999	/	/	/	/	/	/
Aripiprazole	3.25*** (↑) (2.36-4.49) N = 16; n = 1,319	0.84 (↔) (0.57-1.25) N = 11; n = 692	/	/	/	/	/
Clozapine	7.81*** (↑) (6.02-10.22) N = 22; n = 2,398	2.02*** (↑) (1.45-2.83) N = 17; n = 1,177	2.40*** (↑) (1.91-3.03) N = 18; n = 2,091	/	/	/	/
Olanzapine	5.87*** (↑) (4.53-7.67) N = 22; n = 2,633	1.52* (↑) (1.08-2.16) N = 15; n = 2,006	1.81*** (↑) (1.44-2.27) N = 16; n = 2,326	0.75*** (↓) (0.65-0.86) N = 22; n = 3,405	/	/	/
Quetiapine	5.14*** (↑) (3.75-7.07) N = 21; n = 1,266	1.33 (↔) (0.90-1.97) N = 16; n = 639	1.58*** (↑) (1.19-2.11) N = 17; n = 959	0.66*** (↓) (0.53-0.82) N = 23; n = 2,038	0.88 (↔) (0.70-1.09) N = 22; n = 2,273	/	/
Risperidone	4.57*** (↑) (3.48-6.03) N = 30; n = 2,025	1.18 (↔) (0.83-1.69) N = 25; n = 1398	1.40*** (↑) (1.10-1.79) N = 26; n = 1,718	0.58*** (↓) (0.50-0.68) N = 32; n = 2,797	0.78** (↓) (0.66-0.91) N = 30; n = 3,032	0.89 (↔) (0.70-1.12) N = 31; n = 1,665	/
Typical antipsychotics	4.97*** (↑) (3.83-6.51) N = 17; n = 2,525	1.28 (↔) (0.91-1.83) N = 12; n = 1,898	1.53*** (↑) (1.23-1.91) N = 13; n =2,218	0.64*** (↓) (0.55-0.73) N = 19; n = 3,297	0.85* (↓) (0.74-0.97) N = 17; n = 3,532	0.97 (↔) (0.77-1.21) N = 18; n = 2,165	1.09 (↔) (0.93-1.28) N = 27; n = 2,924

*Two-sided p<0.05, two-sided p<0.01, ***two-sided p<0.001
↑ = higher risk, ↓ = lower risk, ↔ = no significant risk difference

Vancampfort et al. 2015

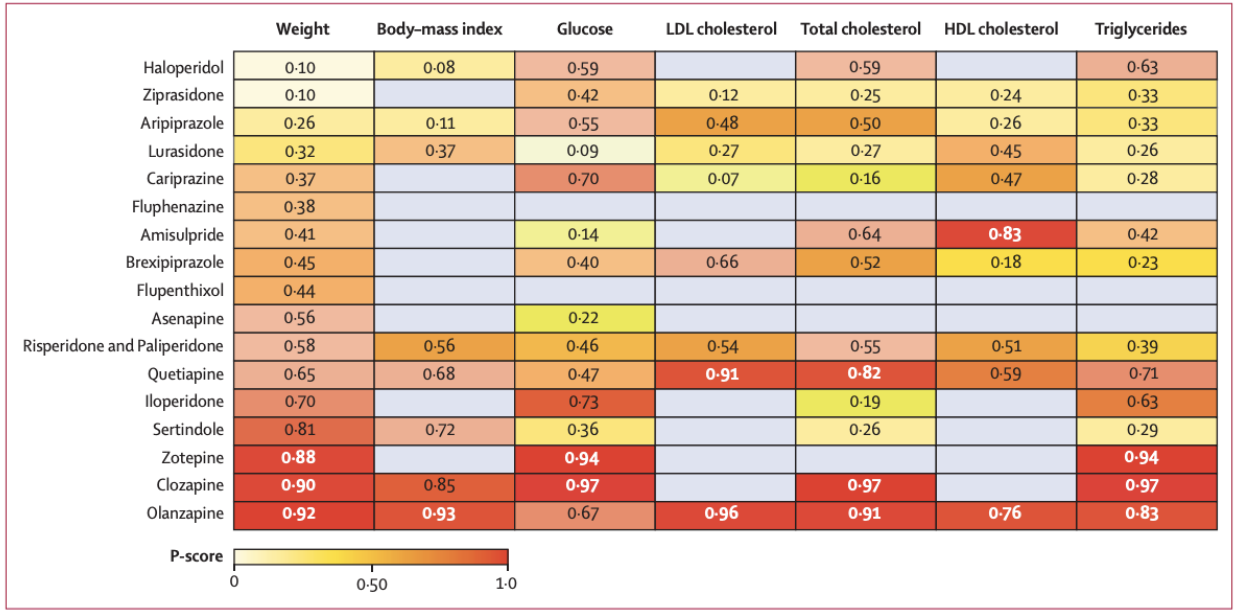


Figure 3: **Heat map of antipsychotic drugs ranked according to associated degree of alteration in bodyweight, body-mass index, and metabolic parameters**
Numbers reflect P-score, which rank antipsychotics on a continuous scale from 0 to 1. A higher P-score indicates a greater increase in the metabolic parameter, with the exception of HDL cholesterol, for which a higher P-score indicates a smaller increase. Grey squares indicate that data were not available.

T. Pillinger et al. Lancet Psychiatry 2020

ANTIPSYCHOTIQUE ET PRISE DE POIDS

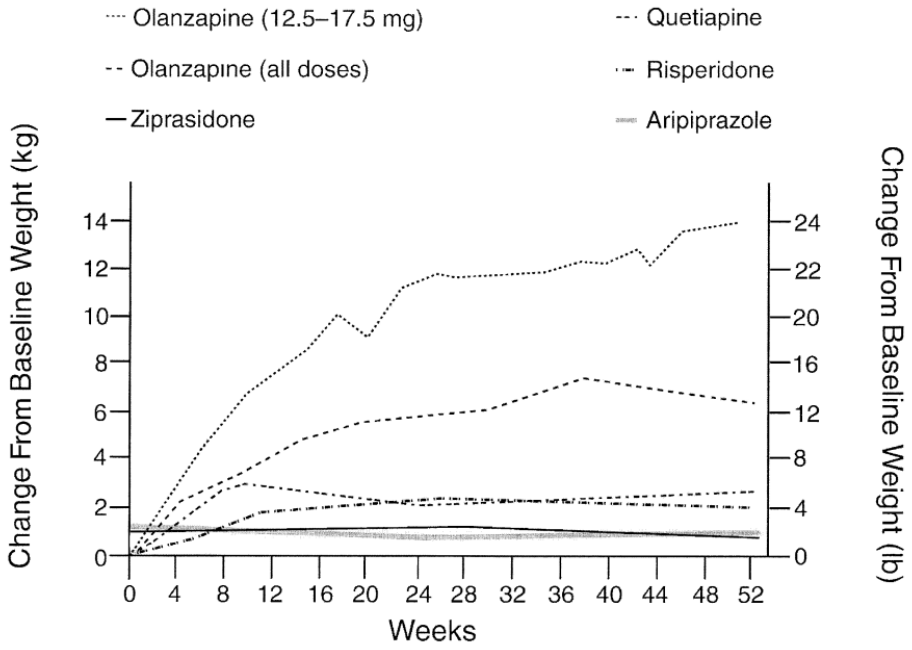


Figure 2 Mean change in weight gain in patients receiving antipsychotic agents. (Adapted with permission from "Factors Associated with Weight Gain During Olanzapine Treatment,"[43] *J Clin Psychiatry*,[44,46] and *Schizophr Res.*[45,48])

Casey DE et al2005

ANTIPSYCHOTIQUE ET PRISE DE POIDS

- **Prise de poids** chez patients sous antipsychotique : 40 à 80 % des individus
- **Facteurs prédictifs** :
  - Antécédent familial d'obésité
  - Jeune âge
  - Femme
  - Faible IMC avant traitement
  - Absence de tabagisme
  - Origine non caucasienne
  - Consommation de cannabis
  - Premier épisode de maladie psychotique ou premier traitement
  - Prise de poids au cours des 3 premières semaines de traitement
  - Facteurs génétiques

Pillinger et al. 2017
Stubbs et al. 2016
Sentissi et al. 2008

ANTIPSYCHOTIQUE ET PRISE DE POIDS

- Antagonisme 5-HT2a, H1 et D2 : **augmentation appétit**
- **Taux de leptine** augmente qq heures après 1ère administration d'antipsychotique. Taux maximum entre 6 et 10 semaines puis stabilisation
- **Sédation** provoquée par antipsychotiques : diminution activité physique

