Medicines Adverse Reactions Committee

Meeting date	10/09/2026	Agenda item	3.2.1
Title	**GLP-1 receptor agonists and suicidality**		
Submitted by	Medsafe Pharmacovigilance Team	Paper type	For advice

Active ingredient	**Product name (therapeutic area)**	**Registration status**	**Sponsor**
dulaglutide	Trulicity (T2DM)	Marketed	Eli Lilly
liraglutide	Saxenda (weight)	Marketed	Novo Nordisk
	Victoza (T2DM)	Marketed	Novo Nordisk
	Benedo (weight)	Not marketed	CARSL Consulting
	Liraglutide RBX (weight)	Not marketed	CARSL Consulting
	Liraglutide SUN (weight)	Not marketed	CARSL Consulting
semaglutide	Wegovy (weight)	Marketed	Novo Nordisk
	Ozempic (T2DM)	Not marketed	Novo Nordisk
tirzepatide	Mounjaro (T2DM, weight)	Marketed	Eli Lilly

Pharmac funding	Trulicity and Victoza are funded by Pharmac
Usage data	Approximately 25,000 New Zealanders received a Pharmac-funded GLP-1 medicine in 2024. [redacted]
Previous MARC meetings	Not previously discussed
International action	TGA requiring a warning on suicidality (Dec 2025) US FDA requiring removal of warning on suicidality (Jan 2026)
Classification	Prescription medicine
Advice sought	**The Committee is asked to advise:** • On the strength of the evidence for a potential association between the use of GLP-1 medicines and the risk of suicidality. • Whether the GLP-1 NZ data sheets should contain a warning on the risk of suicidality.

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1 PURPOSE

GLP-1 receptor agonists are indicated for type 2 diabetes and weight management. In recent years, concerns about the risk of suicidality with the use of these medicines have been raised. There are many published studies evaluating this risk. In addition, regulatory agencies such as the European Medicines Agency (EMA), Australia's Therapeutic Goods Administration (TGA), and United States Food and Drug Administration (US FDA) have reviewed this safety concern.

The conclusions or review outcomes from the published studies and regulatory agencies are not always aligned. Meta-analyses suggest there is no statistically significant association between suicidality and GLP-1 medicines. The EMA's 2024 review found insufficient evidence of a causal association. Then in December 2025 the TGA required a warning in all GLP-1 Australian data sheets on psychiatric disorders, including suicidal behaviour ideation. And subsequently, the US FDA announced in January 2026 that they are asking companies to remove information on suicidal ideation and behaviour from the GLP-1 US data sheets.

The purpose of this paper is to review whether the use of GLP-1 medicines (dulaglutide, liraglutide, semaglutide, tirzepatide) is associated with an increased risk of suicidality. The term 'suicidality' has been used in this paper as an overall term that includes suicidal thoughts, suicidal behaviour, suicidal ideation, suicide, self-harm, self-injurious behaviour etc.

2 BACKGROUND

2.1 GLP-1 receptor agonists

2.1.1 Products, indication, dose

Glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) are incretin hormones secreted in the intestines in response to food intake [1]. Both hormones promote glucose-dependent insulin release [1]. GLP-1 also delays gastric emptying and improves satiety [2].

GLP-1 receptor agonists bind to and activate the GLP-1 receptor. Those that are currently approved for use in New Zealand include dulaglutide, liraglutide, and semaglutide, which are all administered subcutaneously. The approvals for exenatide and lixisenatide have lapsed in New Zealand. An oral form of semaglutide is approved in other countries but not in New Zealand.

Tirzepatide is a dual GLP-1 and GIP receptor agonist.

Table 1 shows the GLP-1 medicines that are currently approved for use in New Zealand along with their therapeutic area (T2DM or weight) and maintenance doses in adults.

The NZF states for blood-glucose lowering in patients with T2DM, metformin is the recommended first-line treatment. An SGLT-2 inhibitor or GLP-1 can be used if metformin is contraindicated. If none of these options are appropriate, affordable or tolerated, a DPP-4 inhibitor may be used. Sulfonylureas are the 3rd or 4th line treatment option.

For the treatment of obesity, medicinal treatments include GLP-1s, pancreatic lipase inhibitors (eg, orlistat (Xenical)), and centrally acting appetite suppressants (eg, phentermine (Duromine), naltrexone + bupropion (Contrave)).

Comments:

GLP-1 receptor agonists are shortened to 'GLP-1s' in this report. Although tirzepatide is a dual GLP-1 and GIP receptor agonist, it is included in the term 'GLP-1s' throughout unless otherwise stated.

For liraglutide and semaglutide, higher doses are used for weight management compared to doses for T2DM.

Table 1: GLP-1 medicines approved for use in New Zealand

Substance	Brand name	Therapeutic area	Adult maintenance dose
dulaglutide	Trulicity	T2DM	1.5 mg once weekly
liraglutide	Victoza	T2DM	1.2 or 1.8 mg daily
	Saxenda	weight	3.0 mg daily
	Benedo	weight	
	Liraglutide RBX	weight	
	Liraglutide SUN	weight	
semaglutide	Ozempic	T2DM	0.5 or 1 mg once weekly
	Wegovy	weight	2.4 mg once weekly
tirzepatide	Mounjaro	T2DM, weight	5 mg, 10 mg, or 15 mg once weekly

Sources: Medsafe Product/Application search, Medsafe product file, Medicine data sheets, Pharmac community schedule online (extracted 28 Apr 2026 & 3 Aug 2026)

Notes:

- Pharmac-funded medicines are highlighted in green.
- Not all brands are currently marketed in New Zealand.

2.1.2 Usage

The number of New Zealanders who have received an initial dispensing of Pharmac-funded GLP-1 medicines from a community pharmacy is shown in Table 2. From 1 May 2024 to 30 Jun 2025, a shortage of GLP-1 medicines resulted in Pharmac funding for existing patients only.

There is use of Wegovy and Mounjaro on the private market but dispensing and/or sales data is not publicly available. The media reported in Apr 2026 that around 50,000 New Zealanders have been prescribed Wegovy, [redacted]

Table 2: Number of New Zealanders with initial dispensings of Pharmac-funded GLP-1s, by year[1]

Medicine	2021	2022	2023	2024
Trulicity (dulaglutide)[2]	4,489	16,143	24,547	22,611
Victoza (liraglutide)[3]	no data		5,687	3,294

Source: Pharmaceutical data web tool (extracted 28 Apr 2026)

[1] Shortage of GLP-1 medicines from 1 May 2024 to 30 Jun 2025 resulting in Pharmac funding for existing patients only.
[2] Trulicity funded since 1 September 2021, therefore data for 2021 is for 4 months only.
[3] Victoza funded since 1 March 2023.

[redacted]

2.2 Suicidality

The Mental Health Foundation of New Zealand states that suicidality is a term used to refer to thoughts, feelings and actions related to suicide. It includes a range of experiences from occasionally thinking about wanting to die, to making plans to die. Suicidality also includes suicide attempts.

ICD-11 describes suicidal ideation as thoughts, ideas or ruminations about the possibility of ending one's life, ranging from thinking that one would be better off dead to formulation of elaborate plans.

2.2.1 Epidemiology

Every year, around 600 New Zealanders die by suicide [3]. New Zealand's suspected suicide rates by ethnicity and year are shown in Table 3. The most recent data available is for the 2021/22 financial year which shows that the rate of suicides has decreased compared to the four previous financial years [4]. The rates for Māori are higher than for non-Māori. Males are more than twice as likely to die by suicide than females [4].

Table 3: Suspected suicide rates, by ethnicity and financial year

[redacted]

Source: Mental Health Foundation statistics on suicide in New Zealand (accessed 28 Apr 2026)

The age-standardised rates of deaths by suicide per 100,000 inhabitants in OECD countries during 2020 are shown in Figure 1. Out of the 36 OECD countries, New Zealand has the 14th highest rate.

Figure 1: Age-standardised suicide rates per 100,000 inhabitants in OECD countries (2020)

[redacted]

Source: OECD data indicators (accessed 6 Aug 2026)

2.2.2 Risk factors, protective factors [5]

Suicide is not caused by a single factor. A combination of factors at the individual, relationship, community and societal levels can increase or decrease the risk of suicide. The risk factors and protective factors for suicide are shown in Table 4.

Risk factors are situations or problems that can increase the likelihood that a person will attempt suicide. However, they may or may not be direct causes.

Similar to risk factors, a range of factors at the individual, relationship, community and societal levels can protect people from suicide.

Table 4: Suicide risk factors and protective factors

	Risk factors	Protective factors
Individual	Previous suicide attempt History of depression and other mental illnesses Serious illness such as chronic pain Criminal/legal problems Job/financial problems or loss Impulsive or aggressive tendencies Substance use Current or prior history of adverse childhood experiences Sense of hopelessness Violence victimisation and/or perpetration	Effective coping and problem-solving skills Reasons for living (eg, family, friends, pets etc.) Strong sense of cultural identity
Relationship	Bullying Family/loved one's history of suicide Loss of relationships High conflict or violent relationships Social isolation	Support from partners, friends and family Feeling connected to others
Community	Lack of access to healthcare Suicide cluster in the community Stress caused by loss of traditional practices and changing beliefs Community violence Discrimination	Feeling connected to school, community and other social institutions Availability of consistent and high quality physical and behavioural healthcare
Societal	Stigma associated with help-seeking and mental illness Easy access to lethal means of suicide among people at risk Unsafe media portrayals of suicide	Reduced access to lethal means of suicide among people at risk Cultural, religious or moral objections to suicide

Source: Adapted from CDC (https://www.cdc.gov/suicide/risk-factors/index.html)

2.2.3 Association with obesity and T2DM

It is possible that suicidality with GLP-1s is confounded by indication (ie, more commonly reported in people using GLP-1 medicines for weight management than in people with T2DM). However, data on the association between suicidal ideation and obesity is mixed. A 2013 systematic review [6] reported that 8 studies evaluating completed suicide found an inverse relationship between BMI and suicide (ie, obese people are less likely to commit suicide than people of low or normal weight). However, 1 study showed no association and 1 showed a positive association. On the other hand, studies on suicide attempts and ideation found results differed depending on gender: while obese women reported more suicide attempts and ideation, obese men reported fewer attempts and thoughts.

Obesity has been found to be a risk factor for suicidal behaviour. Individuals with obesity often face societal stigma, discrimination, and social exclusion due to poor body image which can lead to low self-esteem and social dysfunction. These societal pressures may exacerbate psychological distress increasing the risk of suicide. Excessive circulating adipokines in obese individuals promote the increased expression of inflammatory mediators [7], potentially contributing to a chronic low-grade inflammatory state. These inflammatory mediators may cross the blood-brain-barrier (BBB) disrupting the metabolism and function of neurotransmitters such as serotonin and dopamine which are essential for emotional and behavioural regulation.

Patients with T2DM exhibit higher rates of depression and suicide compared to the general population [8]. This elevated suicide risk stems from a combination of physiological, psychological, social and nutritional factors [9]. Similar to individuals with obesity, T2DM patients often experience chronic inflammatory states which may contribute to depression and suicidal tendencies.

2.2.4 Association with GLP-1s

Studies have shown that GLP-1 receptors are expressed in regions of the brain that are involved in emotional regulation, such as the hypothalamus and limbic system [10-19]. GLP-1 receptor agonists bind to GLP-1 receptors and could therefore influence affective states through various mechanisms. However, these pathways may not necessarily result in clinically significant behaviours in humans.

3 REVIEW OF THE AVAILABLE INFORMATION

3.1 Regulator reviews

3.1.1 EMA PRAC (Apr 2024)

The PRAC requested all GLP-1 sponsors to provide information for their review on suicidal ideation and self-injurious ideation.

PRAC's evaluation included:

- Results from a cohort study by Wang et al (2024) [20] based on electronic health records from a large database (TriNetX) investigating the incidence of suicidal thoughts in patients with overweight or T2DM treated with semaglutide. The study found no causal association between the use of semaglutide and suicidal thoughts (see section 3.1.1.1 below).
- Results from another real-world cohort study initiated by the EMA [21] based on electronic health records. This study investigated the risk of suicide-related and self-injury-related events comparing T2DM patients treated with either GLP-1s or SGLT-2s. The results did not support a causal association (see section 3.1.1.2 below).

The PRAC concluded (meeting highlight published Apr 2024) there was insufficient evidence of a causal association. However, it cannot be definitively ruled out so PRAC continues to investigate.

Comments:
Since the PRAC's review in 2024, several studies have become available and other regulatory agencies (eg, TGA, US FDA) have also conducted reviews, see below.

3.1.1.1 Wang et al 2024 [20]

Title: Association of semaglutide and risk of suicidal ideation in a real-world cohort

Study design: Retrospective cohort study using electronic health records from the TriNetX Analytics Network (United States) aiming to assess the association of semaglutide with suicidal ideation compared to non-GLP-1 receptor agonist anti-obesity or anti-diabetes medicines.

Methods: Hazard ratios (HR) and 95% confidence intervals (CI) of incident and recurrent suicidal ideation were calculated for the 6-month follow-up by comparing propensity score-matched patient groups.

Results – Overweight or obesity: The study population included 232,771 patients who had no previous history of suicidal ideation. The semaglutide group, compared with non-GLP-1 anti-obesity medicine (bupropion, naltrexone, orlistat, topiramate, phentermine, setmelanotide) group, was older, included more males, had a lower prevalence of adverse socioeconomic determinants, mental health disorders, substance use disorders and higher prevalence of T2DM. After propensity score matching, the two groups were balanced (52,783 patients in each group).

The semaglutide group had a significantly lower risk for incident suicidal ideation than the matched non-GLP-1 anti-obesity medicine group (0.11% vs. 0.43%; HR 0.27, 95% CI 0.20-0.36) (Figure 2). Consistently lower risks were observed in patients stratified by sex, age group, ethnicity and ethnic grouping. No patient reported suicide attempts during the 6-month follow-up in the semaglutide group, whereas 14 of the matched non-GLP-1 anti-obesity medicine group reported suicidal attempts.

The analysis of recurrent suicidal ideation included 7,847 patients who had a previous history of suicidal ideation. The semaglutide group was associated with a significantly lower risk for recurrent experience of suicidal ideation (6.5% vs. 14.1%; HR 0.44, 95% CI 0.32-0.60) (Figure 3). Stratification was not performed due to limited sample sizes. The number of patients who had suicide attempt during the 6-month follow-up in both groups was between 1 and 9 but the actual number was not reported because of privacy.