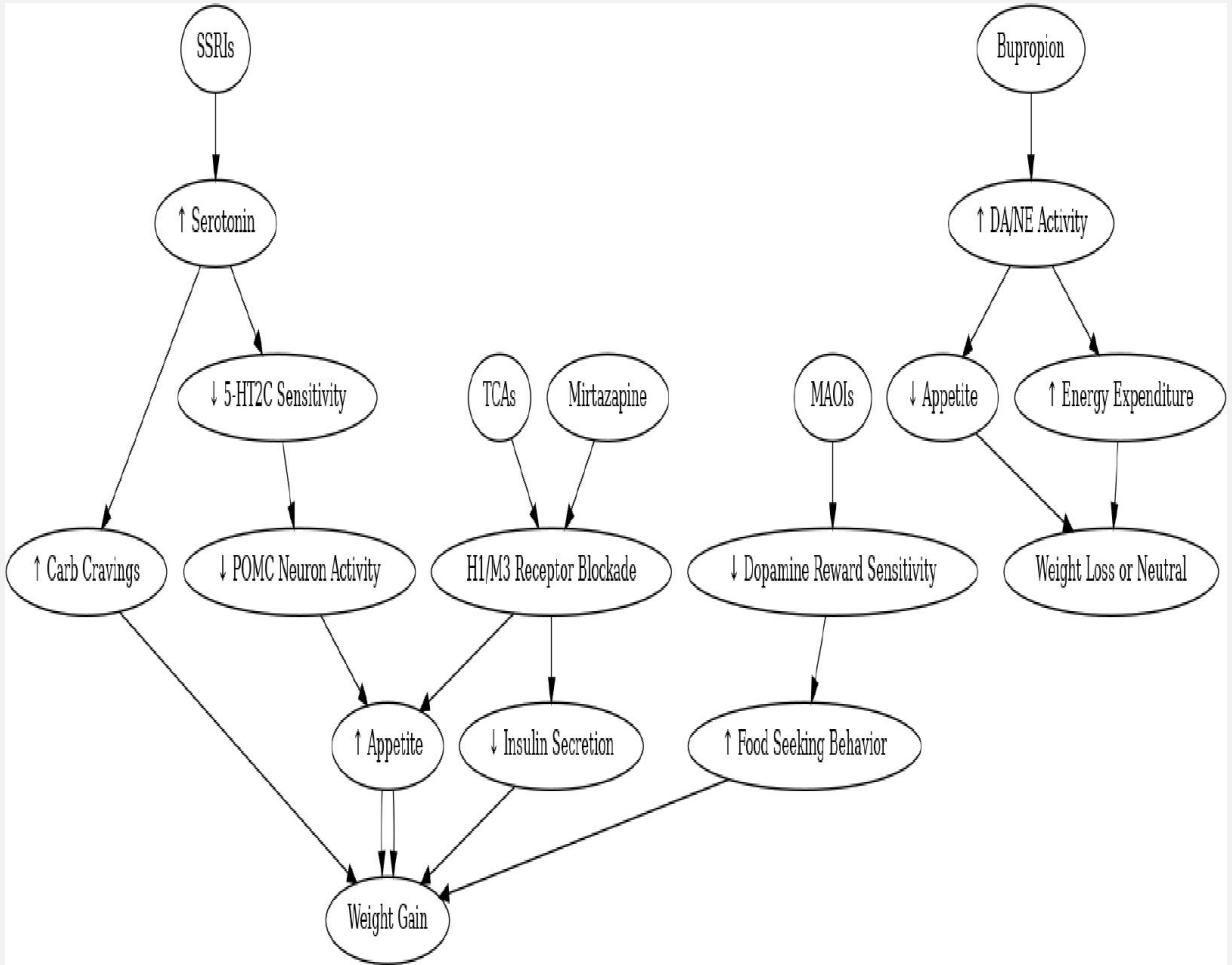
Stubbs et al. 2016
Sentissi et al. 2008

AUTRES PSYCHOTROPES ET PRISE DE POIDS

- **Thymorégulateurs**
  - Lithium:
    - 60% des patients, 4 à 15 kg en 2 ans
    - Augmentation de l'appétit, rétention hydrique, modification du métabolisme des glucides et des graisses
  - Valproate de sodium:
    - stimulation de l'appétit
- **Antidépresseurs**:
  - Inhibiteurs Monoamine Oxydase (IMAO)/tricycliques: Prise de poids
  - ISRS: Risque faible avec mais possibilité de prise de poids à long terme

Baptista et al1995;Deshmukh et al 2003; Bowden et al 2006; Taylor & MacQueen 2006

AUTRES PSYCHOTROPES ET PRISE DE POIDS



Mouawad et al. 2024

PRISE EN CHARGE

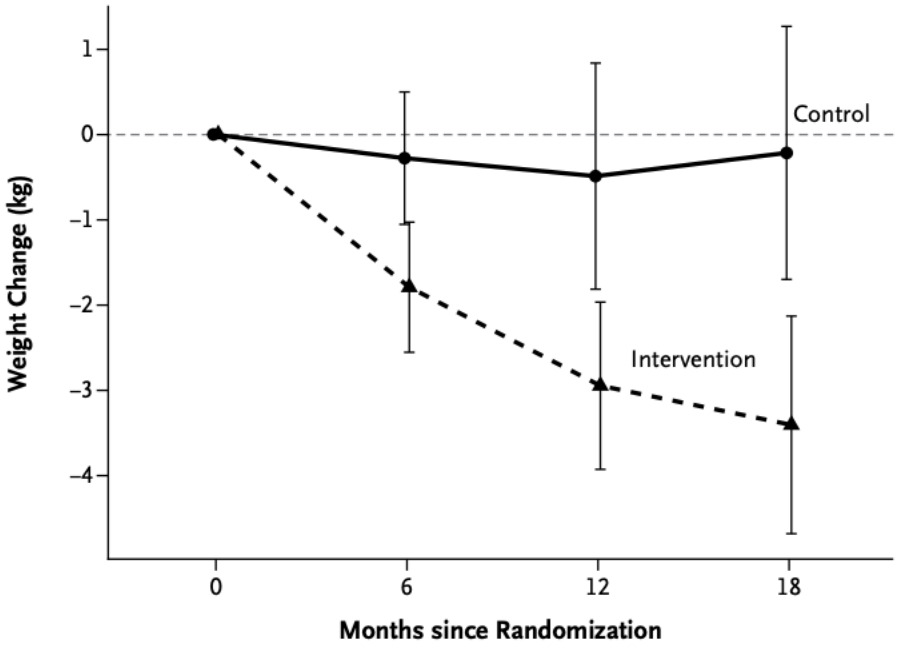
CONSEILS NUTRITIONNELS

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Behavioral Weight-Loss Intervention in Persons with Serious Mental Illness

Gail L. Daumit, M.D., M.H.S., Faith B. Dickerson, Ph.D., M.P.H.,



A 18 mois, perte d'au moins 5% masse corporelle initiale :

- 37.8% des patients avec conseils nutritionnels
- 22.7% des patients du groupe contrôle

RHD: indispensable mais limité

LIMITER LA PRISE DE POIDS LIÉ AUX PSYCHOTROPES

Schizophrenia Bulletin vol. 51 no. 5 pp. 1193–1205, 2025
https://doi.org/10.1093/schbul/sbae205
Advance Access publication December 9, 2024

Metformin for the Prevention of Antipsychotic-Induced Weight Gain: Guideline Development and Consensus Validation

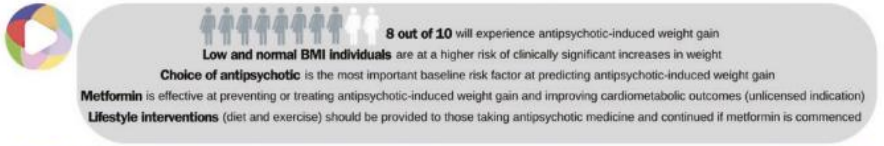
Aoife Carolan[*,1,2,✉]; Caroline Hynes-Ryan[1,2]; Sri Mahavir Agarwal[3,4,5,6]; Rita Bourke; Walter Cullen[7]; Fiona Gaughran[8,9]; Margaret K. Hahn[3,4,5,6,10,11]; Amir Krivoy[12,13,✉]; John Lally[8,14,15]; Stefan Leucht[16,✉]; John Lyne[17,18]; Robert A. McCutcheon[8,19,20]; Michael J. Norton[21,22,✉]; Karen O'Connor[23,24]; Benjamin I. Perry[25,26]; Toby Pillinger[8,✉]; David Shiers[27,28,29]; Dan Siskind[30,31,✉]; Andrew Thompson[32,33]; Donal O'Shea[7,34]; Dolores Keating[1,2]; Brian O'Donoghue[7,15,17,35,✉]

Table 3. Evidence Profile. Metformin compared to placebo or no treatment for the prevention of weight gain

No. of participants taking metformin (studies)	Mean difference change in weight (kg) 95% CI (kg)	Certainty of evidence (grade)
65 (4 RCTs)[17]	−4.03 (−5.78, −2.28)	⊕⊕⊖⊖ Low
563 (14 RCTs)	−3.12 (−4.22, −2.01)	⊕⊖⊖⊖ Very low
69 (1 cohort study)[19]	−3.14 (−0.78, −5.52)	⊕⊕⊖⊖ Low

Metformin compared to placebo or no treatment for the prevention of weight gain.
Outcome: Average endpoint change in body weight.

Guideline on Metformin for Prevention of Antipsychotic-Induced Weight Gain



8 out of 10 will experience antipsychotic-induced weight gain

Low and normal BMI individuals are at a higher risk of clinically significant increases in weight

Choice of antipsychotic is the most important baseline risk factor at predicting antipsychotic-induced weight gain

Metformin is effective at preventing or treating antipsychotic-induced weight gain and improving cardiometabolic outcomes (unlicensed indication)

Lifestyle interventions (diet and exercise) should be provided to those taking antipsychotic medicine and continued if metformin is commenced

To be applied at antipsychotic initiation or following a switch from one antipsychotic to another

High risk
(Not first line)
Olanzapine
Clozapine

Medium risk
Quetiapine
Paliperidone
Risperidone

Lower risk
All other antipsychotics

BMI ≥30
BMI 27-30 with <u>one of the following</u>:
Hypertension
Dyslipidaemia
Diabetes (Type 1 and 2)
Pre-diabetes
(HbA1c 42-47mmol/mol
Fasting glucose 6.1-6.9mmol/L)
Obstructive sleep apnoea

+ <u>One of the following:</u>
Hypertension
Dyslipidaemia
Diabetes (Type 1 and 2)
Pre-diabetes
(HbA1c 42-47mmol/mol
Fasting glucose 6.1-6.9mmol/L)
BMI >25 *(Adjust for ethnicity)*
Age 10-25

+ >3% weight gained at any time during the first year
<u>Adult:</u> 60Kg + 3% = 1.8Kg
70Kg + 3% = 2.1Kg
80Kg + 3% = 2.4Kg
90Kg + 3% = 2.7Kg
<u>Young Person:</u> >3% weight gained outside expected growth trajectory

Co-commence metformin | **Commence metformin** | If unavailable → **Commence GLP-1 Agonist**

Avoid metformin with:
- Acute metabolic acidosis
- Severe renal failure (GFR < 30 mL/min)
- Hepatic insufficiency
- Acute physical illness or harmful use of alcohol - see 'When to stop' below

Useful information
- Metformin lowers appetite, lowers hepatic glucose production and improves insulin response
- It does not stimulate insulin secretion and so does not cause hypoglycaemia
- Metformin is a low cost medicine

Pre-treatment Monitoring
- Renal function (GFR)

Dose escalation

	Morning	Evening
Week 1	500mg	
Week 2	500mg	500mg
	Check for efficacy	
Week 4	1g	500mg
	Check for efficacy	
Week 6	1g	1g

- Take with or after food to minimise GI side-effects
- Target dose of 1-2g/day - BMI/weight or increases in appetite should inform dose escalation schedule
- Available as a slow release tablet once a day - could be considered if GI side-effects persist, twice daily dosing is likely to lead to poor adherence or if preferred by the individual
- Special considerations:
  - GFR 30-44mL/min = Max 1g/day

Side-effects

<1 in 10
- Transient - Nausea, vomiting, diarrhoea, abdominal pain and loss of appetite
- Vitamin B12 decrease/deficiency

<1 in 100
- Taste disturbance

<1 in 10,000
- Lactic acidosis
- LFT abnormalities/hepatitis
- Skin reactions such as erythema, pruritus, urticaria

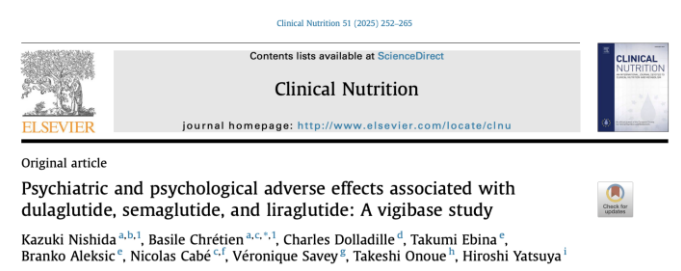
Ongoing Monitoring
- Weight/BMI
- Signs and symptoms of lactic acidosis - dyspnoea, muscle cramps, abdominal pain, hypothermia, or asthenia
- Liver function and HbA1c annually
- Renal function annually or 6 monthly for those >75 years or taking concomitant NSAIDs, ACE inhibitors, angiotensin II receptor antagonists and diuretics (especially loop diuretics)
- Vitamin B12 annually or 6 monthly for those with vegan diet, bariatric surgery, prescribed PPI or colchicine, older age or with gastrointestinal disorders affecting absorption - administer corrective treatment for vitamin B12 deficiency in line with current clinical guidelines; continue metformin therapy for as long as it is tolerated and not contraindicated

When to stop
- If lactic acidosis is suspected or if risks for lactic acidosis present - dehydration (severe diarrhoea or vomiting, fever or reduced fluid intake), acute alcohol intoxication, harmful use of alcohol, decompensated heart failure, respiratory failure, recent myocardial infarction, hypovolemeic shock, severe infection
- Prior to or at the time of administration of iodinated contrast agents (restarted at least 48 hours after)
- If GFR drops below 30mL/min
- BMI <20
- Sick day rule - Stop if systemically unwell (restart when well)
- If antipsychotic is stopped

PROGRESS | St John of God Hospital | HRB | ST. VINCENT'S UNIVERSITY HOSPITAL

ANALOGUE GLP-1 ET PSYCHIATRIE

ANALOGUES DU GLP1 ET PSYCHIATRIE



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Original article

Psychiatric and psychological adverse effects associated with dulaglutide, semaglutide, and liraglutide: A vigibase study

Kazuki Nishida [a,b,1], Basile Chrétien [a,c,*,1], Charles Dolladille [d], Takumi Ebina [e], Branko Aleksic [e], Nicolas Cabé [c,f], Véronique Savey [g], Takeshi Onoue [h], Hiroshi Yatsuya [i]

- Les agonistes GLP-1 sont efficaces pour le diabète et l'obésité, mais leur sécurité psychiatrique fait débat.
- analyse mondiale de pharmacovigilance:
  - Pas d'augmentation d'effets secondaires psychiatriques observé.
  - Sémaglutide: signaux pour la dépression et l'anxiété:
    - Biais de recrutement à prendre en considération

ANALOGUES DU GLP1 ET PSYCHIATRIE

A C. S. Pierret,Glucagon-Like Peptide 1 Receptor Agonists and Mental Health A Systematic Review and Meta-Analysis, Jama Psychiatry, 2025

- 80 RCT, 107860 patients DT2/obèses, Liraglutide (30%), semaglutide (20%)
- Adverse effects/QOL/eating behavior

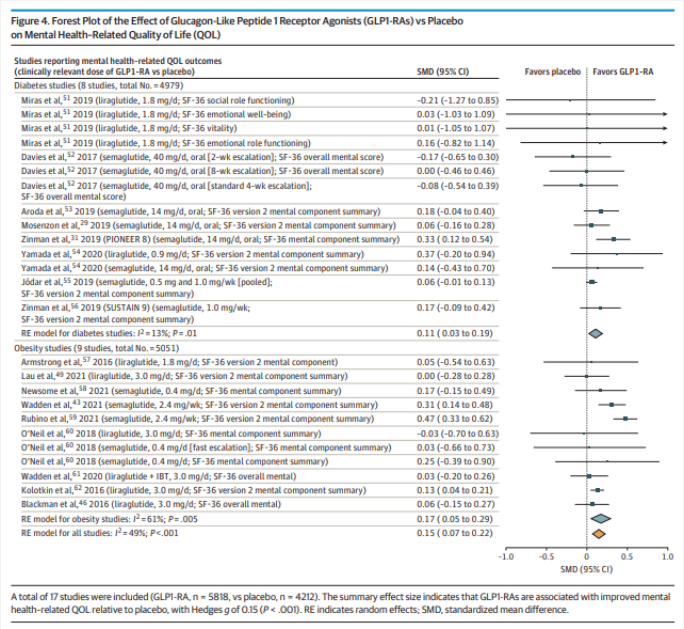


Figure 4. Forest Plot of the Effect of Glucagon-Like Peptide 1 Receptor Agonists (GLP1-RAs) vs Placebo on Mental Health–Related Quality of Life (QOL)

Studies reporting mental health–related QOL outcomes (clinically relevant dose of GLP1-RA vs placebo)	SMD (95% CI)
Diabetes studies (8 studies, total No. = 4979)	
Miras et al,[51] 2019 (liraglutide, 1.8 mg/d; SF-36 social role functioning)	-0.21 (-1.27 to 0.85)
Miras et al,[51] 2019 (liraglutide, 1.8 mg/d; SF-36 emotional well-being)	0.03 (-1.03 to 1.09)
Miras et al,[51] 2019 (liraglutide, 1.8 mg/d; SF-36 vitality)	0.01 (-1.05 to 1.07)
Miras et al,[51] 2019 (liraglutide, 1.8 mg/d; SF-36 emotional role functioning)	0.16 (-0.82 to 1.14)
Davies et al,[52] 2017 (semaglutide, 40 mg/d, oral [2-wk escalation]; SF-36 overall mental score)	-0.17 (-0.65 to 0.30)
Davies et al,[52] 2017 (semaglutide, 40 mg/d, oral [8-wk escalation]; SF-36 overall mental score)	0.00 (-0.46 to 0.46)
Davies et al,[52] 2017 (semaglutide, 40 mg/d, oral [standard 4-wk escalation]; SF-36 overall mental score)	-0.08 (-0.54 to 0.39)
Aroda et al,[53] 2019 (semaglutide, 14 mg/d, oral; SF-36 version 2 mental component summary)	0.18 (-0.04 to 0.40)
Mosenzon et al,[29] 2019 (semaglutide, 14 mg/d, oral; SF-36 version 2 mental component summary)	0.06 (-0.16 to 0.28)
Zinman et al,[31] 2019 (PIONEER 8) (semaglutide, 14 mg/d, oral; SF-36 mental component summary)	0.33 (0.12 to 0.54)
Yamada et al,[54] 2020 (liraglutide, 0.9 mg/d; SF-36 version 2 mental component summary)	0.37 (-0.20 to 0.94)
Yamada et al,[54] 2020 (semaglutide, 14 mg/d, oral; SF-36 version 2 mental component summary)	0.14 (-0.43 to 0.70)
Jódar et al,[55] 2019 (semaglutide, 0.5 mg and 1.0 mg/wk [pooled]; SF-36 version 2 mental component summary)	0.06 (-0.01 to 0.13)
Zinman et al,[56] 2019 (SUSTAIN 9) (semaglutide, 1.0 mg/wk; SF-36 version 2 mental component summary)	0.17 (-0.09 to 0.42)
RE model for diabetes studies: I^2 = 13%; P = .01	0.11 (0.03 to 0.19)
Obesity studies (9 studies, total No. = 5051)	
Armstrong et al,[57] 2016 (liraglutide, 1.8 mg/d; SF-36 version 2 mental component)	0.05 (-0.54 to 0.63)
Lau et al,[49] 2021 (liraglutide, 3.0 mg/d; SF-36 version 2 mental component summary)	0.00 (-0.28 to 0.28)
Newsome et al,[58] 2021 (semaglutide, 0.4 mg/d; SF-36 mental component summary)	0.17 (-0.15 to 0.49)
Wadden et al,[43] 2021 (semaglutide, 2.4 mg/wk; SF-36 version 2 mental component summary)	0.31 (0.14 to 0.48)
Rubino et al,[59] 2021 (semaglutide, 2.4 mg/wk; SF-36 version 2 mental component summary)	0.47 (0.33 to 0.62)
O'Neil et al,[60] 2018 (liraglutide, 3.0 mg/d; SF-36 mental component summary)	-0.03 (-0.70 to 0.63)
O'Neil et al,[60] 2018 (semaglutide, 0.4 mg/d [fast escalation]; SF-36 mental component summary)	0.03 (-0.66 to 0.73)
O'Neil et al,[60] 2018 (semaglutide, 0.4 mg/d; SF-36 mental component summary)	0.25 (-0.39 to 0.90)
Wadden et al,[61] 2020 (liraglutide + IBT, 3.0 mg/d; SF-36 overall mental)	0.03 (-0.20 to 0.26)
Kolotkin et al,[62] 2016 (liraglutide, 3.0 mg/d; SF-36 version 2 mental component summary)	0.13 (0.04 to 0.21)
Blackman et al,[46] 2016 (liraglutide, 3.0 mg/d; SF-36 overall mental)	0.06 (-0.15 to 0.27)
RE model for obesity studies: I^2 = 61%; P = .005	0.17 (0.05 to 0.29)
RE model for all studies: I^2 = 49%; P < .001	0.15 (0.07 to 0.22)