Figure 2: Incident suicidal ideation in the study population with overweight or obesity



Source: Figure 1 of Wang et al [20]

Figure 3: Recurrent suicidal ideation in the study population with overweight or obesity



Results – T2DM: The study population consisted of 1,572,885 patients with no previous history of suicidal ideation. The semaglutide group compared with the non-GLP-1 anti-diabetes medicine group (insulin, metformin, sulfonylureas, alpha glucosidase inhibitors, thiazolidinediones, DPP-4 inhibitors, SGLT-2 inhibitors) was younger, and had a higher prevalence of overweight and obesity, cancer, chronic pain and mental disorders. After propensity score matching, the two groups (27,726 in each group) were balanced.

The semaglutide group had a significantly lower risk for incident suicidal ideation than the matched non-GLP-1 anti-diabetes medicine group (0.13% vs. 0.36%; HR 0.36, 95% CI 0.25-0.53) (Figure 4). Consistently lower risks were seen in patients stratified according to sex, age subgroup and ethnic grouping. The number of patients who had a suicide attempt during the 6-month follow-up in both groups was between 1 and 9 (actual number not reported due to privacy).

The analysis of recurrent suicidal ideation included 16,970 patients who had a previous history of suicidal ideation. The semaglutide group was associated with a significantly lower risk for recurrent suicidal ideation compared to the matched non-GLP-1 anti-diabetes medicine group (10% vs. 17.9%; HR 0.51, 95% CI 0.31-0.83) (Figure 4). The number of patients who had a suicide attempt during the 6-month follow-up in both groups was between 1 and 9 (actual number not reported due to privacy).

The association for longer follow-ups (1, 2 and 3 years) was also examined. Compared with non-GLP-1 anti-diabetes medicines, semaglutide was associated with a lower risk of incident suicidal ideation at longer follow-ups (Figure 4).

Figure 4: Incident and recurrent suicidal ideation in the study population with T2DM, by follow-up period



Source: Figure 4 of Wang et al [20]

Conclusion: These findings do not support higher risks of suicidal ideation with semaglutide compared with non-GLP-1 receptor agonist anti-obesity or anti-diabetes medicines.

Comments:
This study only included semaglutide. The authors conducted their analysis by indication (weight, T2DM) and non-GLP-1 comparison groups were used.
Their analyses consistently showed that semaglutide had statistically significant lower risks of incident and recurrent suicidal ideation compared to non-GLP-1s.

3.1.1.2 Real-world cohort study [21]

In July 2023, an EMA PRAC review was started to investigate the signal of suicidal ideation and self-injurious ideation after exposure to liraglutide and semaglutide. To support the evaluation of this signal, this real-world study was proposed to assess whether there is an association between exposure to GLP-1 receptor agonists and increased risk of suicide-related and self-harm-related events among patients with T2DM compared to patients who are prescribed SGLT-2 inhibitors.

Study design

This was a comparative cohort design (active comparator, new user design) study that covered 1 Mar 2013 to 1 Jun 2023. The IQVIA™ Medical Research Data (IMRD) UK database was used. New users of GLP-1 receptor agonists or SGLT-2 inhibitors were identified based on the date of first prescription in the database (index date). Patients were eligible if they had no recorded history of suicide-related or self-harm-related events prior to the index date. The primary outcome consisted of a composite endpoint which included the first recorded occurrence of any of the following:

- Suicide-related events including suicidal ideation, attempted suicide, intentional overdose/self-poisoning, completed suicide.
- Self-harm-related events in which intention of self-harm is clearly specified (eg, deliberate self-harm/self-injury, self-inflicted harm, self-injurious behaviour) to differentiate from unintentional/accidental harm.

Participants

Overall, 38,336 patients who were prescribed GLP-1 receptor agonists or SGLT-2 inhibitors were identified. After excluding patients who did not meet the selection criteria or who initiated both study treatments on the same day or had missing data for deprivation index, 6027 patients prescribed GLP-1 receptor agonists and 20,855 patients prescribed SGLT-2 inhibitors were included in the study.

The GLP-1 receptor agonist and SGLT-2 inhibitor cohorts were followed for a median of 3.5 (IQR 1.5-6.2) and 2.0 (IQR 0.8-4.3) years, respectively. A total of 300 incident cases of suicide-related and self-harm related events were identified. The clinical terms which contributed most to the composite endpoint definition were suicidal thoughts (28%), thoughts of suicide or self-harm (26%), suicidal ideation (15%), intentional drug overdose (5%), and thoughts of deliberate self-harm (4%).

Before inverse probability of treatment weighting (IPTW), patients starting GLP-1 receptor agonists were more likely to be female, obese, had a higher prevalence of insulin, sulfonylureas or glitazone use history, and of psychiatric conditions (eg, anxiety, depression) or renal disease, and were less likely to have suffered cardiovascular disease (eg, congestive heart failure, cerebrovascular disease) compared with those starting SGLT-2 inhibitors.

Results – Intention-to-treat (ITT) analysis

The results shown here are for the composite endpoint (including both suicide-related and self-harm-related events).

The unadjusted incidence rate (IR) of the composite endpoint was higher in the GLP-1 receptor agonist cohort than the SGLT-2 inhibitor cohorts with IR 0.50 (95% CI 0.42-0.60) vs. 0.30 (95% CI 0.26-0.35) events per 100 person-years, respectively (Table 5). This difference was attenuated after IPTW adjustment (IR 0.36 (95% CI 0.30-0.44) vs. 0.33 (95% CI 0.29-0.39)).

Table 5: Incidence rates per 100 person-years and hazard ratios for the composite endpoint

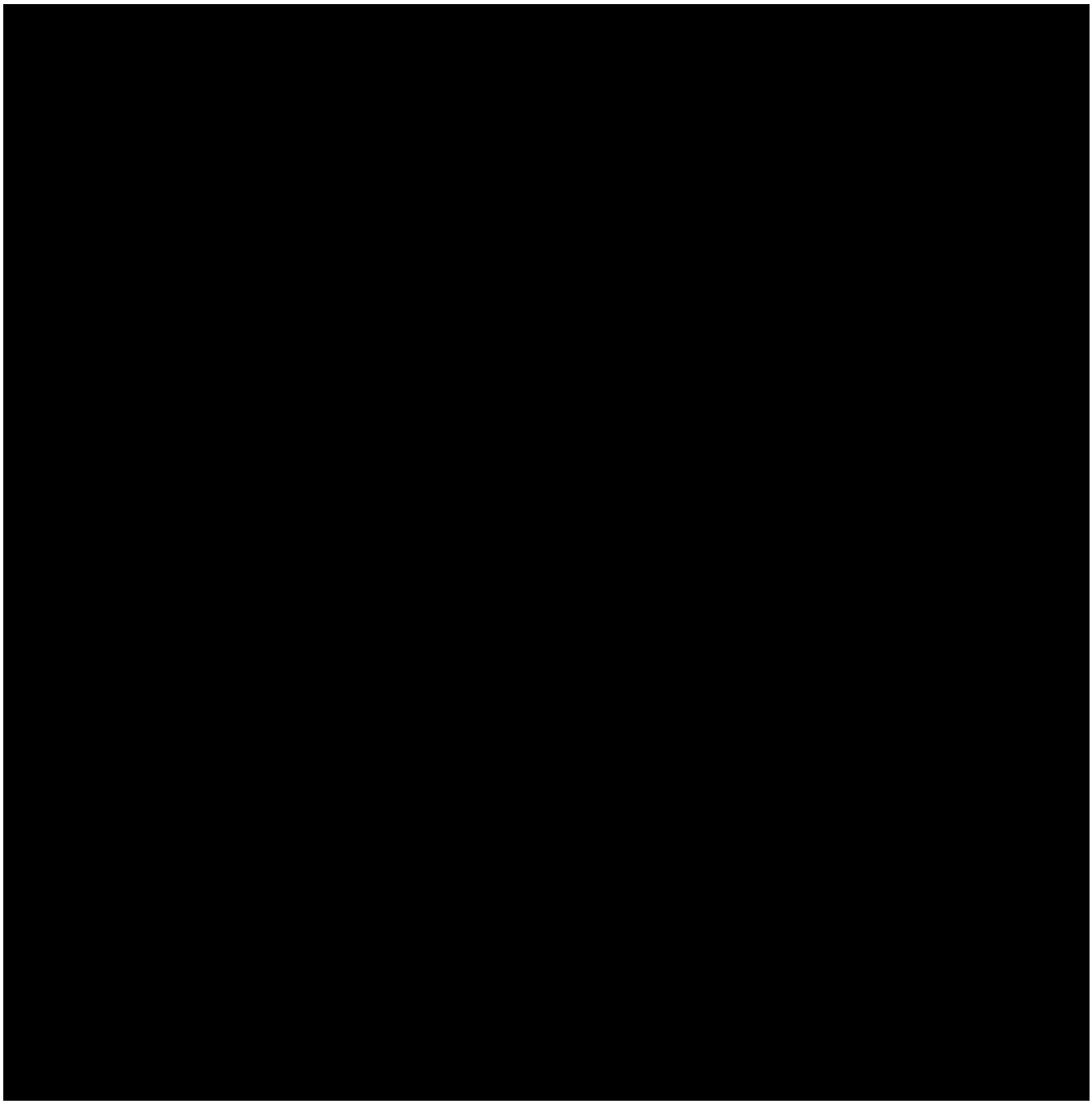


Source: Table 2 of final study report

The unadjusted cumulative incidence of the composite endpoint diverged soon after treatment initiation and throughout the follow-up period (Figure 5a). At 8.8 years of follow-up (around the time of the last outcome events observed in each treatment arm) the unadjusted cumulative incidence was 3.9% (95% CI 3.1-4.8%) for the GLP-1 receptor agonist cohort vs. 3.1% (95% CI 1.8-4.4%) for the SGLT-2 inhibitor cohort. After IPTW adjustment, the cumulative incidence curves overlapped throughout the follow-up period (Figure 5b).

In the unadjusted hazard ratio (HR) analysis, the use of GLP-1 receptor agonists was associated with a 71% increased risk of suicide-related and self-harm related events compared with the use of SGLT-2 inhibitors (HR 1.71, 95% CI 1.35-2.16) (Table 4). However, the HR was substantially attenuated after IPTW adjustment (HR 1.10, 95% CI 0.86-1.41).

Figure 5: Unadjusted (a) and IPTW adjusted (b) cumulative incidence of composite endpoint (ITT)



Source: Figure 2 of final study report

Results – Sensitivity analysis

Suicide-related events only: The composite endpoint consisted largely of suicide-related events (115 of 125 in the GLP-1 cohort). When restricting the outcome definition to suicide-related events only, the unadjusted and IPTW adjusted incidence rates, hazard ratios and cumulative incidence curves were consistent with those for the composite endpoint in the ITT analysis (unadjusted HR: 1.67 (95% CI 1.30-2.13) and IPTW adjusted HR: 1.08 (95% CI 083-1.39) for GLP-1s). The differences in incidence rate, cumulative incidence between the two treatment cohorts, and hazard ratio were also attenuated after IPTW adjustment.

Asymmetric propensity score (PS) trimming: When excluding patients with extreme PS from each treatment cohort, unadjusted and IPTW adjusted results were consistent with the main ITT composite endpoint analysis.

On-treatment (OT) analysis: The results based on the OT analytic approach using the composite outcome were consistent with those for the main ITT composite endpoint analysis and with the results from the trimmed study population analysis. The follow-up time was shorter under OT for both treatment arms compared to the ITT analysis (median of 1.3 vs. 3.5 years for the GLP-1 cohort, median of 1.0 vs. 2.0 years for SGLT-2 cohort). The percentage of patients censored by discontinuing baseline treatment or crossing over was 57% for the GLP-1 cohort and 39% for the SGLT-2 cohort.

Results – Post-hoc analyses

Restricting the population to T2DM patients with obesity: This subpopulation included 5472 patients initiating GLP-1s and 12,815 patients initiating SGLT-2s. A total of 254 incident cases of suicide-related and self-harm related events were identified. In the ITT analysis, the unadjusted risk for the composite endpoint was higher in GLP-1 users compared with SGLT-2 users (0.55 vs. 0.35 events per 100 person-years) corresponding to a HR of 1.66 (95% CI 1.30-2.13). The HR dropped to 1.33 (95% CI 1.02-1.72) after adjusting for confounders. Similarly, the contrast observed between the unadjusted cumulative incidence curves of the 2 treatment arms was attenuated after IPTW adjustment. OT analysis results were consistent with these results.

Restricting the population to those with a history of depression: This subpopulation included 2617 patients initiating GLP-1s and 7370 patients initiating SGLT-2s. A total of 220 incident cases of suicide-related and self-harm related events were identified. In the ITT analysis, the unadjusted risk for the composite endpoint was higher in GLP-1 users compared with SGLT-2 users (0.96 vs. 0.65 events per 100 person-years) corresponding to a HR of 1.52 (95% CI 1.16-2.00). However, the HR dropped to 1.14 (95% CI 0.86-1.52) after adjusting for confounders. Similarly, the contrast observed between the unadjusted cumulative incidence curves of the 2 treatment arms was attenuated after IPTW adjustment. OT analysis results were consistent with these results.

Use of shorter gap periods (ie, 90 days) as a cut-off for treatment discontinuation: When a 90-day period was used in the OT analysis, the unadjusted risk of suicide-related and self-harm related events was higher in GLP-1 users compared to SGLT-2 users (0.53 vs. 0.29 events per 100 person-years) corresponding to a HR of 1.81 (95% CI 1.28-2.56). This HR dropped to 1.24 (95% CI 0.86-1.79) after adjusting for confounders. Similarly, the contrast observed between the unadjusted cumulative incidence curves of the 2 treatment arms was attenuated after IPTW adjustment. Consistent with the main OT analysis which used a 180-day prescription gap, this OT analysis using a shorter 90-day gap showed a marginally numerically higher risk of suicide-related and self-harm related events in the GLP-1 arm (HR 1.24, 95% CI 0.86-1.79 when using a 90-day gap vs. 1.11, 95% CI 0.80-1.56 when using a 180-day gap).

Conclusion

These study results do not support a clinically relevant increased risk of suicide-/self-harm-related events associated with GLP-1s vs. SGLT-2s in T2DM patients. However, further research is needed, and studies for individuals receiving GLP-1s for weight management are of particular interest.

Comments:

The EMA has a centralised repository of real-world data (RWD) sources and studies. The aim is to enhance transparency in RWD research and support regulators, pharmaceutical companies and researchers in identifying and using real-world data to investigate the use, safety and effectiveness of medicines.