A total of 17 studies were included (GLP1-RA, n = 5818, vs placebo, n = 4212). The summary effect size indicates that GLP1-RAs are associated with improved mental health-related QOL relative to placebo, with Hedges *g* of 0.15 (P < .001). RE indicates random effects; SMD, standardized mean difference.

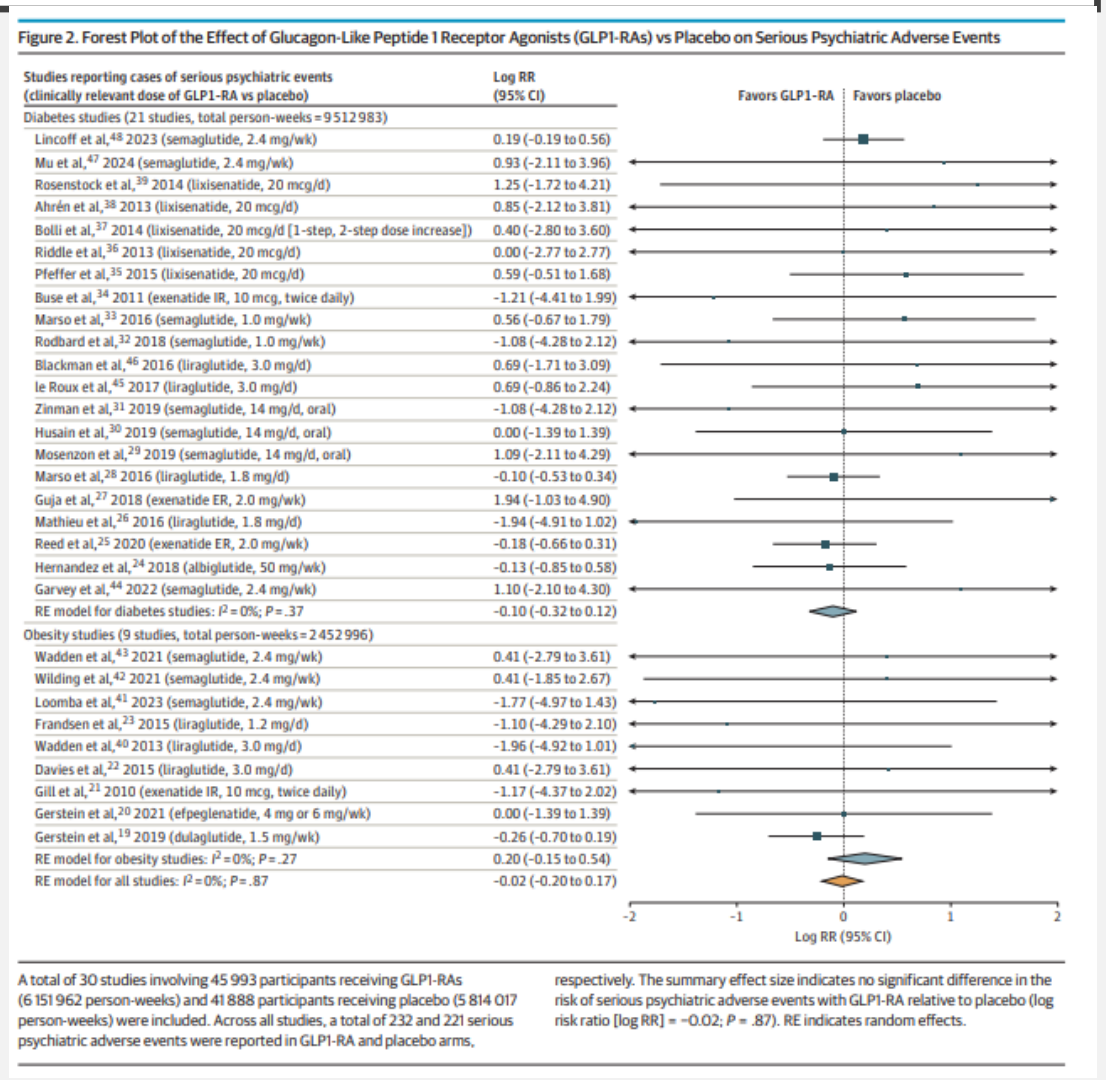


Figure 2. Forest Plot of the Effect of Glucagon-Like Peptide 1 Receptor Agonists (GLP1-RAs) vs Placebo on Serious Psychiatric Adverse Events

Studies reporting cases of serious psychiatric events (clinically relevant dose of GLP1-RA vs placebo)	Log RR (95% CI)
Diabetes studies (21 studies, total person-weeks = 9 512 983)	
Lincoff et al,[48] 2023 (semaglutide, 2.4 mg/wk)	0.19 (-0.19 to 0.56)
Mu et al,[47] 2024 (semaglutide, 2.4 mg/wk)	0.93 (-2.11 to 3.96)
Rosenstock et al,[39] 2014 (lixisenatide, 20 mcg/d)	1.25 (-1.72 to 4.21)
Ahrén et al,[38] 2013 (lixisenatide, 20 mcg/d)	0.85 (-2.12 to 3.81)
Bolli et al,[37] 2014 (lixisenatide, 20 mcg/d [1-step, 2-step dose increase])	0.40 (-2.80 to 3.60)
Riddle et al,[36] 2013 (lixisenatide, 20 mcg/d)	0.00 (-2.77 to 2.77)
Pfeffer et al,[35] 2015 (lixisenatide, 20 mcg/d)	0.59 (-0.51 to 1.68)
Buse et al,[34] 2011 (exenatide IR, 10 mcg, twice daily)	-1.21 (-4.41 to 1.99)
Marso et al,[33] 2016 (semaglutide, 1.0 mg/wk)	0.56 (-0.67 to 1.79)
Rodbard et al,[32] 2018 (semaglutide, 1.0 mg/wk)	-1.08 (-4.28 to 2.12)
Blackman et al,[46] 2016 (liraglutide, 3.0 mg/d)	0.69 (-1.71 to 3.09)
le Roux et al,[45] 2017 (liraglutide, 3.0 mg/d)	0.69 (-0.86 to 2.24)
Zinman et al,[31] 2019 (semaglutide, 14 mg/d, oral)	-1.08 (-4.28 to 2.12)
Husain et al,[30] 2019 (semaglutide, 14 mg/d, oral)	0.00 (-1.39 to 1.39)
Mosenzon et al,[29] 2019 (semaglutide, 14 mg/d, oral)	1.09 (-2.11 to 4.29)
Marso et al,[28] 2016 (liraglutide, 1.8 mg/d)	-0.10 (-0.53 to 0.34)
Guja et al,[27] 2018 (exenatide ER, 2.0 mg/wk)	1.94 (-1.03 to 4.90)
Mathieu et al,[26] 2016 (liraglutide, 1.8 mg/d)	-1.94 (-4.91 to 1.02)
Reed et al,[25] 2020 (exenatide ER, 2.0 mg/wk)	-0.18 (-0.66 to 0.31)
Hernandez et al,[24] 2018 (albiglutide, 50 mg/wk)	-0.13 (-0.85 to 0.58)
Garvey et al,[44] 2022 (semaglutide, 2.4 mg/wk)	1.10 (-2.10 to 4.30)
RE model for diabetes studies: I^2 = 0%; P = .37	-0.10 (-0.32 to 0.12)
Obesity studies (9 studies, total person-weeks = 2 452 996)	
Wadden et al,[43] 2021 (semaglutide, 2.4 mg/wk)	0.41 (-2.79 to 3.61)
Wilding et al,[42] 2021 (semaglutide, 2.4 mg/wk)	0.41 (-1.85 to 2.67)
Loomba et al,[41] 2023 (semaglutide, 2.4 mg/wk)	-1.77 (-4.97 to 1.43)
Frandsen et al,[23] 2015 (liraglutide, 1.2 mg/d)	-1.10 (-4.29 to 2.10)
Wadden et al,[40] 2013 (liraglutide, 3.0 mg/d)	-1.96 (-4.92 to 1.01)
Davies et al,[22] 2015 (liraglutide, 3.0 mg/d)	0.41 (-2.79 to 3.61)
Gill et al,[21] 2010 (exenatide IR, 10 mcg, twice daily)	-1.17 (-4.37 to 2.02)
Gerstein et al,[20] 2021 (efpeglenatide, 4 mg or 6 mg/wk)	0.00 (-1.39 to 1.39)
Gerstein et al,[19] 2019 (dulaglutide, 1.5 mg/wk)	-0.26 (-0.70 to 0.19)
RE model for obesity studies: I^2 = 0%; P = .27	0.20 (-0.15 to 0.54)
RE model for all studies: I^2 = 0%; P = .87	-0.02 (-0.20 to 0.17)

A total of 30 studies involving 45 993 participants receiving GLP1-RAs (6 151 962 person-weeks) and 41 888 participants receiving placebo (5 814 017 person-weeks) were included. Across all studies, a total of 232 and 221 serious psychiatric adverse events were reported in GLP1-RA and placebo arms, respectively. The summary effect size indicates no significant difference in the risk of serious psychiatric adverse events with GLP1-RA relative to placebo (log risk ratio [log RR] = −0.02; P = .87). RE indicates random effects.

ANALOGUES DU GLP1 ET TROUBLES DE L'HUMEUR

X Chen, The Antidepressant Effects of GLP-1 Receptor Agonists: A Systematic Review and Meta-Analysis, Am J Geriatr Psychiatry, 2024

Méta-analyse : 2071 patients (DT2/parkinson) sur 5 RCTs et 1 étude prospective

TABLE 1. Main Characteristics of the Included Studies

First Author, Year, Country	Study Type	Study Duration	Population	Male%	Age (Avg.)	Depression Rating Scale	GLP-1RAs (Number of Patients)	Control (Number of Patients)
Athauda, 2017, UK[7]	DBRCT	60 weeks	Patients with moderate Parkinson's disease	73	60	MADRS	Exenatide (n = 31)	Placebo (n = 29)
Best, 2011, USA[16]	DBRCT	26 weeks	T2DM	52	53	PGWB subscale depression[a]	Exenatide (n = 133)	Pioglitazone (n = 130)
Bode, 2010, USA[17]	DBRCT	52 weeks	T2DM	49	53	HRQoL subscale depression[a]	Liraglutide (n = 247)	Glimepiride (n = 248)
De Wit, 2014, Netherlands[18]	Unblinded RCT	26 weeks	T2DM patients with ≥4% weight gain during short-term (≤16 months) insulin therapy	62	58	BDI-II	Liraglutide (n = 26)	Insulin (n = 24)
Miras, 2019, UK[19]	DBRCT	26 weeks	Obese patients with T2DM who had undergone metabolic surgery at least 1 year before randomization	41	56	HADS, BDI-II	Liraglutide (n = 45)	Placebo (n = 21)
Reaney, 2013, 6 European countries[20]	Cohort study	24 weeks	T2DM	56	61	HADS	Exenatide (n = 605)	Insulin (n = 532)

DBRCT: double-blind randomized clinical trial; RCT: randomized clinical trial; T2DM: Type 2 diabetes mellitus.
[a]The higher scores reflect better emotional well-being; to ensure comparison with studies that utilized scales in which lower scores indicated better outcomes, the negative scores were used to report these scores.

FIGURE 2. The change in depression rating scale scores for GLP-1RA groups compared to control groups.

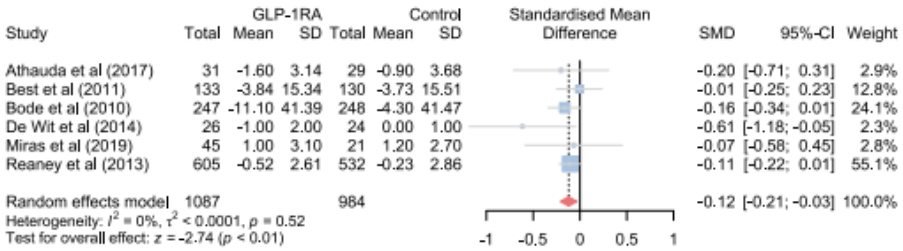
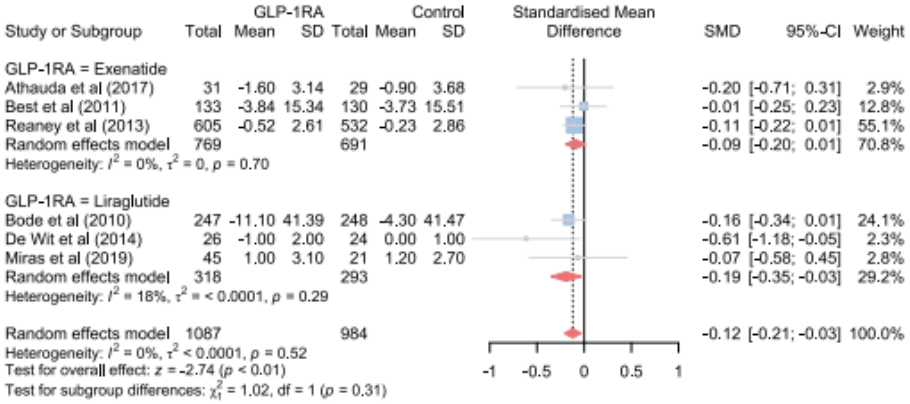


FIGURE 4. Subgroup analysis of the change in depression rating scale scores for GLP-1RA groups compared to control groups based on intervention (exenatide, liraglutide).



ANALOGUES DU GLP1 ET TROUBLES DE L'HUMEUR

R.Mansur, Liraglutide promotes improvements in objective measures of cognitive dysfunction in individuals with mood disorders: A pilot, open-label study, Journal of Affective Disorders, 2017

- Étude pilote, ouverte, 4 semaines
- 19 patients : dépression sévère ou maladie bipolaire, non diabétique
- ajout Liraglutide 1,8 mg/j
- Mesure cognition/fonctions exécutives par test TMTB

> Le Liraglutide est sécure et bien toléré dans cette population et a des effets favorables sur les fonctions cognitives

Table 1
Differences between baseline and endpoint in cognitive measures.

	Baseline		Endpoint			
	Mean	SD	Mean	SD	% Change	*p*-value
TMTB (T-score)	46.41	11.71	53.18	9.36	14.59	0.009
TMTB (time)	65.80	27.81	50.39	14.15	−23.42	0.021
TMTA (time)	28.58	8.23	25.74	5.50	−9.94	0.172
DSST (number of symbols)	53.47	10.93	60.00	13.36	12.21	< 0.001
RAVLT acquisition (number of words)	7.18	3.67	8.53	2.91	18.80	0.021
RAVLT delayed recall (number of words)	7.35	3.92	8.41	3.31	14.42	0.185
STROOP – Congruent (time)	39.94	13.11	30.29	7.30	−24.16	0.001
STROOP – Incongruent (time)	58.00	13.07	51.94	10.25	−10.45	0.005
Composite z-score (all tests)	−0.26	0.74	0.26	0.60	20.51	< 0.00
PDQ (total score)	44.17	14.30	24.94	14.15	−43.54	< 0.00

SD: standard deviation; TMT, trail making test; DSST, Digit Symbol Substitution T
RAVLT, Rey Auditory Verbal Learning Test; PDQ, Perceived Deficits Questionnaire

Avis n° 25 du GT

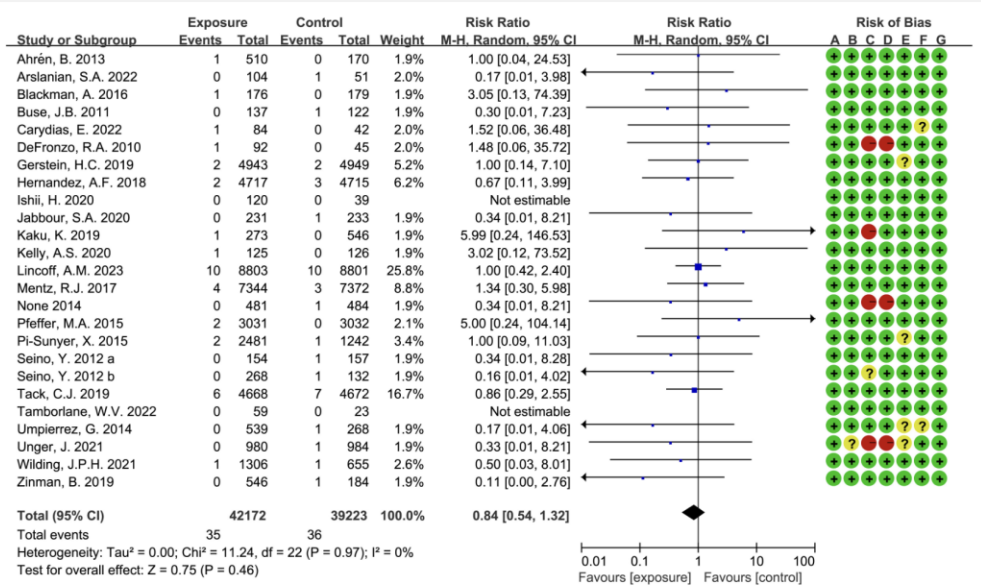
- Les données récentes auprès de populations sélectionnées ne suggèrent pas de risque psychiatrique accru associé aux TMO **(B)**.
- Toutefois, le GT indique qu'il faut prendre en compte l'état de santé global d'un individu, y compris son état psychologique, avant d'initier un TMO **(AE)**.
- En cas de pathologie psychiatrique connue, ou d'une fragilité psychique identifiée à l'initiation du TMO, le GT recommande que le prescripteur évalue régulièrement l'évolution de l'état psychique lors du suivi du traitement. En effet, toute perte de poids importante et rapide peut s'accompagner d'une déstabilisation psychique. Au besoin, une sollicitation du psychiatre référent doit être envisagée pour un suivi coordonné **(AE)**.