This RWD cohort study investigated suicide-related and self-harm-related events in patients with T2DM using GLP-1s vs. SGLT-2s. Patients were followed for a median of 3.5 and 2.0 years, respectively. Patients starting GLP-1s had higher prevalence of psychiatric conditions (anxiety, depression) than SGLT-2s.

In the main intention-to-treat (ITT) analysis, there was a consistent association between GLP-1 initiation and suicide- and self-harm-related events (composite endpoint) compared to SGLT-2 initiation. However, this association was attenuated following adjustment for confounders using an inverse probability of treatment weighting (IPTW) approach.

Results from sensitivity analyses (restricting to suicide-related events only, excluding patients with extreme propensity scores, on-treatment analysis) were consistent with the composite endpoint ITT analysis.

In the post-hoc analyses, restricting the population to obese patients with T2DM found a higher risk of suicide- and self-harm-related events in GLP-1 users in the ITT analysis which was attenuated following IPTW adjustment, with a similar sized but non-significant association in the on-treatment (OT) analysis. No association was observed in either ITT or OT analyses following IPTW adjustment in T2DM patients with prior history of depression.

3.1.2 TGA (Dec 2025)

The TGA requested GLP-1 sponsors to review suicidal ideation and self-injurious ideation.

On 1 December 2025, a medicine safety update article was published to inform the public that the TGA is requiring consistent warnings on the potential risk of suicidal thoughts or behaviours across the GLP-1 Australian data sheets. The following warning was added:

> **Psychiatric disorders**
>
> Suicidal behaviour and ideation have been reported with GLP-1 receptor agonists. Monitor patients for the emergence or worsening of depression, suicidal thoughts or behaviours, and/or any unusual changes in mood or behaviour. Consider the benefits and risks for individual patients prior to initiating or continuing therapy in patients with suicidal thoughts or behaviours or have a history of suicidal attempts.

Comments:

Around the time of the TGA's review, Medsafe also noted that information on suicidality in the GLP-1 NZ data sheets was not consistent, with some containing a warning and others containing no information. This was inconsistent for the individual GLP-1 substance, and also inconsistent by product indication (ie, T2DM vs. weight management).

Medsafe requested sponsors to add the TGA required wording to the GLP-1 data sheets that did not include any information on suicidality (see section 3.3). This is currently on hold following the US FDA's announcement to remove these warnings (see section 3.1.3) and pending the outcome of the MARC's review.

3.1.3 US FDA (Jan 2026)

In January 2024, the FDA published a communication to say their preliminary evaluation does not suggest a causal link between suicidal thoughts or actions and GLP-1 medicines. Their review was completed in March 2024 and concluded that a clear relationship was not demonstrated. The US labels for GLP-1s used for weight management already contain information on the risk of suicidal thoughts and actions, which is consistent for other weight loss medicines. However, because of the small number of suicidal thoughts or actions observed in both people using GLP-1s and the comparative groups, the FDA could not definitively rule out that a small risk may exist. Therefore, the FDA would continue monitoring this issue.

Finally in January 2026, the FDA announced they are requesting sponsors to remove information on suicidal ideation and behaviour from labelling of GLP-1 medicines. This action follows a comprehensive FDA review that found no increased risk.

- FDA's initial review of clinical trial data did not find an association between the use of GLP-1s and suicidal ideation. However, because of the small number of cases observed in individual trials, there was considerable uncertainty in the risk estimate. To address this, FDA performed a comprehensive meta-analysis of clinical trials across the GLP-1 drug development programs. The meta-analysis assessed the risk by comparing GLP-1s vs. placebo. There were 91 placebo-controlled trials that included 107,910 patients

(60,338 treated with GLP-1; 47,572 treated with placebo). The results did not show an increased risk of suicidal ideation or for other relevant psychiatric adverse events such as anxiety, depression, irritability, or psychosis. Results from this meta-analysis are not yet published.

- FDA conducted a retrospective cohort study using administrative healthcare claims data from the Sentinel System to compare the risk between new users of GLP-1s and SGLT-2s in patients with T2DM [22] (see section 3.1.3.1 below). The study population included 2,243,138 users (1,161,983 initiated on GLP-1 and 1,081,155 initiated on a SGLT-2) from 10 data partners during 1 Oct 2015 and 20 Sep 2023. After controlling for baseline confounders, FDA did not find an increased risk of intentional self-harm in GLP-1 users compared to SGLT-2 users. Similarly, FDA did not find an increased risk in the subgroup of patients with both T2DM and obesity.
- FDA also reviewed published observational and pooled studies evaluating the relationship between GLP-1s and suicidal ideation including related outcomes. FDA concluded the totality of these studies does not support a causal relationship between the use of GLP-1s and occurrence of suicidal ideation.

3.1.3.1 Kuzucan et al 2026 [22]

Title: Association of GLP-1 receptor agonists with intentional self-harm in patients with type 2 diabetes: a Sentinel distributed database study

Methods: An active-comparator, new-user cohort study using the FDA's Sentinel System with data from 1 Oct 2015 to 30 Sep 2023. The study included health plan members aged ≥18 years diagnosed with T2DM, newly initiated on GLP-1s (albiglutide, dulaglutide, exenatide, liraglutide, lixisenatide, semaglutide, tirzepatide), SGLT-2s (bexagliflozin, canagliflozin, dapagliflozin, empagliflozin, ertugliflozin, sotagliflozin), or DPP-4s (alogliptin, linagliptin, saxagliptin, sitagliptin) and continuously enrolled in a health plan with medical and drug coverage for ≥183 days.

The main outcome was intentional self-harm rather than suicidal ideation/behaviour because of the known inadequacies of claims data to capture suicidal intent. Inverse probability of treatment weighting (IPTW) of propensity scores was used to control for confounding.

Results: The study included 1,161,983 patients in the GLP-1 group, 1,081,155 in the SGLT-2 group, and 1,396,382 in the DPP-4 group. The mean age was slightly above 60 years. Adjusted incidence rates of intentional self-harm per 1000 person-years were 1.13 for GLP-1s, 1.22 for SGLT-2s, and 1.37 for DPP-4s.

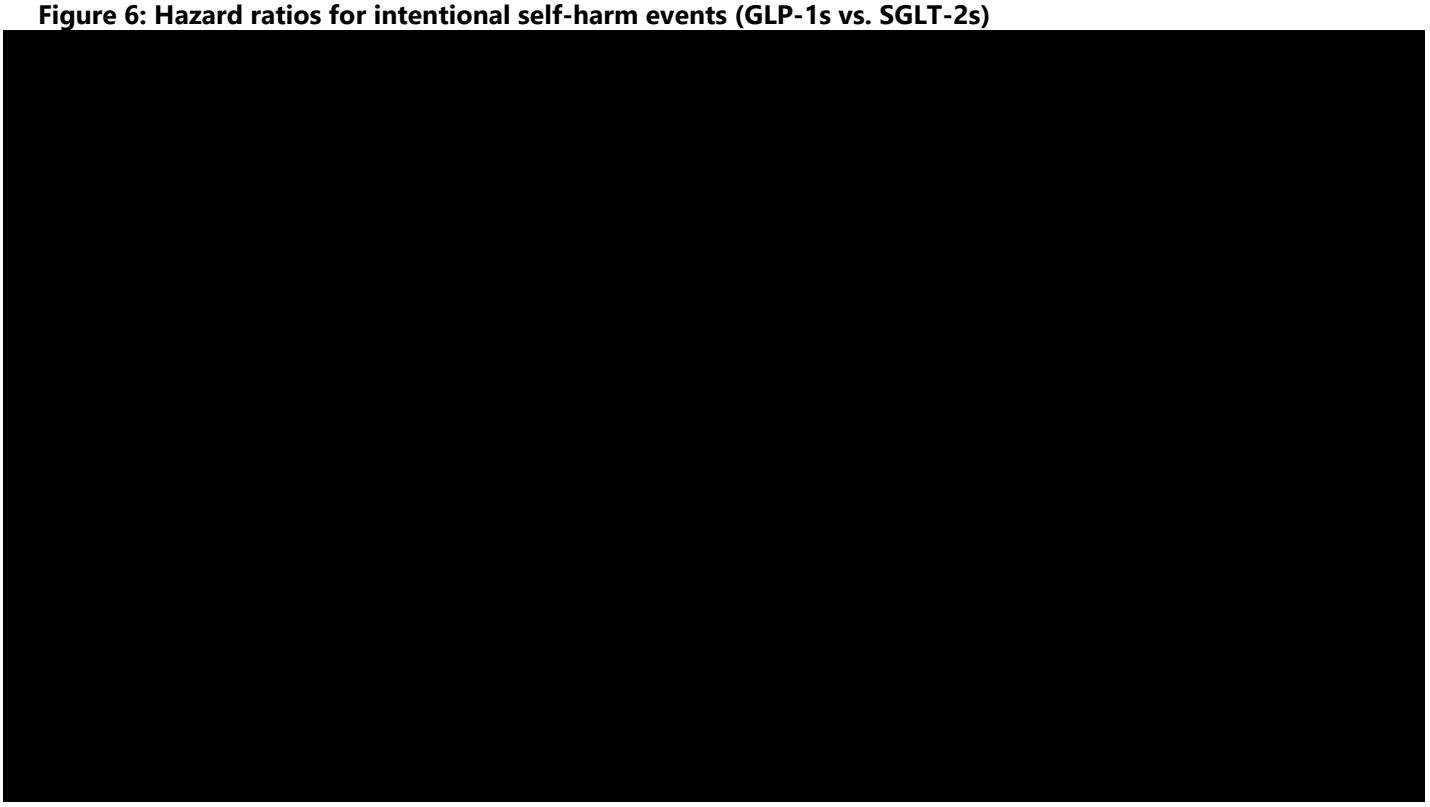
Adjusted HRs indicated no increased risk of intentional self-harm comparing GLP-1s to SGLT-2s (HR 0.93, 95% CI 0.81 to 1.08) or DPP-4s (HR 0.94, 95% CI 0.82 to 1.07).

Subgroup HR estimates comparing GLP-1 users to SGLT-2 users ranged from 0.64 to 1.10 with 95% CIs that included the null (Figure 6). For both GLP-1 and SGLT-2 users: (1) those with psychiatric history showed a higher IR compared with those with no psychiatric history; (2) those with prior intentional self-harm events showed a higher IR compared with those with no prior intentional self-harm; (3) females showed a higher IR compared with males, and (4) younger age generally showed a higher IR. Sensitivity analyses with varying IPTW truncation thresholds, outcome definitions, and exposure definitions resulted in HRs close to 1.0 with 95% CIs that included 1.0 (Figure 6).

Subgroup and sensitivity analyses of GLP-1s vs. DPP-4s resulted in HRs that were either close to 1.0 or had a 95% CI that included 1.0 (Figure 7).

Conclusions: The use of GLP-1s did not show increased risk of intentional self-harm compared with SGLT-2s or DPP-4s, which provides some reassurance on the safety of GLP-1 use in patients with T2DM.

Figure 6: Hazard ratios for intentional self-harm events (GLP-1s vs. SGLT-2s)



Source: Figure 2 of Kuzucan et al 2026 [22].

Notes: IPTW adjusted analysis included 1% truncation and average treatment effect stabilisation. [a] Incidence rate: number of events per 1000 person-years; hazard ratio estimates plotted on the natural log scale. [b] Analyses were conducted in a subset of data where Sentinel Data Partners had at least one event in each subgroup. ED, emergency department; IP, inpatient; IPTW, inverse probability of treatment weight.

Figure 7: Hazard ratios for intentional self-harm events (GLP-1s vs. DPP-4s)



Source: Figure of Kuzucan et al 2026 [22].

Notes: IPTW adjusted analysis included 1% truncation and average treatment effect stabilisation. [a] Incidence rate: number of events per 1000 person-years; hazard ratio estimates plotted on the natural log scale. [b] Analyses were conducted in a subset of data where Sentinel Data Partners had at least one event in each subgroup. IPTW, inverse probability of treatment weight.

Comments:

The study using data from FDA's Sentinel System compared the rates of intentional self-harm in patients with T2DM newly initiated on GLP-1s, SGLT-2s or DPP-4s.

For the comparison of GLP-1s vs. SGLT-2s, the unadjusted HR was statistically significant (1.38, 95% CI 1.25 to 1.54) but was no longer statistically significant following IPTW adjustment (0.93, 95% CI 0.81 to 1.08).

A similar situation occurred when GLP-1s were compared with DPP-4s with a statistically significant unadjusted HR (1.23, 95% CI 1.12 to 1.35) which became non-statistically significant following IPTW adjustment (0.94, 95% CI 0.82 to 1.07).



[redacted]

3.3 NZ data sheets

Information on suicidal ideation in GLP-1 NZ data sheets is shown in Table 6 along with the sponsor's proposed actions. The wording is generally aligned with the TGA's requested wording.

The packaging for GLP-1 medicines, particularly for Novo Nordisk's products, are harmonised between Australia and New Zealand – for products supplied to New Zealand, the Australian product information is used as the pack insert which currently includes the TGA-required warning.

Table 6: Information on psychiatric disorders, including suicidal ideation in GLP-1 NZ data sheets

GLP-1 medicine	Suicidality warning
Ozempic (semaglutide)	Psychiatric disorders Suicidal behaviour and ideation have been reported with GLP-1 receptor agonists. Monitor patients for the emergence or worsening of depression, suicidal thoughts or behaviours, and/or any unusual changes in mood or behaviour. Consider the benefits and risks for individual patients prior to initiating or continuing therapy in patients with suicidal thoughts or behaviours or have a history of suicidal attempts.
Wegovy (semaglutide)	No information
Victoza (liraglutide)	No information
Saxenda (liraglutide)	Suicide behaviour and ideation Patients treated with SAXENDA should be monitored for the emergence of depression, suicide thoughts or behaviour, or any unusual changes in mood or behaviour. Discontinue SAXENDA in patients who experience suicidal thoughts or behaviours or who develop other symptoms of depression [see Section 4.8]. Patients with a history of major depressive disorder or other major psychiatric disorder were excluded from the SAXENDA clinical trials. Because of the lack of data on efficacy and safety in patients with a history of major depressive disorder or other major psychiatric disorder, SAXENDA is not recommended in these patients.
Benedo (liraglutide) Liraglutide RBX Liraglutide SUN	As for Saxenda
Trulicity (dulaglutide)	Psychiatric disorders Suicidal behaviour and ideation have been reported with GLP-1 receptor agonists. Monitor patients for the emergence or worsening of depression, suicidal thoughts or behaviours, and/or any unusual changes in mood or behaviour. Consider the benefits and risks for individual patients prior to initiating or continuing therapy in patients with suicidal thoughts or behaviours or have a history of suicidal attempts.
Mounjaro (tirzepatide)	Psychiatric disorders Suicidal behaviour and ideation have been reported with GLP-1 receptor agonists. Monitor patients for the emergence or worsening of depression, suicidal thoughts or behaviours, and/or any unusual changes in mood or behaviour. Consider the benefits and risks for individual patients prior to initiating or continuing therapy in patients with suicidal thoughts or behaviours or have a history of suicidal attempts.

3.4 Spontaneous reports

3.4.1 New Zealand cases

Up to 4 August 2026, there are 6 cases of suicide/self-injury-related terms reporting a GLP-1 as the suspect medicine in the NZ pharmacovigilance database. An overview of these 6 cases is shown in Table 7, and a line-listing in Table 8.

All 6 cases were serious, and a GLP-1 medicine was the only medicine reported in all 6 cases.

Table 7: Overview of suicide/self-injury-related cases with a GLP-1 medicine as the suspect in New Zealand (n=6)

Subgroup	Number
GLP-1 medicine	
liraglutide	3
semaglutide	2
tirzepatide	1
Gender	
Male	2
Female	4
Age	
30-44 years	2
45-59 years	1
60+ years	1
Unknown	2
Median	49 years
Range	39 to 62 years
Ethnicity	
[redacted]	
Time to onset	
[redacted]	
Outcome	
[redacted]	

Source: New Zealand pharmacovigilance database (data extracted via Qlik app)
Notes:

- Data last updated 4 Aug 2026
- Search criteria: MedDRA SMQ Suicide/self-injury + ATC A10BJ + ATC A10BX

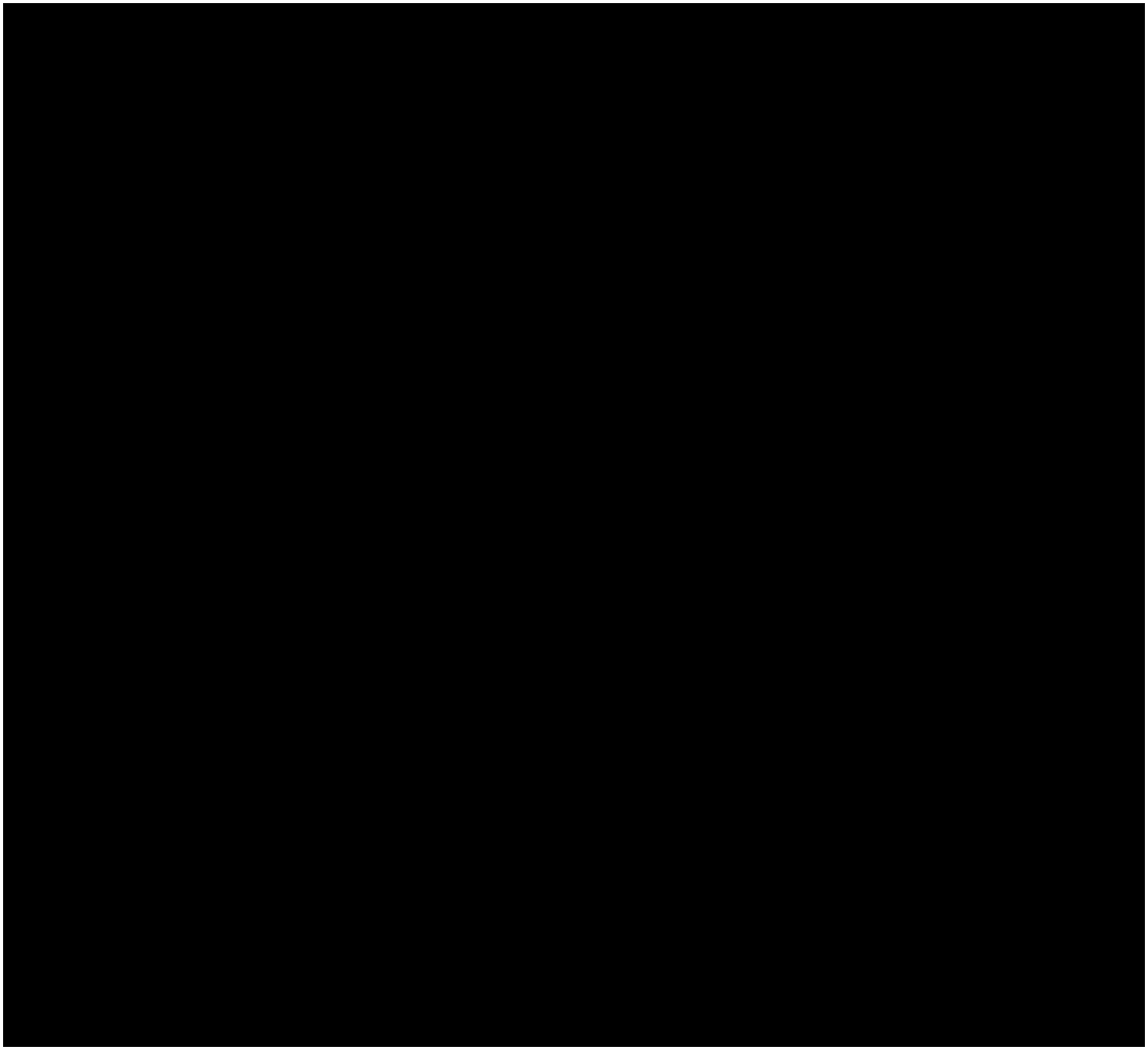
Table 8: Line-listing of suicide/self-injury-related cases with a GLP-1 medicine as the suspect

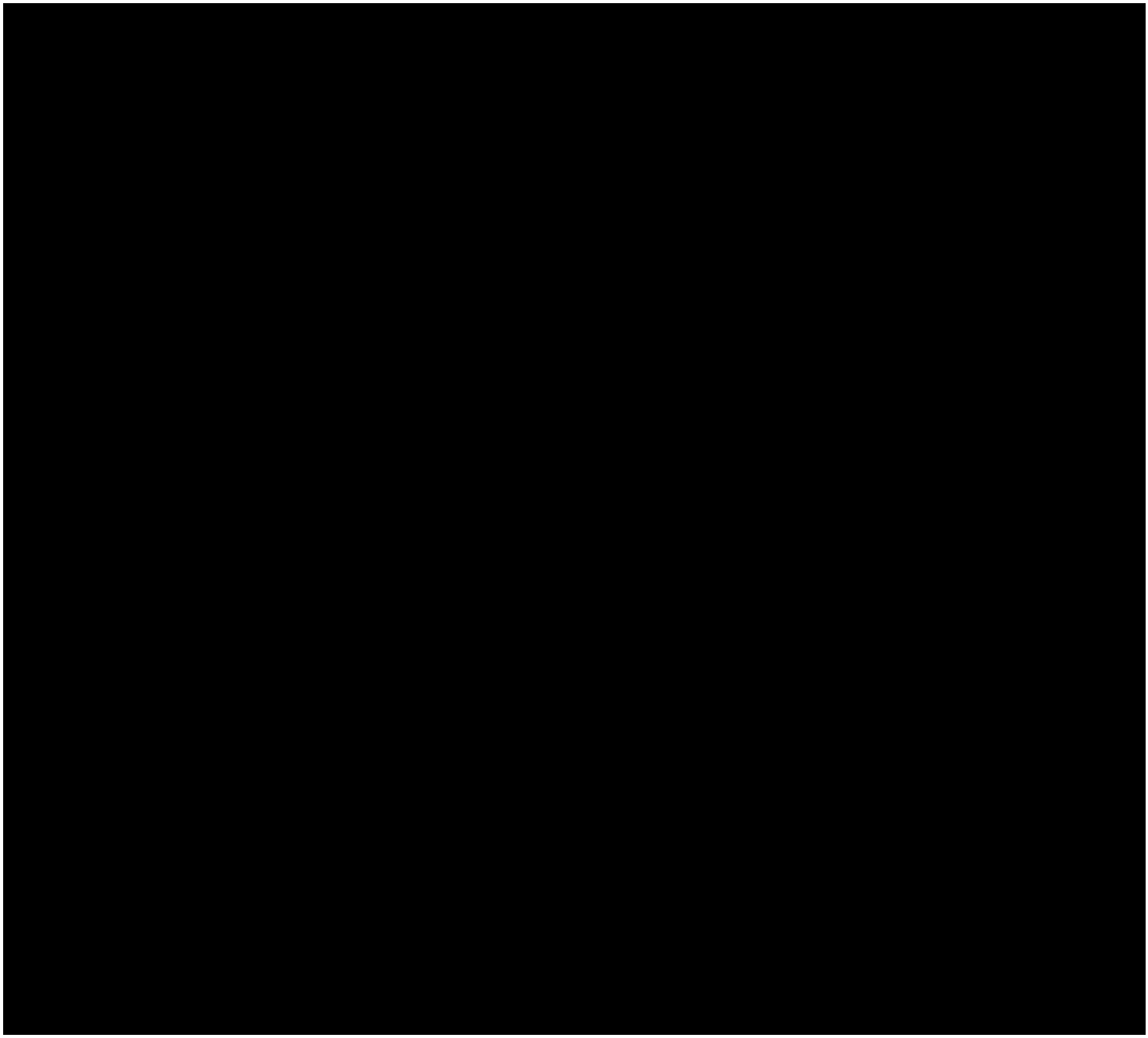
Report ID	Date	Age	Sex	Medicine	Reactions(s)	Notes
161338	Mar 2025	-	M	Saxenda (liraglutide)	suicidal ideation, violent thoughts	[redacted]
161342	Mar 2025	39	M	Saxenda (liraglutide)	intrusive thoughts, thoughts of self-harm	
161856	Apr 2025	-	F	Saxenda (liraglutide)	suicidal ideation	
167224	Apr 2026	39	F	semaglutide	suicidal ideation, anhedonia	
167441	May 2026	62	F	semaglutide	suicidal ideation	
167792	Jun 2026	58	F	Mounjaro (tirzepatide)	suicidal ideation, anxiety	

Source: NZ pharmacovigilance database (data extracted via Qlik app)
Notes:

- Data last updated 4 Aug 2026
- Search criteria: MedDRA SMQ Suicide/self-injury + ATC A10BJ + ATC A10BX

3.4.2 International cases





4 META-ANALYSES & SYSTEMATIC REVIEWS

A search of PubMed using (glp) AND (suicid*) was conducted on 20 Jul 2026 and retrieved 123 results. These were manually reviewed for relevant articles.

Meta-analyses and systematic reviews are summarised below in sections 4.1 and 4.2.

There were also individual studies retrieved using observational methods (eg, cohort studies of large datasets like the TriNetX, UK CPRD) and those using pharmacovigilance methods (eg, disproportionality analyses of US FAERS, VigiBase) many of which were included in the meta-analyses and systematic reviews.

4.1 Meta-analyses (+/- systematic reviews)

4.1.1 Alansari et al 2025 [23]

Title: Assessing the shadows: A meta-analysis of GLP-1 agonists and suicidal ideation

Methods: Eligible studies were RCTs and observational studies. A search of 6 databases up to Oct 2024 identified 354 studies, of which 23 were eligible and 12 were included in the final meta-analysis. All included studies were of medium/good quality based on the Newcastle Ottawa Scale risk of bias.

Results – Suicidal ideation: A total of 5 studies were included (510,962 patients with 1399 events). No significant statistical difference in suicidal ideation in patients on GLP-1s compared to other obesity and diabetes medicines (OR 1.0, 95% CI 1.0-1.0) (Figure 8). Significant heterogeneity was observed.

Figure 8: Suicidal ideation among patients on GLP-1s and controls



Source: Figure 2 of Alansari et al [23]

Results – Suicide: A total of 4 studies assessed completed suicide. No significant difference observed between patients on GLP-1s and other comparable medicines for completed suicide (OR 1.77, 95% CI 0.80-3.91) (Figure 9). Substantial heterogeneity was observed.

Figure 9: Completed suicide among patients on GLP-1s and controls



Results – Subgroup analysis: In a subgroup analysis, suicide was higher among patients on liraglutide vs. semaglutide (OR 1.48, 95% CI 1.17-1.89) with no heterogeneity found (I^2 = 0%, P-value for heterogeneity = 0.47, standard difference = 3). No significant statistical difference observed when comparing tirzepatide and

semaglutide (OR 0.98, 95% CI 0.94-1.03) but significant heterogeneity was observed (I^2 = 90%, P-value for heterogeneity = <0.001, standard difference = 2).

Conclusion: No significant statistical difference was found in suicide, suicidal ideation in patients taking GLP-1 agonist, and other obesity and diabetes medicines. A RCT that assess the association between GLP-1 agonists and suicidality is highly recommended.

Comments:

Eligible studies for this meta-analysis were RCTs and observational studies. 12 studies were included in the final meta-analysis.

No significant statistical difference was found between GLP-1s and other comparable medicines for both suicidal ideation, and complete suicide. In subgroup analyses, suicide was higher among patients on liraglutide compared to semaglutide, and no statistically significant difference between patients using tirzepatide vs. semaglutide.

4.1.2 Bushi et al 2025 [24]

Title: Association of GLP-1 receptor agonists with risk of suicidal ideation and behaviour: A systematic review and meta-analysis

Methods: A search of PubMed, Embase and Web of Science through Sep 2024 to identify observational cohort and case-control studies. 126 studies were identified of which 11 met inclusion criteria for the final systematic review and meta-analysis. Risk of bias was assessed using the Newcastle-Ottawa scale for observational studies and indicated the included studies had a moderate to high quality.

Included studies: The 11 studies had diverse designs: 4 pharmacovigilance analyses, 2 retrospective cohort studies, 1 population-based cohort study, 1 post hoc analysis, 1 case-control study, 1 retrospective observational study, and 1 retrospective European pharmacovigilance study (Table 12).

Various neuropsychiatric outcomes were assessed including suicidal ideation, suicide attempts, suicidal behaviours, and self-injury. Study populations ranged from T2DM patients, overweight/obese adults, and other users of GLP-1s.

Overall, the majority of studies reported no increased risk of suicidality with GLP-1s, and some suggested a lower risk compared with other antihyperglycemic medicines or placebo.

Table 12: Basic characteristics of included studies (n=11)

[redacted]

Source: Table 1 of Bushi et al [24]

Results – Meta-analysis: Of the 11 studies, 4 were eligible for meta-analysis which found no statistically significant difference in suicidal outcomes between GLP-1 users and users of other anti-hyperglycaemic medicines (RR 0.568, 95% CI 0.077-4.205) (Figure 10). Substantial heterogeneity was observed (I^2 = 98%).