ANALOGUES DU GLP1 ET SUICIDE

ORIGINAL ARTICLE OPEN ACCESS

Impact of GLP-1 Receptor Agonists on Suicide Behavior: A Meta-Analysis Based on Randomized Controlled Trials

Jingqi Chen[1] | Qiufeng Zhang[1] | Qingping Wu[1] | Xiaoming Zhang[1] | Zhiyi Xiang[1] | Sidong Zhu[1] | Tianfu Dai[1] | Yuexiu Si[2]



Study or Subgroup	Exposure Events	Exposure Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Ahrén, B. 2013	1	510	0	170	1.9%	1.00 [0.04, 24.53]
Arslanian, S.A. 2022	0	104	1	51	2.0%	0.17 [0.01, 3.98]
Blackman, A. 2016	1	176	0	179	1.9%	3.05 [0.13, 74.39]
Buse, J.B. 2011	0	137	1	122	1.9%	0.30 [0.01, 7.23]
Carydias, E. 2022	1	84	0	42	2.0%	1.52 [0.06, 36.48]
DeFronzo, R.A. 2010	1	92	0	45	2.0%	1.48 [0.06, 35.72]
Gerstein, H.C. 2019	2	4943	2	4949	5.2%	1.00 [0.14, 7.10]
Hernandez, A.F. 2018	2	4717	3	4715	6.2%	0.67 [0.11, 3.99]
Ishii, H. 2020	0	120	0	39		Not estimable
Jabbour, S.A. 2020	0	231	1	233	1.9%	0.34 [0.01, 8.21]
Kaku, K. 2019	1	273	0	546	1.9%	5.99 [0.24, 146.53]
Kelly, A.S. 2020	1	125	0	126	1.9%	3.02 [0.12, 73.52]
Lincoff, A.M. 2023	10	8803	10	8801	25.8%	1.00 [0.42, 2.40]
Mentz, R.J. 2017	4	7344	3	7372	8.8%	1.34 [0.30, 5.98]
None 2014	0	481	1	484	1.9%	0.34 [0.01, 8.21]
Pfeffer, M.A. 2015	2	3031	0	3032	2.1%	5.00 [0.24, 104.14]
Pi-Sunyer, X. 2015	2	2481	1	1242	3.4%	1.00 [0.09, 11.03]
Seino, Y. 2012 a	0	154	1	157	1.9%	0.34 [0.01, 8.28]
Seino, Y. 2012 b	0	268	1	132	1.9%	0.16 [0.01, 4.02]
Tack, C.J. 2019	6	4668	7	4672	16.7%	0.86 [0.29, 2.55]
Tamborlane, W.V. 2022	0	59	0	23		Not estimable
Umpierrez, G. 2014	0	539	1	268	1.9%	0.17 [0.01, 4.06]
Unger, J. 2021	0	980	1	984	1.9%	0.33 [0.01, 8.21]
Wilding, J.P.H. 2021	1	1306	1	655	2.6%	0.50 [0.03, 8.01]
Zinman, B. 2019	0	546	1	184	1.9%	0.11 [0.00, 2.76]
Total (95% CI)		**42172**		**39223**	**100.0%**	**0.84 [0.54, 1.32]**
Total events	35		36			

Heterogeneity: Tau² = 0.00; Chi² = 11.24, df = 22 (P = 0.97); I² = 0%
Test for overall effect: Z = 0.75 (P = 0.46)

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

FIGURE 2 | Forest plot depicting the association between GLP-1 RAs exposure and suicidal behavior in participants with T2DM or obesity.

ANALOGUES DU GLP1 ET SCHIZOPHRÉNIE

BMI

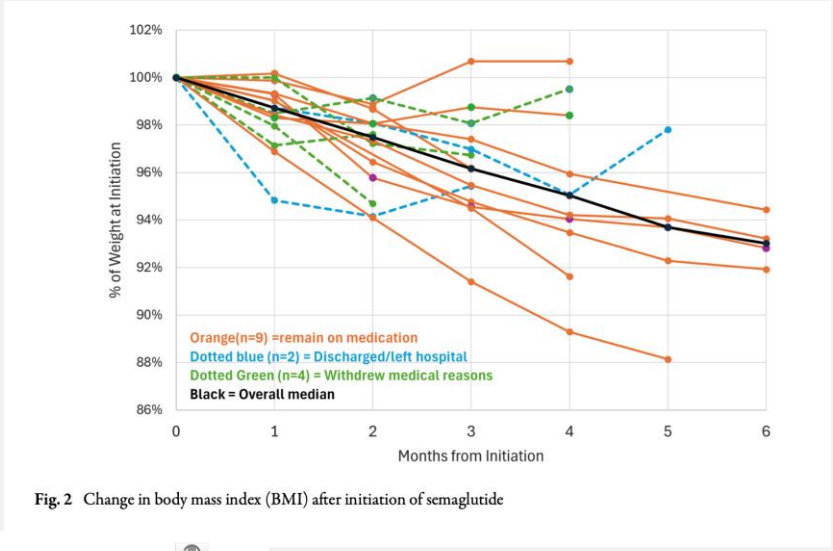


Fig. 2 Change in body mass index (BMI) after initiation of semaglutide

HBA1C

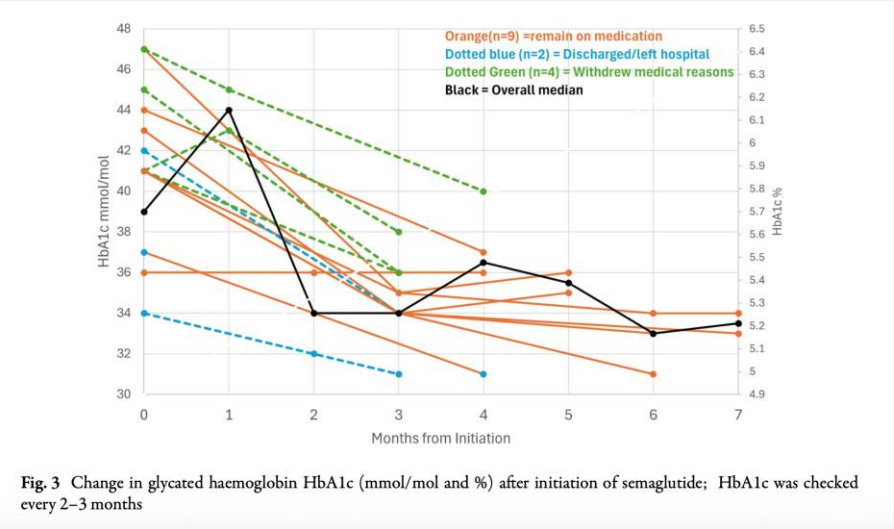


Fig. 3 Change in glycated haemoglobin HbA1c (mmol/mol and %) after initiation of semaglutide; HbA1c was checked every 2–3 months

Adv Ther (2025) 42:4013–4022
https://doi.org/10.1007/s12325-025-03261-0

ORIGINAL RESEARCH

Obesity and Schizophrenia: Results of a Feasibility Study with Semaglutide to Assist Weight Loss

Adrian H. Heald · Gavin Reynolds · Isabel Nash · Onagh Boyle · Chris Daly · Damien Longson · Donal O'Shea · Joseph Ingram · Richard Holt · Joseph Firth · Mike Stedman · Akheel Syed · Marc de Hert

ANALOGUES DU GLP1 ET ANTIPSYCHOTIQUE

Therapeutic Advances in Psychopharmacology
Volume 13, 2023

https://doi.org/10.1177/20451253231165169

SAGE journals

Case Series

Semaglutide for the treatment of antipsychotic-associated weight gain in patients not responding to metformin – a case series

Abstract

Metformin is the currently accepted first-line treatment for antipsychotic-associated weight gain (AAWG). However, not all patients benefit from metformin. Glucagon-like peptide-1 receptor agonists (GLP1-RA) have shown promise in the management of obesity in the general population, with preliminary evidence supporting efficacy in AAWG. Semaglutide is a weekly injectable GLP-1RA which received recent approval for obesity management and noted superiority over other GLP-1RAs. This study explored the efficacy and tolerability of semaglutide in AAWG among individuals with severe mental illness. A retrospective chart review of patients treated with semaglutide in the Metabolic Clinic at the Center for Addiction and Mental Health (CAMH) between 2019 and 2021 was conducted. Patients failing a trial of metformin (<5% weight loss or continuing to meet criteria for metabolic syndrome) after 3 months at the maximum tolerated dose (1500–2000 mg/day) were initiated on semaglutide up to 2 mg/week. The primary outcome measure was a change in weight at 3, 6, and 12 months. Twelve patients on weekly semaglutide injections of 0.71 ± 0.47 mg/week were included in the analysis. About 50% were female; the average age was 36.09 ± 13.32 years. At baseline, mean weight was 111.4 ± 31.7 kg, BMI was 36.7 ± 8.2 kg/m^2, with a mean waist circumference of 118.1 ± 19.3 cm. A weight loss of 4.56 ± 3.15 kg ($p < 0.001$), 5.16 ± 6.27 kg ($p = 0.04$) and 8.67 ± 9 kg ($p = 0.04$) was seen at 3, 6, and 12 months, respectively, after initiation of semaglutide with relatively well-tolerated side-effects. Initial evidence from our real-world clinical setting suggests that semaglutide may be effective in reducing AAWG in patients not responding to metformin. Randomized control trials investigating semaglutide for AAWG are needed to corroborate these findings.