Figure 10: Forest plot illustrating the risk of suicidal outcomes with GLP-1s



Source: Figure 2 of Bushi et al [24]

Conclusion: This review found no significant link between GLP-1 use and increased suicidal ideation or behaviour. However, the high heterogeneity and reliance on pharmacovigilance data suggest caution.

Comments:

Eligible studies for this meta-analysis were observational studies, including those using pharmacovigilance datasets. 11 studies were eligible for inclusion of which 4 were included in the meta-analysis.

The meta-analysis found there was no statistically significant difference in suicidal outcomes between GLP-1 users and users of other anti-hyperglycaemics (RR 0.568). However, there was substantial heterogeneity (I^2 = 98%) and the confidence interval was wide (0.077-4.205).

4.1.3 Chen et al 2025 [25]

Title: Impact of GLP-1 receptor agonists on suicide behaviour: A meta-analysis based on randomized controlled trials

Methods: A search of databases including PubMed, Web of Science, Cochrane Library, clinicaltrials.gov up to Oct 2024 for RCTs in participants with T2DM or obesity, intervention with GLP-1 RAs, a comparison group, and outcomes including suicide-related adverse events. Risk of bias was evaluated using the Cochrane collaboration risk of bias tool (CCRBT) for RCTs. Data from 25 RCTs were included in the meta-analysis.

Included RCTs: The 25 RCTs (Table 13) enrolled over 81,000 participants (42,000 assigned to GLP-1 exposure group, 39,000 controls). 20 RCTs involved participants with T2DM, and 5 with obesity. In the control group, T2DM participants received either placebo or other hypoglycaemic agents, while participants with obesity received only placebo. There were 4 studies that included adolescents (<18 years) while the remaining 21 enrolled adults.

All 25 studies were evaluated using CCRBT and met requirements for inclusion in the meta-analysis. Four studies were classified as having a high risk of bias due to lack of blinding for participants and personnel, as a result of non-stratified randomisation. Three studies were deemed to have a high risk of detection bias due to unblinded outcome assessment. Overall, the majority of studies were classified as low risk of bias, and all studies were considered to be of high quality.

Table 13: Characteristics of the 25 RCTs included in the meta-analysis



Results: No significant difference in the incidence of suicidal behaviour between GLP-1s and controls (RR 0.84, 95% CI 0.54-1.32) (Figure 11). Results from subgroup analyses (Table 14) were consistent with the main analysis:

- No significant differences in the incidence of suicidal behaviour among participants with T2DM (RR 0.74), obesity (RR 1.07), adolescents (RR 0.91) and adults (RR 0.84).
- No significant differences between the 2 groups in any type of suicidal behaviour, including suicidal ideation (RR 1.04), suicide attempts (RR 0.68), depression-related suicides (RR 0.65), and completed suicides (RR 1.06).
- No significant differences between the groups for any type of GLP-1 including dulaglutide (RR 0.46), exenatide (RR 0.98), semaglutide (RR 0.82), lixisenatide (RR 1.25), and liraglutide (RR 0.92).
- No significant differences observed between the exposure and control groups according to different comparators including placebo (RR 0.91) and others (RR 1.08).

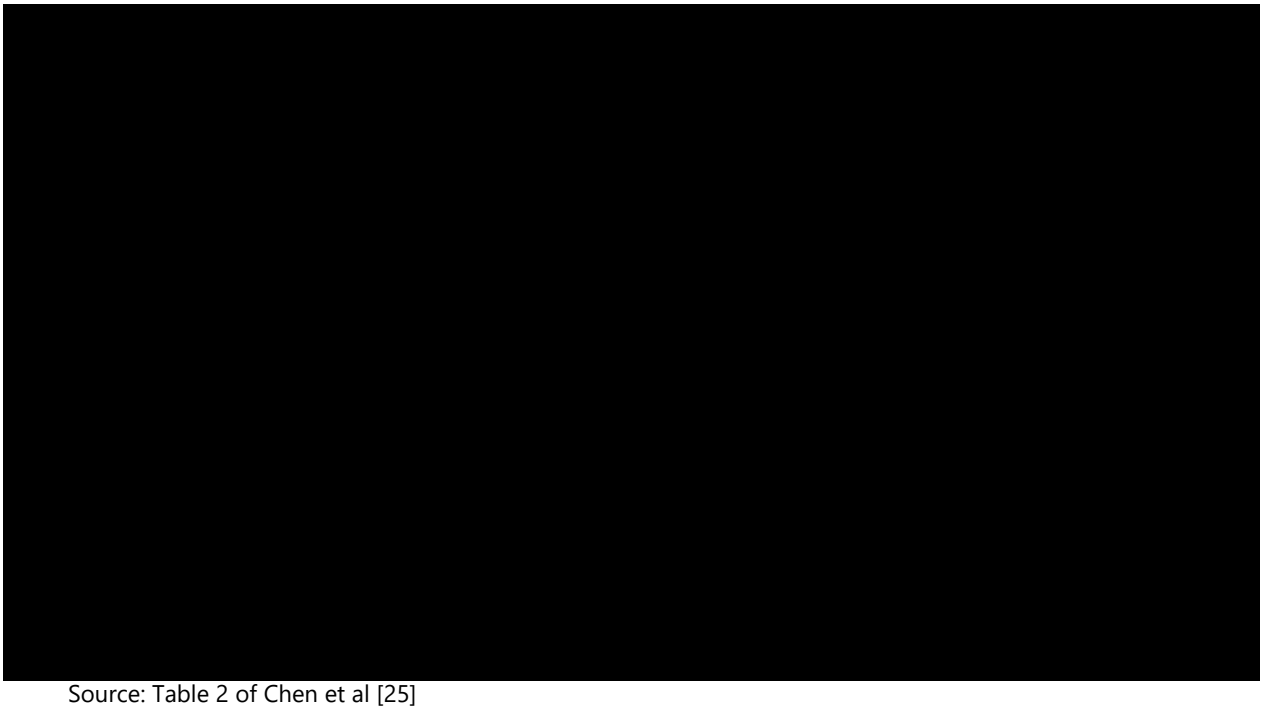
All subgroup analyses showed p-values greater than 0.05 (two-sided tests) and I^2 values of 0%.

Figure 11: Forest plot showing the association between GLP-1s and suicidal behaviour in participants with T2DM or obesity



Source: Figure 2 of Chen et al [25]

Table 14: Subgroup analysis of the association between GLP-1s and suicidal behaviour in participants with T2DM or obesity



Source: Table 2 of Chen et al [25]

Conclusion: These findings suggest there is no significant association between GLP-1s and suicidal behaviours in patients with T2DM or obesity.

Comments:

This meta-analysis included 25 RCTs. Some studies were assessed as high risk of bias mostly due to lack of blinding. However overall, the majority of studies were classified as low risk of bias and all studies were considered to be of high quality.

There was no significant difference in the incidence of suicidal behaviour between GLP-1s and controls (RR 0.84, 95% CI 0.54-1.32) and results from subgroup analyses were consistent with the main analysis.

4.1.4 Choudhury et al 2026 [26]

Title: Effect of glucagon-like-peptide-1 receptor agonists (GLP-1 RA) on neuropsychiatric outcomes: A systematic review and meta-analysis

Methods: A systematic review and meta-analysis of RCTs and observational studies assessing the effect of GLP-1s on neuropsychiatric outcomes. Searches were performed in Medline, Scopus, Central and Web of Science up to Oct 2025. Risk of bias was assessed using Cochrane 'Rob2' for RCTs, and ROBINS-I for observational studies. The GRADE system was used to assess the quality of evidence of each outcome.

A range of neuropsychiatric outcomes were assessed including Parkinson's disease, substance use disorders, suicidal behaviour, anxiety, depression, binge eating disorder, dementia etc.

Included studies: 82 studies met inclusion criteria. Most RCTs were of moderate or serious risk of bias, and the majority of observational studies were of serious or critical risk of bias. Overall, the certainty of evidence across meta-analysed outcomes ranged from very low to moderate. Most outcomes, including Parkinson's disease incidence and symptoms, substance use disorders, suicidality, affective disorders, and dementia were graded as low or very low certainty primarily due to study limitations, heterogeneity and imprecision.

Results: There were 10 studies pooled for the suicidality meta-analysis. In observational studies, compared to non-users controls, GLP-1 use was associated with a lower reported risk of suicidality (pooled OR 0.34, 95% CI 0.18-0.63, I^2 = 99%) (Figure 12), but no such association was seen with semaglutide alone (pooled OR 0.71, 95% CI 0.29-1.73, I^2 = 99%), active-comparator studies (pooled HR 0.96, 95% CI 0.81-1.15, I^2 = 0%) or RCTs (pooled RR 1.13, 95% CI 0.53-2.41, I^2 = 0%).

Figure 12: Suicidality, cohort studies



Source: Portions of Figure 4(a) of Choudhury et al [26]

Conclusions: Findings should be interpreted as hypothesis-generating due to significant heterogeneity and wide confidence intervals, indicating imprecision. Longer-term studies with neuropsychiatric outcomes as the primary endpoint are required.

Comments:
This meta-analysis looked at a number of neuropsychiatric outcomes. For suicidality, they found that from observational studies, GLP-1 use was associated with a lower reported risk of suicidality compared to non-users/controls while no such association was seen with semaglutide alone. However, there was significant heterogeneity. The authors state these findings should be considered hypothesis-generating.

4.1.5 Ebrahimi et al 2025 [27]

Title: Suicide and self-harm events with GLP-1 receptor agonists in adults with diabetes or obesity: A systematic review and meta-analysis

Methods: Medline, Embase, Clinicaltrials.gov, and Cochrane databases were systematically searched up to Aug 2023. RCTs lasting ≥6 months comparing GLP-1s with placebo for the treatment of diabetes or obesity were identified. The PICO criteria were used for study selection. The Cochrane Risk of Bias Tool was used to assess bias.

Included studies: A total of 27 of 144 RCTs meeting inclusion criteria systematically recorded suicide and/or self-harm-related events comprising a total of 32,354 individuals receiving GLP-1s and 27,042 receiving placebo (Table 15). Five studies were considered at risk of bias due to loss of >5% of participants to follow-up. Otherwise, studies were not found to be heterogeneous nor at high risk of bias.

Results: The overall findings, subgroup and sensitivity analyses are summarised in Table 16. There were 33 recorded occurrences of death by suicide, suicide attempts, suicidal ideation, or self-harm in the GLP-1 group and 27 events in the placebo group. Event incidence was very low in the GLP-1 (0.047 per 100 person-years) and placebo (0.042 per 100 person-years) groups with no statistically significant difference between the groups (RR 0.76, 95% CI 0.48-1.21).

11 studies including 5992 participants had a history of suicide attempts or depression as an exclusion criterion. Removing these studies did not change the overall findings. Subgroup analyses indicated no difference in association between GLP-1 users with or without diabetes (Figures 13 and 14). Another subgroup analysis based on specific GLP-1s did not suggest a difference in outcomes. The inclusion of additional suicidal ideation events reported within the Columbia suicide severity rating scale (C-SSRS) did not alter results from the main analysis (RR 0.81, 95% CI 0.60-1.10).

Table 15: Characteristics of participants

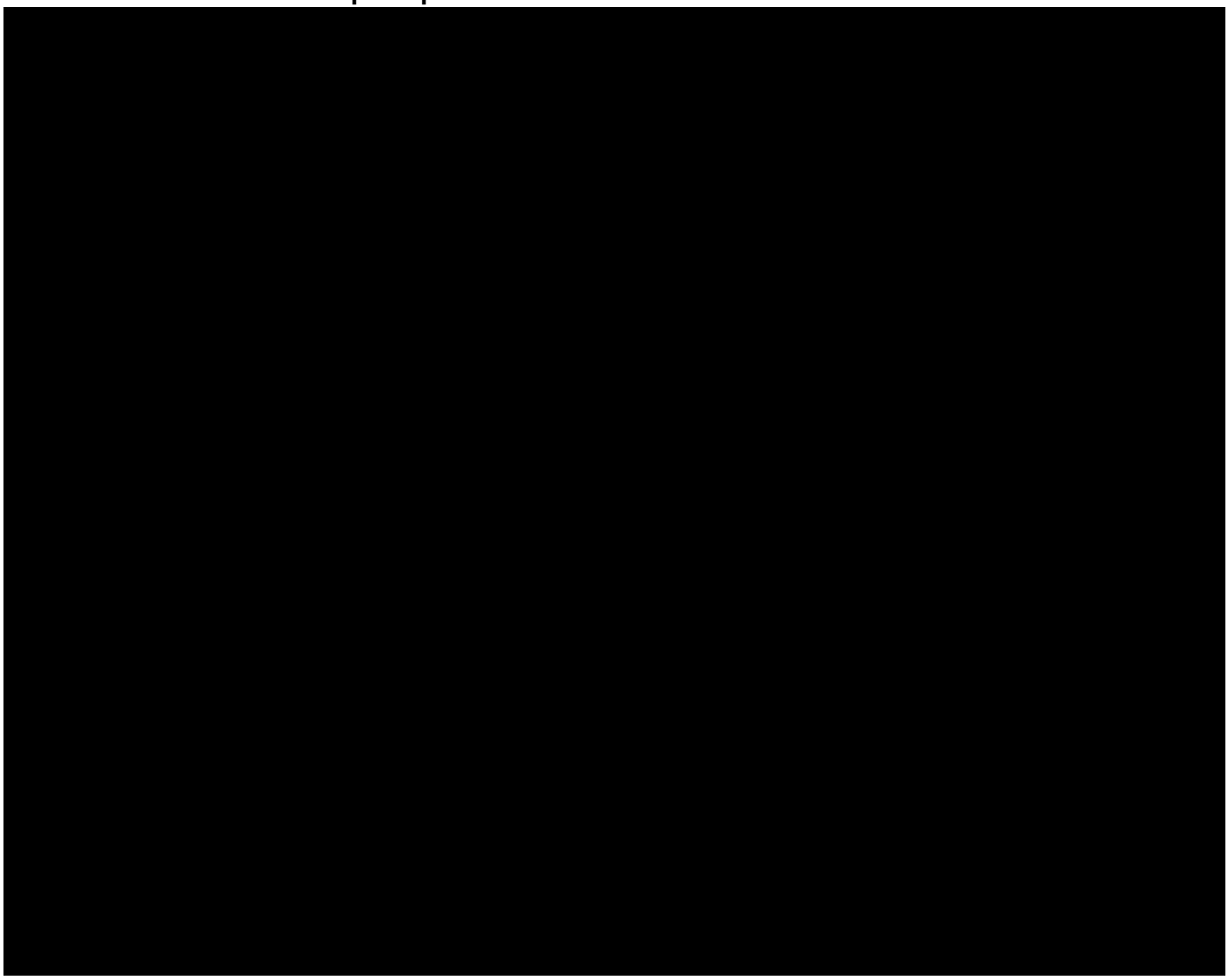
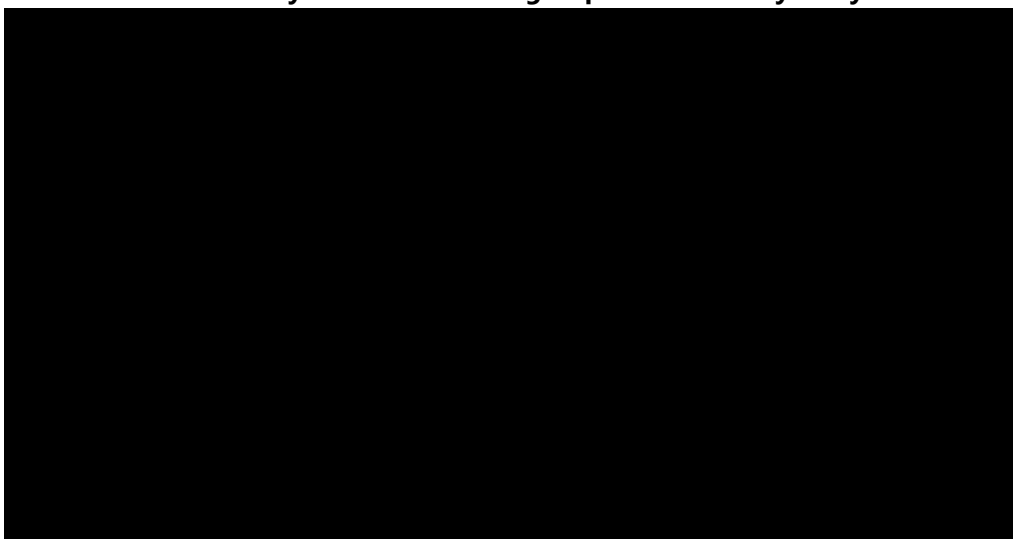


Table 16: Summary estimates for subgroup and sensitivity analyses



Source: Table 2 of Ebrahimi et al [27]

Figure 13: GLP-1s vs. placebo in adults with diabetes



Source: Figure 3 of Ebrahimi et al [27]

Conclusion: It is unlikely that there is an increase in the very low incidence of suicide-related adverse events among individuals receiving GLP-1s within the context of RCTs. However, continued monitoring is warranted to identify particular patients who may be at risk as use of GLP-1 expands.

Comments:

This meta-analysis included 27 RCTs, of which 5 were considered at risk of bias due to loss of >5% of participants to follow-up. Otherwise, studies were not found to be heterogeneous nor at high risk of bias.

The difference in suicide-related events between the GLP-1 and placebo groups was not statistically significant (RR 0.76, 95% CI 0.48-1.21). However, there was a low number of suicide-related events with 33 in the GLP-1 group and 27 in the placebo group. Subgroup analyses particularly by individual GLP-1 should be interpreted with caution due to the low number of events.

4.1.6 Han et al 2026 [28]

Title: Association of glucagon-like peptide-1 receptor agonist use with risk of psychiatric disorders: A systematic review and meta-analysis of randomised controlled trials

Methods: A systematic search of PubMed, Embase, Cochrane library and Web of Science up to 13 Jun 2025. RCTs that compared the use of GLP-1s with either placebo or other non-GLP-1 were included. Psychiatric disorders were collected based on reported treatment-emergent adverse events. The quality of each study was assessed using the Cochrane tool and evidence quality using the GRADE framework.

Included studies: Of the 13,701 potentially relevant studies identified, 86 RCTs were included in the meta-analysis. The majority of the trials (79.1%) included T2DM participants.

Results: A total of 133,378 participants across 86 RCTs. No significant statistical difference found in the incidence of psychiatric disorders between the GLP-1 group and the control group (RR 0.96, 95% CI 0.85-1.08, I^2 = 0%).

GLP-1 treatment was not associated with suicide (RR 0.90, 95% CI 0.59-1.38) depression, anxiety, sleep disorder, bipolar disorder, delirium, addictive disorder or schizophrenia (Figure 15).

Figure 15: Risk of psychiatric disorders associated with GLP-1s



Source: Figure 2 of Han et al 2026 [28]

No statistically significant associations were observed for drug type, indication, dose, treatment duration, comparator type, baseline BMI, trial designation, age, inclusion of baseline psychiatric disorders or reporting category. Meta-regression analyses revealed no significant effect of changes in fasting blood glucose, haemoglobin A1c, weight or BMI on the risk of psychiatric disorders.

Conclusion: GLP-1 use was not associated with the risk of psychiatric disorders, including depression, suicide or anxiety.

Comments:
This meta-analysis investigated the risk of psychiatric disorders, including suicide. Of the 86 RCTs included in the meta-analysis, 32 looked at suicide and found no association between GLP-1 use and suicide (RR 0.90, 95% CI 0.59 to 1.38).

4.2 Systematic reviews

4.2.1 Au et al 2026 [29]

Title: Association of glucagon-like peptide-1 receptor agonists and suicidality: A systematic review

Methods: Relevant articles were retrieved from OVID, PubMed and Web of Science up to May 2024. Primary research examining the association between GLP-1s and suicidality were included for analysis. The NIH quality assessment tools were used to assess risk of bias.

Included studies: 14 studies that met the eligibility criteria were included in the systematic review: 5 were pharmacovigilance analyses, 4 were retrospective cohort studies, 3 were RCTs, and 2 were post-hoc analyses of RCTs (Table 17).

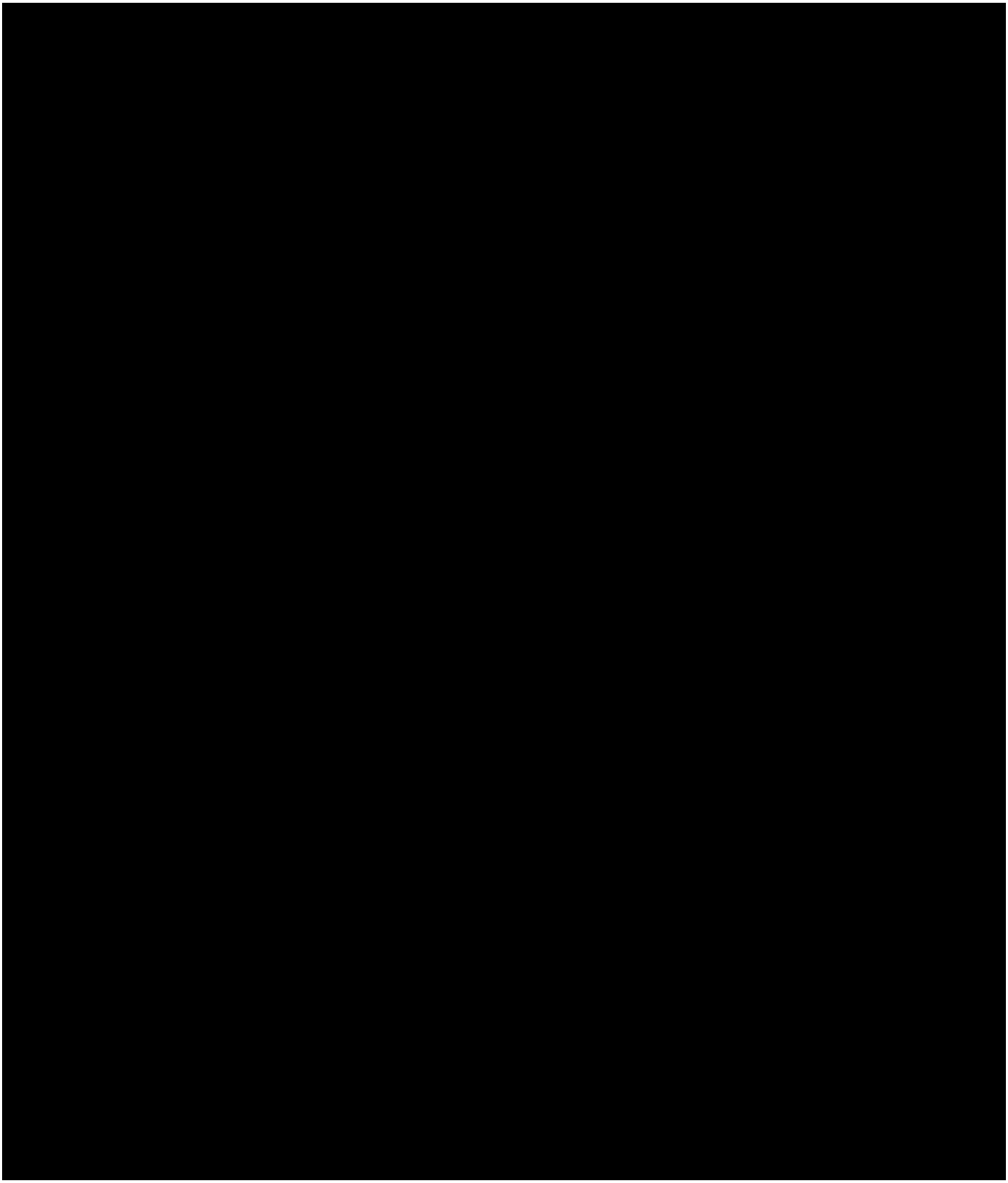
- RCTs: None with a high risk of bias. The most common limitation was the lack of provided information on randomisation and treatment blinding. The overall dropout rate due to treatment-emergent adverse events was >20% in some studies.
- Observational: None with a high risk of bias. Common limitations were missing reports of patient recruitment, omission of sample size justification, and a lack of adjustment for confounders.

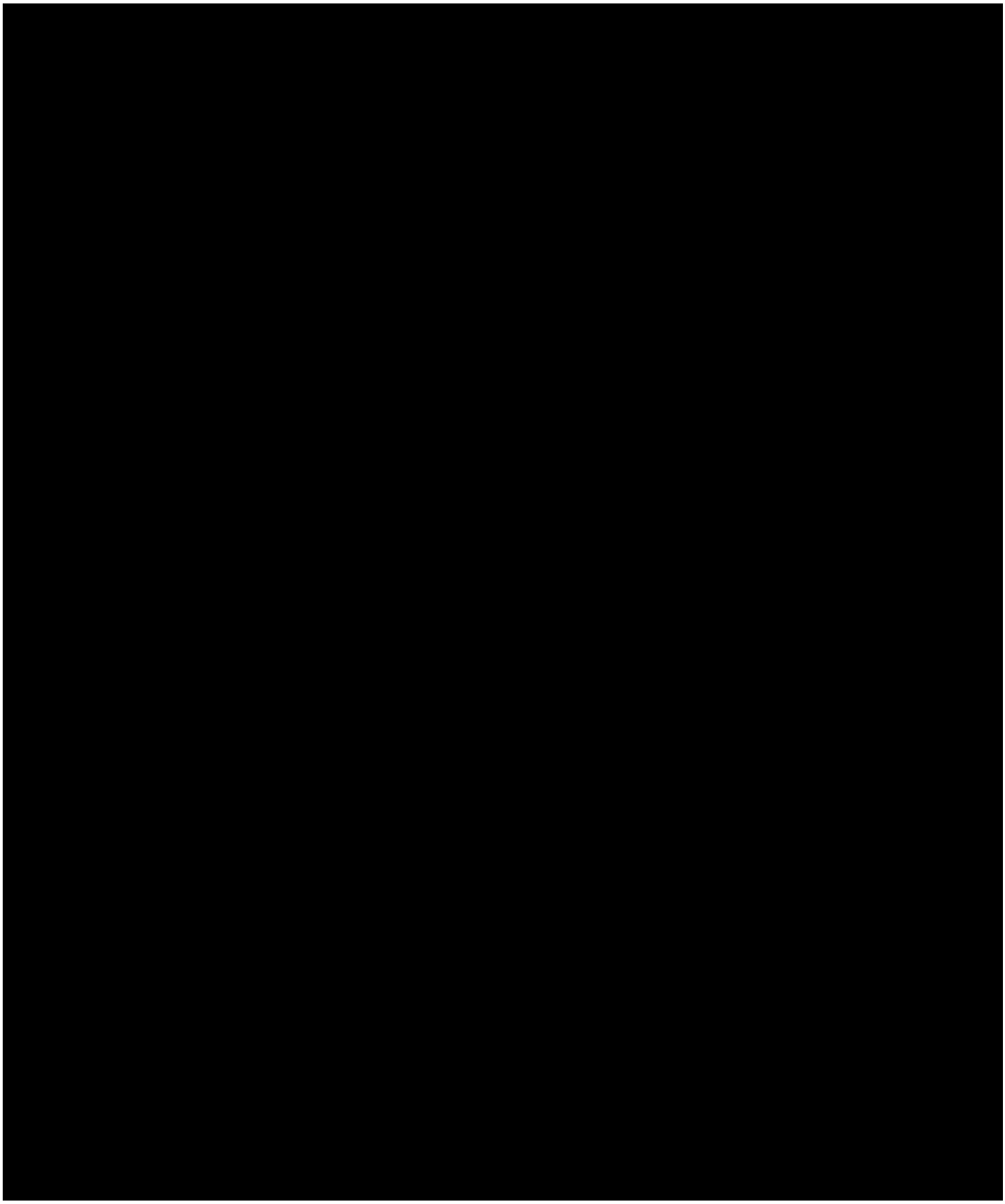
Discussion: In this review, an association between liraglutide, semaglutide and tirzepatide and the risk of suicidal ideation across multiple studies was observed. However, there was no association between suicidality and other GLP-1s including dulaglutide, exenatide and lixisenatide.