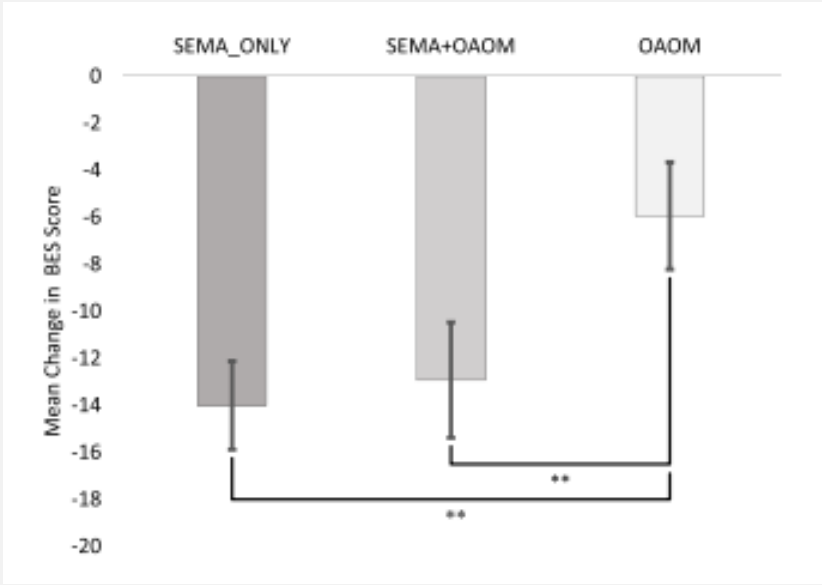
ANALOGUES DU GLP1 ET TCA (BED)

Jesse Richards, Successful treatment of binge eating disorder with the GLP-1 agonist semaglutide: A retrospective cohort study, Obesity Pillars, 2023

- Traitements : Psychothérapie, Lisdexamfetamine, Topiramate
- Etude rétrospective : 48 patients avec BED (BES score) 06/21 > 12/22

Table 1
Moderate/severe initial BES score patient characteristics.

	SEMA Only	SEMA + OAOM	OAOM
n	19	13	16
Female	17	10	14
Race/Ethnicity	White 15 Black 3 American Indian 1	White 5 American Indian 3	White 9 Black 1 American Indian 1 Multiracial 1
Age (yrs) *M [SD, range]*	43.5 *[13.6, 22-74]*	43.1 *[9.8, 32-64]*	39.6 *[12.8, 21-67]*
Initial weight (lbs) *M [SD, range]*	257.6 *[58.1, 162.4-360.6]*	327.1 *[127.6, 209.9-606.4]*	268.4 *[57.7, 179.5-358.2]*
Total body weight loss (lbs) *M [SD, range]*	22.5 *[14.3, 6.4-52.6]*	53 *[64.2, 1.3-224.9]*	13.2 *[20.1, -23.54-67.1]*
Baseline BES Score *M [SD, range]*	23.89 *[5.7, 18-36]*	22.7 *[6.3, 17-35]*	26.1 *[7.4, 17-44]*
Average Change in BES Score *M [SD, range]*	14 *[8.2, -2-25]*	12.9 *[8.9, 0-29]*	5.9 *[9.1, -7-24]*
Prescribed Vyvanse	0	2	1
Prescribed Topiramate	0	13	12
Prescribed both Vyvanse and Topiramate	0	2	1



ANALOGUES DU GLPI ET TCA (BED)

Kelly C. Allison, A pilot randomized controlled trial of liraglutide 3.0 mg for binge eating disorder, Obesity Science and Practice, 2022

- Essai pilote randomisé liraglutide 3mg/placebo
- Nombre de crises de BE /17 semaines
- 37 patients > 27 dans l'analyse (erreur de traitement)

TABLE 2 Participant characteristics at randomization

Characteristic	Total (*N* = 27)	Placebo (*N* = 14)	Liraglutide 3.0 mg (*N* = 13)	*Cohen's d (95% CI)*	*p*
Sex (female), *n* (%)	17 (63.0%)	11 (78.6%)	6 (46.2%)	--	0.09
Race, *n* (%)					
Black	11 (40.7%)	6 (42.9%)	5 (38.5%)	--	0.82
White	16 (59.3%)	8 (57.1%)	8 (61.5%)		
Age (years)	44.5 ± 10.5	42.8 ± 12.5	46.3 ± 7.8	0.34 (−0.43, 1.09)	0.39
Objective binge episodes per week[a]	3.8 ± 2.7	2.8 ± 1.8	4.9 ± 3.1	0.74 (−0.05, 1.52)	0.07
Weight (kg)	106.4 ± 21.4	105.1 ± 23.6	107.7 ± 19.6	0.12 (−0.64, 0.87)	0.76
Height (cm)	169.1 ± 14.2	170.6 ± 10.7	167.6 ± 17.6	−0.21 (−0.96, 0.55)	0.59
BMI (kg/m^2)	37.9 ± 11.8	35.8 ± 5.7	40.1 ± 16.0	0.36 (−0.40, 1.12)	0.36
Waist circumference (cm)	110.8 ± 12.9	110.5 ± 14.5	111.0 ± 11.6	0.04 (−0.72, 0.79)	0.92
Depressed mood (PHQ-9)[b]	6.5 ± 4.8	6.6 ± 5.5	6.3 ± 3.9	−0.06 (−0.83, 0.71)	0.88
Quality of life (Q-LES-Q General)[c]	72.4 ± 13.0	71.7 ± 12.6	73.4 ± 14.0	0.13 (−0.67, 0.92)	0.76
Eating inventory					
Cognitive restraint[c]	7.8 ± 3.5	7.8 ± 3.7	7.8 ± 3.5	0.02 (−0.77, 0.81)	0.96
Disinhibition[c]	13.0 ± 2.8	12.7 ± 3.6	13.3 ± 1.3	0.19 (−0.60, 0.98)	0.64
Hunger[c]	10.0 ± 2.9	8.5 ± 3.0	11.9 ± 0.9	1.47 (0.56, 2.35)	0.001

TABLE 3 Changes from week 0 to week 17 in binge episodes, clinical improvement ratings, anthropometrics and psychosocial functioning in the placebo and liraglutide 3.0 mg groups

Characteristic	Placebo (*N* = 14) Mean ± SE	Liraglutide 3.0 mg (*N* = 13) Mean ± SE	Mean difference (95% CI)	*p*
Objective binge episodes per week[a]	−2.5 ± 0.5	−4.0 ± 0.6	1.2 (−1.3, 2.0)	0.37
CGII	1.9 ± 0.3	1.5 ± 0.3	0.4 (−0.4, 1.2)	0.30
Body weight (kg)	−0.9 ± 0.7	−4.7 ± 0.8	3.7 (1.4, 6.0)	0.003
Percent change in weight	−0.9 ± 0.9	−5.1 ± 1.0	4.2 (1.4, 7.1)	0.005
BMI (kg/m^2)	−0.3 ± 0.4	−1.3 ± 0.4	1.0 (−0.2, 2.2)	0.10
Waist circumference (cm)	−1.2 ± 0.9	−4.0 ± 1.1	2.8 (−0.1, 5.8)	0.06
Depression (PHQ-9)	−3.4 ± 1.0	−3.7 ± 1.1	0.3 (−2.7, 3.4)	0.83
Quality of life (Q-LES-Q-General)	5.1 ± 2.9	4.5 ± 3.3	0.6 (−8.4, 9.7)	0.89
Eating inventory				
Cognitive restraint	1.9 ± 1.0	3.0 ± 1.0	1.2 (−1.8, 4.1)	0.38
Disinhibition	−1.6 ± 0.7	−2.6 ± 0.8	1.0 (−1.0, 2.9)	0.25
Hunger	−2.1 ± 1.0	−2.7 ± 1.0	0.6 (−2.3, 3.4)	0.58

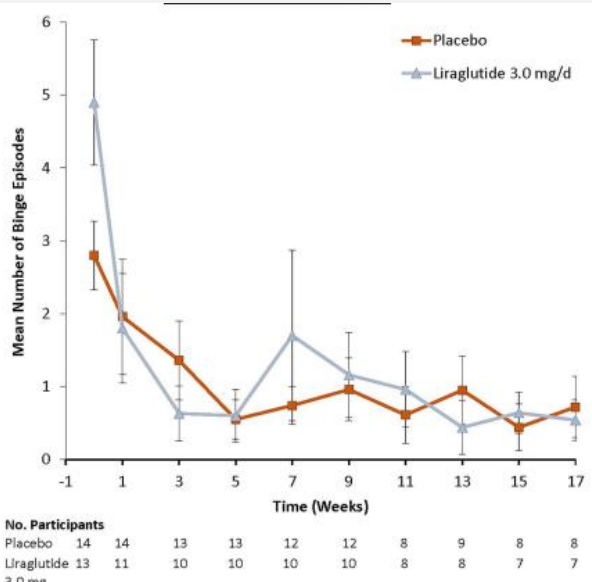


FIGURE 2 Observed mean (SE) number of binge episodes per week in the liraglutide 3.0 mg and placebo groups by treatment week