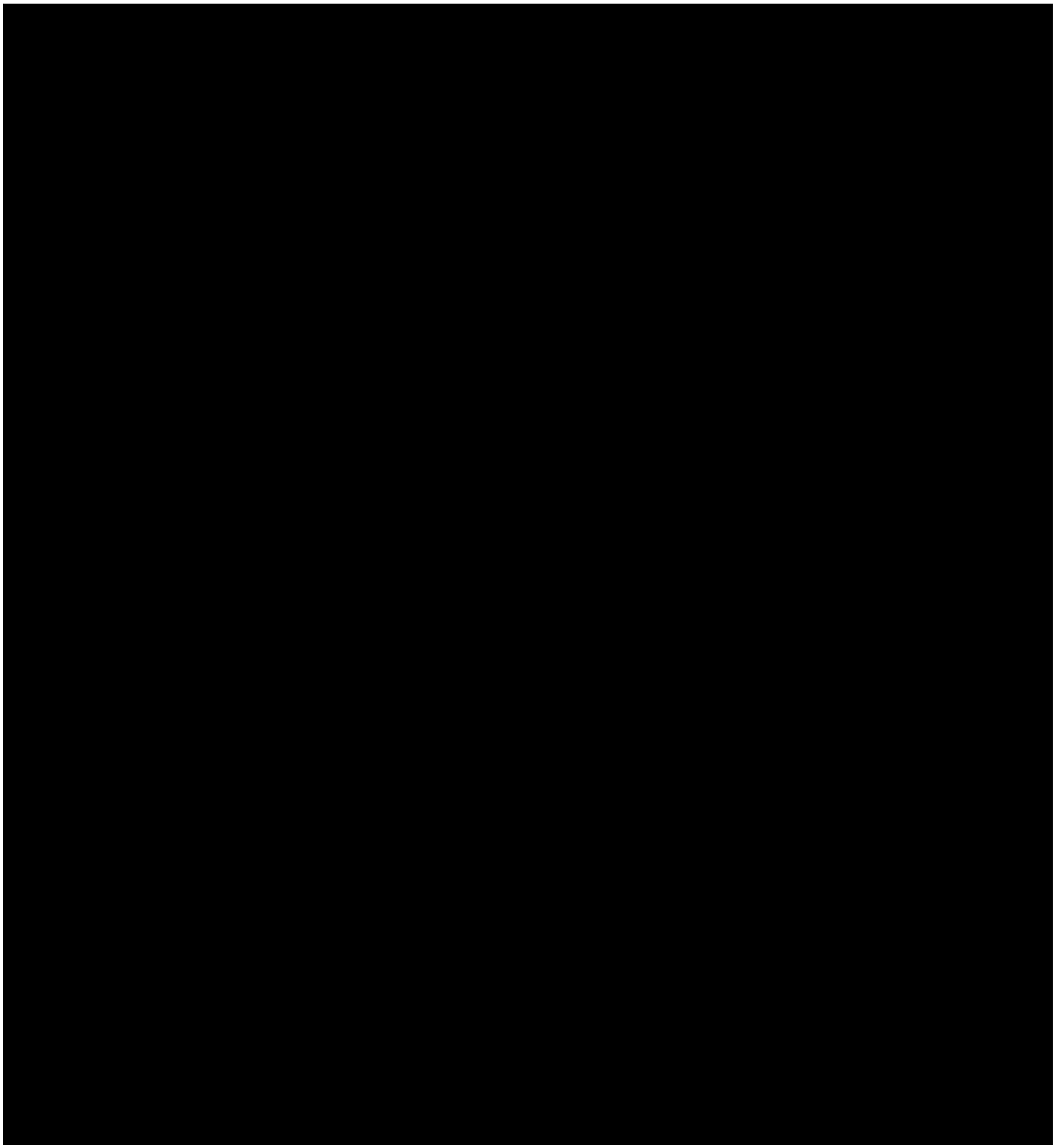
Despite the relationship observed between some GLP-1s and suicidality, causation cannot be established. No causal link between GLP-1s and suicidality can be established when using the Bradford Hill criteria.

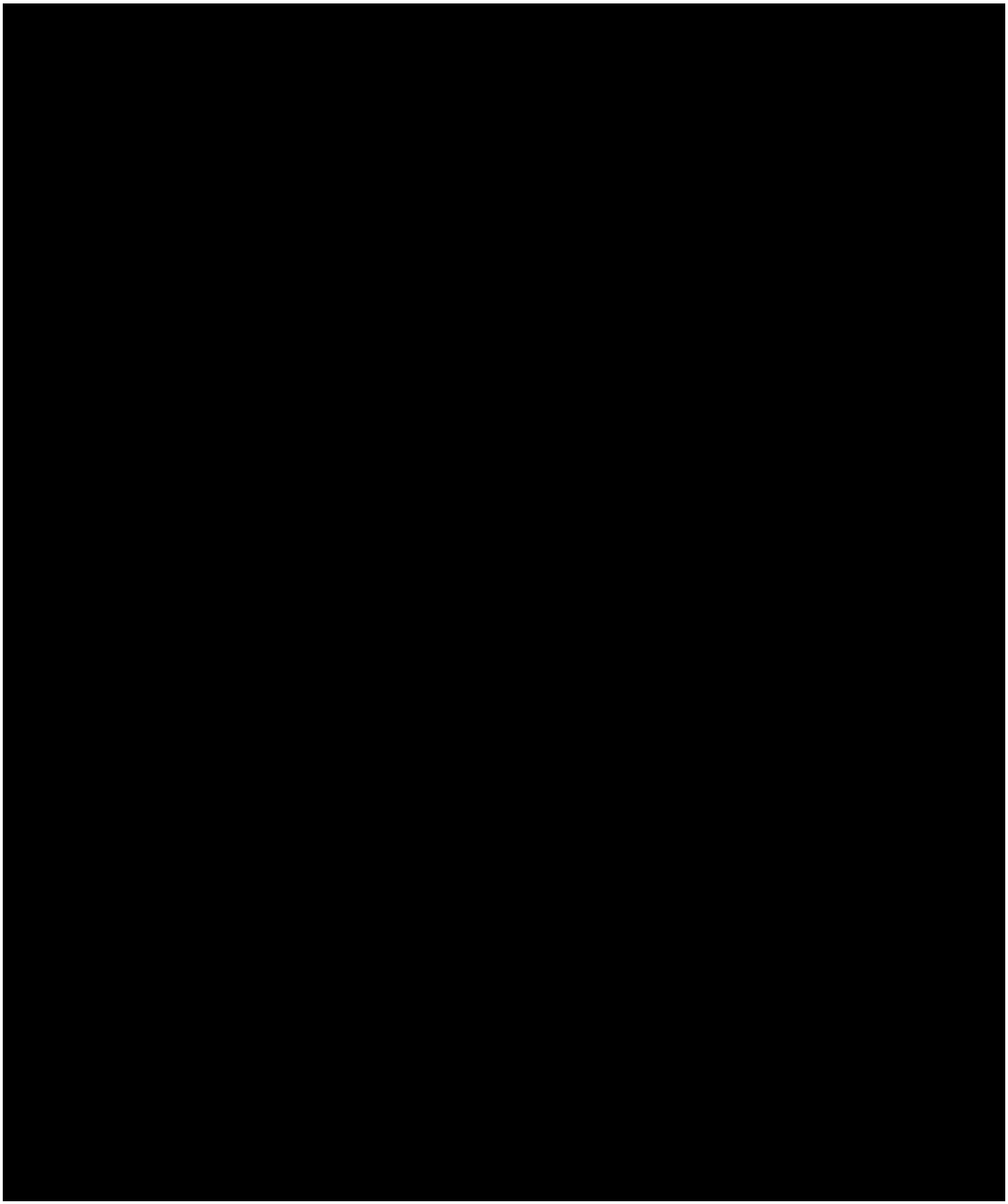
Conclusion: Reports of suicidality with exposure to some GLP-1s exist, but no causality is apparent.

Table 17: Characteristics of studies examining the association between GLP-1s and suicidality









[redacted]

Comments:

The authors note that although there are mixed results reported in the literature, they found an association between liraglutide, semaglutide and tirzepatide with suicidality. No significant association between other GLP-1s and suicidality was observed.

4.2.2 Chan et al 2026 [30]

Title: Association between glucagon-like peptide-1 receptor agonists and suicidality: A systematic review

Methods: Search of Medline, PubMed, Embase, CINAHL and PsycINFO up to 11 Dec 2025. Observational studies investigating suicidal ideation, suicide attempts or complete suicide among adults using GLP-1s were included.

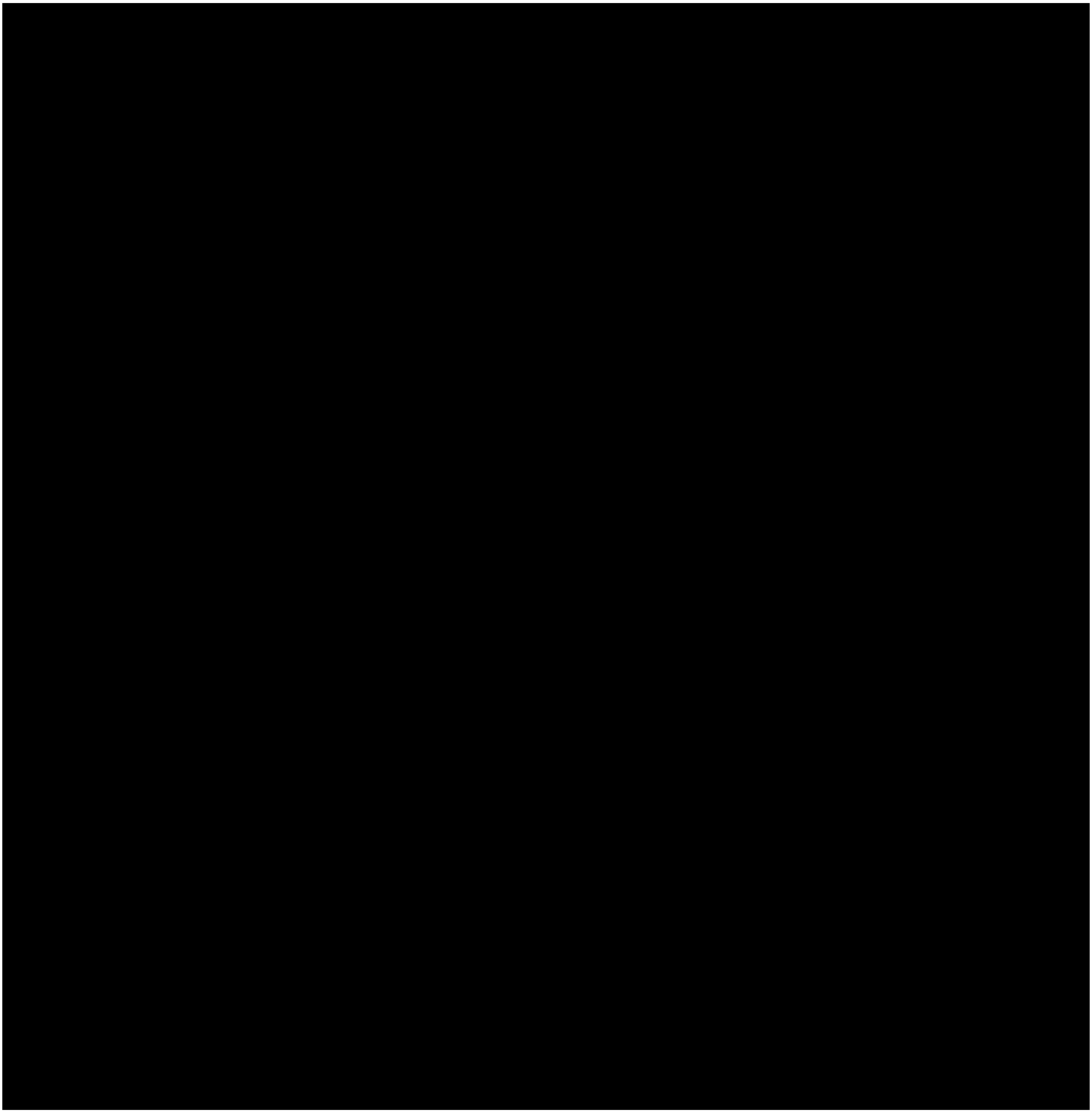
Included studies: 43 studies were included: retrospective cohorts (n=17), case-control (n=1), pharmacovigilance (n=16), cross-sectional (n=2) and case reports/series (n=6).

The authors did not conduct a meta-analysis due to duplication of data (eg, multiple studies using the same data sources) and the heterogeneity in interventions, comparators and outcomes.

Results: Findings varied by study design. Some case reports suggested a temporal relationship between GLP-1s and suicidal ideation. Cross-sectional studies and case-control studies identified a negative association between GLP-1s and suicidal attempts (Table 18). Pharmacovigilance and cohort studies showed more mixed results with some identifying a positive association between semaglutide or liraglutide and suicidal ideation, while others paradoxically reported a negative association with suicidal behaviours (ie, attempts and intentional self-harm) or completed suicide.

In the pharmacovigilance studies, statistical methodologies were broadly similar, yet heterogeneity in exposures (eg, pooled vs. specific GLP-1s), comparators (eg non GLP-1 medicines, other T2DM treatments) and outcomes (eg, suicidal ideation, attempts, completed suicide) hindered the ability to synthesise findings. Some pharmacovigilance studies highlighted liraglutide and semaglutide as potentially associated with increased suicidal ideation, though these findings lacked consistency across comparator groups and outcomes.

Table 18: Summary of retrospective cohort studies





Source: Table 3 of Chan et al 2026 [30]

Conclusions: While evidence does not support GLP-1s as a causative agent for suicidality, due to multiple risk factors in this population, clinicians should routinely assess mental health status before and during GLP-1 treatment regardless of indication. Importantly, a history of concurrent mental health conditions should not preclude use of a GLP-1; rather, individual patient factors should be accounted for when making prescribing decisions.

Comments:

Findings were mixed depending on the study design. The authors note initial concerns about suicidality with GLP-1 use was largely driven by case reports. However, other studies that have less bias have made this association less evident.