ANALOGUES DU GLP1 ET TCA (BED)

Hanieh Radkhah, The impact of glucagon-like peptide-1 (GLP-1) agonists in the treatment of eating disorders: a systematic review and meta-analysis, Eating and Weight Disorders - Studies on Anorexia, Bulimia and Obesity (2025)

Table 1 Description of the studies

First author, year	Type of study	Intervention/ control	Female %	Age	Number for intervention/ control	Duration of intervention	Weight change (Kg)	BMI change (Kg/m2)	WC change (cm)	BES score change
Allison et al. 2023	Randomized double-blind controlled trial	Liraglutide (3 mg)	46.1%	46.3 ± 7.8	(*n* = 13/7 completed)	17 weeks	−4.7 ± 2.88	−1.3 ± 1.44	−4 ± 3.97	NR
		Placebo	78.5%	42.8 ± 12.5	(*n* = 14/7 completed)		−0.9 ± 2.62	−0.3 ± 1.49	−1.2 ± 3.67	NR
Richard et al. 2023	Open-label retrospective cohort study	Semaglutide	89.4%	43.5 [13.6, 22–74]	*n* = 19	Average of change in 180 days	−10.2 ± 6.48	NR	NR	−14 ± 8.2
		alternative anti-obesity medications but not receiving semaglutide	87.5%	39.6 [12.8, 21–67]	*n* = 16		−13.2 [20.1, −23.54–67.1]	NR	NR	−5.9 ± 9.1
Lanius et al. 2022	Abstract, trial	Metformin and liraglutide 1.8 mg daily -12 weeks	NR		*n* = 8	12 weeks	−4.3 ± 1.3	NR	NR	NR
		Metformin and SGLT-2 inhibitors			*n* = 10		−1.7 ± 0.8	NR	NR	NR
Robert et al. 2015	Randomized, prospective, controlled trial	Liraglutide 1.8 mg daily, exercise and diet	NR		*n* = 21	12 weeks	−4.4 ± 8.59	−1.75 ± 2.12	−3.71 ± 6.2	−10.44 ± 3.19
		Exercise and diet			*n* = 21		−0.76 ± 7.11	−0.76 ± 2.36	−0.25 ± 2.36	−6.15 ± 3.55
Da Porto et al. 2020	Pilot open-label, prospective controlled study	Dulaglutide	47.7%	54,2 ± 8,9	*n* = 30	12 weeks	−4.53 ± 2.17	−1.65 ± 0.81	NR	−11.93 ± 7.11
		Gliclazide	60%	55,1 ± 6,433	*n* = 30		0.49 ± 1.91	0.1 ± 0.77	NR	0.3 ± 3.23

BED: Binge eating disorder; BES: Binge eating scale

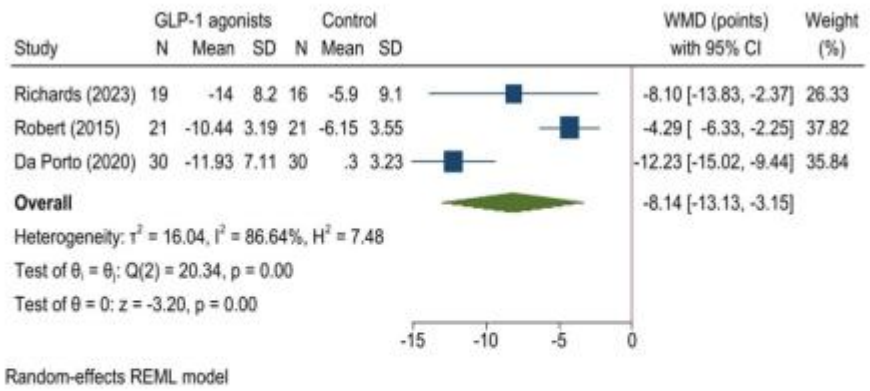


Fig. 5 Forest plot for analysis comparing the BES score (points) in patients with BED administrated with GLP-1 agonist (GLP-1 agonist) to controls (control) at follow-up. This forest plot presents the weighted mean difference (WMD) with 95% confidence intervals (CI) for BES score (points) in patients with BED administrated with GLP-1 agonist (GLP-1 agonist) compared to controls (control). Each study's sample size (N), mean, and standard deviation (SD) for treatment and control groups are shown. The diamond shapes represent pooled estimates, with the overall effect size at the bottom. Heterogeneity statistics and *p*-values are also provided

Avis n° 32 du GT

Il existe encore très peu de données sur l'utilisation des TMO chez les patients en situation d'obésité présentant une hyperphagie boulimique :

- **les TMO ne sont pas contre indiqués dans l'HB**, mais une prise en charge spécialisée de l'hyperphagie boulimique doit être débutée avant de se questionner sur l'initiation d'un TMO pour la prise en charge de l'obésité **(AE)**,
- **le TMO n'est pas un traitement de l'hyperphagie boulimique.** Les TMO actuels (aRGLP1 et aRGIP/GLP1) **pourraient toutefois** avoir un effet bénéfique en limitant la fréquence/sévérité des crises d'hyperphagie chez les patients en situation d'obésité présentant une hyperphagie boulimique **(AE)**.

ANALOGUES DU GLP1 ET ADDICTION OH

Scheen AJ. Glucagon-like peptide-1 receptor agonists and alcohol use disorders: An emerging unexpected beneficial effect. Diabetes Obes Metab. 2025;

- Données favorables chez les rongeurs/primates : diminution activation système mésolimbique dopaminergique > diminution prise d'alcool
- Données observationnelles chez l'homme
  - > diminution 35 % incidence ou récurrence AUD
  - > Population obese/DT2
  - > Effet semblerait indépendant du BMI
  - > ≠ chirurgie bariatrique
  - > une étude rétrospective : diminution de survenue d'une hépatopathie OH ou diminution aggravation si préexistence
- Peu d'études interventionnelles randomisées mais vont dans le même sens
- données génétiques/imagerie cérébrale fonctionnelle: pistes d'explications

TABLE 1 Decreased alcohol use disorders with glucagon-like peptide-1 receptor agonists in observational studies (only studies that included >1000 patients were considered in this table).

References	Country	Study type	Data collection	GLP-1RA	Patients	Prior AUD (n patients)	Follow-up (years)	Risk of AUD on treatment	Alcohol outcomes
Wium-Andersen et al. 2022[34]	Denmark	Nationwide cohort study	Danish National Prescription Registry	GLP-1RAs vs. DPP-4is	T2DM/ Obesity	Mainly No (5.3% with AUD) (38 454)	1	0.62 (0.45–0.85)	Alcohol-related events
Wang et al. 2024[35]	U.S.	Retrospective cohort	Electronic health record data	Semaglutide vs. anti-obesity agents (naltrexone or topiramate) (PSM)	Obesity	No (26 566)	1	0.50 (0.39–0.63)	Incidence of AUD diagnosis
					Obesity	Yes (1051)	1	0.44 (0.38–0.52)	Recurrence of AUD diagnosis
					T2DM	No (25 670)	1	0.56 (0.43–0.74)	Incidence of AUD diagnosis
					T2DM	Yes (653)	1	0.61 (0.50–0.75)	Recurrence of AUD diagnosis
Qeadan et al. 2024[36]	U.S.	Retrospective cohort	Electronic health record data	GLP-1RA or tirzepatide vs. usual care	T2DM	Yes (NA)	2	0.51 (0.40–0.65)	Alcohol intoxication
					Obesity	Yes (NA)	2	0.58 (0.45–0.75)	
Lahteenvuo et al. 2024[37]	Sweden	Retrospective cohort	Population registry	Semaglutide vs. no use of GLP-1RA	Obesity/ T2DM	Yes (4321)	8.8	0.64 (0.50–0.83)	AUD hospitalisation
				Liraglutide vs. no use of GLP-1RA	Obesity/ T2DM	Yes (2509)	8.8	0.72 (0.57–0.92) (†)	
Miller-Matero et al. 2024[38]	U.S.	Retrospective cohort	WeightWatchers Clinic telehealth medical weight management programme	Semaglutide or tirzepatide vs. metformin	Obesity	Both (12 116)	0.6	0.84 (0.65–1.10)	Self-reported alcohol use
Xie et al. 2025[39]	U.S.	Retrospective	US Department of Veterans Affairs database	GLP-1RA vs. usual care	T2DM	Both (215 970)	3.7	0.89 (0.86–0.92)	AUD
Kuo et al. 2025[40]	U.S.	Retrospective	TriNetX Research Network	GLP-1 RA vs. DPP-4is (PSM)	T2DM	Yes (3566)	5.3	0.89 (0.81–0.98)	Alcohol-related liver disease

Note: Results are expressed as hazard ratio (± 95% confidence interval).
Abbreviations: AUD, alcohol use disorder; DDP-4is, dipeptidyl peptidase-4 inhibitors; GLP-1RAs, glucagon-like peptide-1 receptor agonists; NA, not available; PSM, propensity score matching; T2DM, type 2 diabetes mellitus.

CONCLUSION

CONCLUSION

- Risque cardio métabolique et obésité: ++++ en population avec maladie psychiatrique
- Facteurs:
  - Physiopathologie
  - Traitements
- Prise en charge:
  - RHD
  - Place metformin et a-GLP1