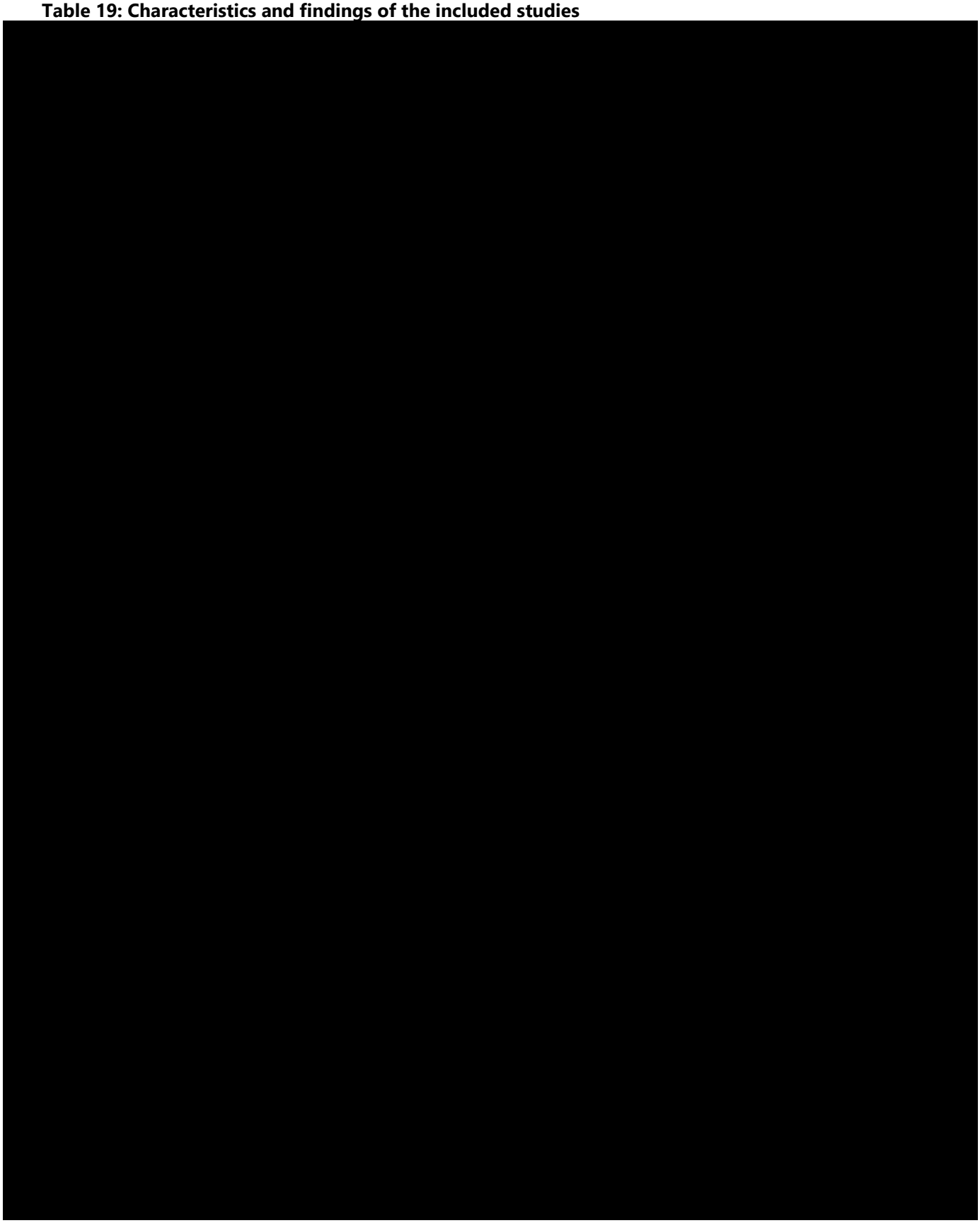
4.2.3 Di Stefano et al 2025 [31]

Title: Glucagon-like peptide-1 receptor agonists, dual GIP/GLP-1 receptor agonist tirzepatide and suicidal ideation and behaviour: A systematic review of clinical studies and pharmacovigilance reports

Methods: A search was performed in Medline, Embase, and APA PsycInfo up to 24 Sep 2024. Risk of bias was evaluated using the Newcastle-Ottawa Scale for cohort studies and ROB2 for RCTs.

Included studies: The review identified 16 studies consisting of 5 observational studies, 2 RCTs, 8 pharmacovigilance analyses, and 1 post-hoc analysis of RCTs (Table 19). Quality appraisal of the observational studies resulted in a mean score of 7.8 indicating an overall low risk of bias.

Table 19: Characteristics and findings of the included studies





Source: Table 1 of Di Stefano et al [31]

Results: No consistent evidence indicated an increased suicide risk among GLP-1 users. Pharmacovigilance analyses produced mixed findings. While some disproportionality analyses reported higher rates relative to other antihyperglycaemics, no causal link was confirmed.

Cohort studies involving diabetic and obese populations generally did not demonstrate a significant increase in suicidal behaviour.

Conclusions: Although current data do not warrant changes in prescribing practices, further research is needed before definite conclusions can be drawn. Moreover, the generalisability and reliability of these findings should be interpreted in light of the methodological limitations of the included studies.

4.2.4 Sa et al 2026 [32]

Title: Psychiatric effects of GLP-1 receptor agonists: A systematic review of emerging evidence

Methods: Electronic databases searched were Pubmed/Medline, Cochrane central register of controlled trials, Embase and Web of Science.

Eligible studies included RCTs, non-RCTs, controlled before-and-after studies and observational designs that incorporated control or comparator groups. Meta-analyses that addressed the primary or secondary outcomes of interest were also included to capture aggregated findings across studies.

The Cochrane risk of bias tool was used to assess RCTs, and the ROBINS-I tool for non-randomised studies.

Included studies: 38 studies were included.

Results: Findings suggest modest antidepressant effects, inconsistent associations with suicidality and potential therapeutic benefit in disorders of reward regulation (Table 20). These findings are constrained by limited sample diversity, variability in outcome measures and the consistent underrepresentation of individuals with psychiatric comorbidities.

Table 20: Summary of the evidence

[redacted]

Note: References 17 and 18 for suicidality are Ueda et al (2024) and Bushi et al (2025).

For suicidality, the association with GLP-1s remains uncertain and controversial. A large cohort study conducted in Sweden and Denmark by Ueda et al (2024) found no statistically significant increase in suicidality associated with GLP-1 exposure. The upper bound of the confidence interval corresponded to an absolute risk of 0.16 events per 1000 person-years [33]. A meta-analysis of 4 studies by Bushi et al (2025) reported a non-significant relative risk of 0.568 (95% CI 0.077-4.205. Substantial heterogeneity was observed across studies (I2 = 98%) likely reflecting differences in study design, populations and outcome ascertainment. The extremely wide prediction interval (0.001-218.938) further underscores the high degree of uncertainty and variability in effect estimates. However, pharmacovigilance data suggest a potential increased risk of suicidal ideation with semaglutide use in individuals concurrently prescribed antidepressants or benzodiazepines, with ROR of 4.45 and 4.07, respectively [24].

Understanding whether suicidality reflects a direct mechanistic effect (eg, dysregulated stress response or limbic modulation) or is a downstream consequence of rapid weight loss, metabolic shifts or medicine interactions remains an important area for future research. The absence of a robust safety signal should not be interpreted as evidence of safety in high-risk populations, and clinicians should exercise caution when prescribing GLP=1s to individuals with a history of suicidality or severe mood disorders. Regulatory agencies may need to consider population-specific monitoring recommendations as the use of GLP-1s continues to expand.

Conclusion: This review highlights key findings on neuropsychiatric effects of GLP-1s. The heterogeneity among studies in terms of dosing, clinical indications and baseline psychiatric status complicates interpretation, but preliminary evidence suggests modest antidepressant effects and potential therapeutic roles in eating and SUD. Concerns regarding suicidality remain unresolved. In schizophrenia, GLP-1s provide clear metabolic benefits but have not demonstrated consistent effects on psychiatric symptomatology.

4.2.5 Ştefănescu et al 2025 [34]

Title: Evaluating suicidal risk in GLP-1RA therapy: An umbrella review of meta-analytic evidence

Methods: A search of Medline, PubMed, PsychInfo, Web of Science, Science Direct, Sage, Wiley, Scopus, Google Scholar, Proquest and Cochrane library up to July 2025. Quality of included studies was assessed using the JBI checklist for systematic reviews and research syntheses.

Included studies: Out of 50 initial studies, a final number of 12 reviews and meta-analyses were included in the study comprising of 4 systematic reviews, 2 meta-analyses, 4 systematic reviews and meta-analyses, 1 scoping review, and 1 narrative review (Table 21).

The number of included studies relevant to suicide varied from 2 to 36 and assessed studies employing various methodological approaches: RCTs, observational studies, post hoc analyses, case series, and pharmacovigilance studies.

Sample sizes ranged from 6 to 131,255,418 participants covering both children and adults (age range 0 to 85 years) although only 2 studies included children. All participants were diagnosed with T2DM and/or obesity and a significant proportion of studies also included participants diagnosed with several psychological conditions (eg, depression, schizoaffective disorders, substance use, obstructive sleep apnoea etc.).

Table 21: Study characteristics



[redacted]

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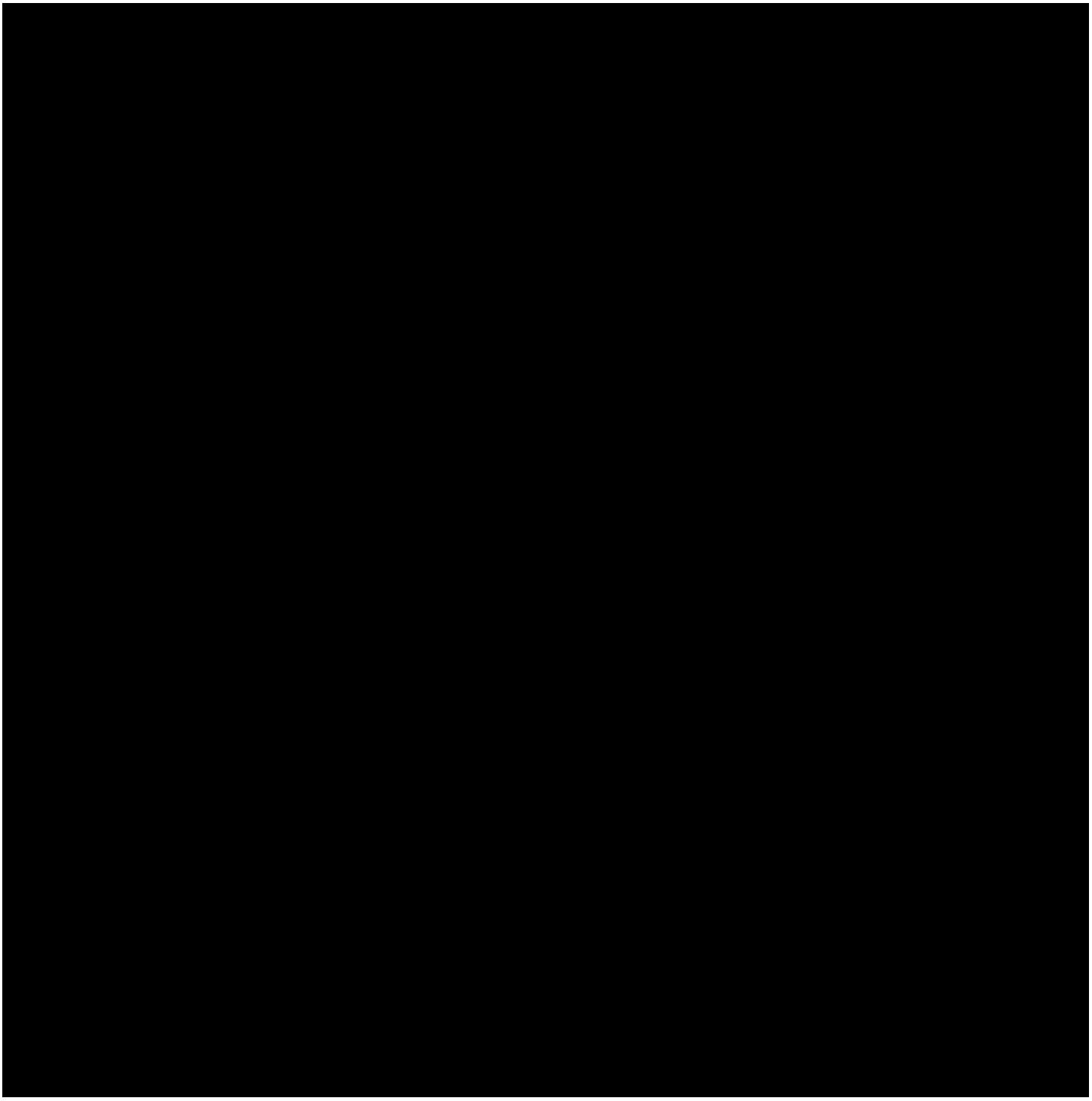
Results: The most consistent pattern was that there were no effects of GLP-1s on any aspect of suicidality (Table 22). Furthermore, although limited by high heterogeneity, 1 narrative review by Strumila et al (2024) found a small risk of suicide in patients treated with GLP-1s but there was insufficient evidence for a direct causal link [35]. Additionally, quantitative data confirmed this result: across the 6 studies, the risk ratio for suicidality ranged from 0.56 to 0.83 without a significance level (p varying from 0.06 to 0.82 in some cases) but with varying levels of heterogeneity (from 0.00% without significance, to 98% with a significant impact ($p<0.01$).

Despite this clear trend, 2 studies composed of observational data found suicidal ideation to be present (not increased) in patients taking GLP-1s as reported by Chao et al (2023) [36], and self-harm behaviours in underweight patients as reported by Neeland et al (2024) [37], although a causal relationship cannot be inferred. At the same time, 2 meta-analyses showed a more nuanced pattern, based on the methodology of studies and of the GLP-1 type as reported by Barroso et al (2024) [38], and based on patient expectations as reported by Sharma et al 2025 [39]. Firstly, mixed results were found in terms of pharmacovigilance, meaning an increased risk was observed for semaglutide and liraglutide, whereas for the rest of the GLP-1s this trend was not supported [38]. Secondly, unrealistic expectations and treatments' failure to meet these expectations were associated with an increased risk of suicide attempts, while GLP-1s alone did not have a direct link to the attempts [39].

Table 22: Summary of results from included studies





Source: Table 2 of Ştefănescu et al 2025 [34]

Conclusion: GLP-1 treatment represents a safe option when treating diabetes/obesity. However, a careful assessment of treatment expectations and of suicide risk is needed in order to attenuate potential suicidal tendencies that already exist.

4.2.6 Valentino et al 2025 [40]

Title: The effect of glucagon-like peptide-1 receptor agonists on measures of suicidality: A systematic review

Methods: A search of PubMed, Medline, Cochrane library, PsychInfo, Embase, Scopus and Web of Science for pharmacovigilance and cohort studies up to 20 Nov 2024 in accordance with PRISMA guidelines. A manual search using Google Scholar to identify additional studies.

Cohort studies were assessed for quality using the Newcastle-Ottawa Scale (NOS). Studies scoring ≥7 were denoted as high quality, 5-6 as moderate, and <5 as low. Pharmacovigilance studies were not assessed for risk of bias due to unavailability of standardised assessment of these studies.

Included studies: 22 studies met inclusion criteria comprised of pharmacovigilance (n=10) and cohort studies (n=12). In general, the cohort studies received a moderate rating on the NOS. Common methodological limitations include a statement on the adequacy of the follow-up cohort(s) and a demonstration that the outcome(s) of interest were not present at the start of the study.

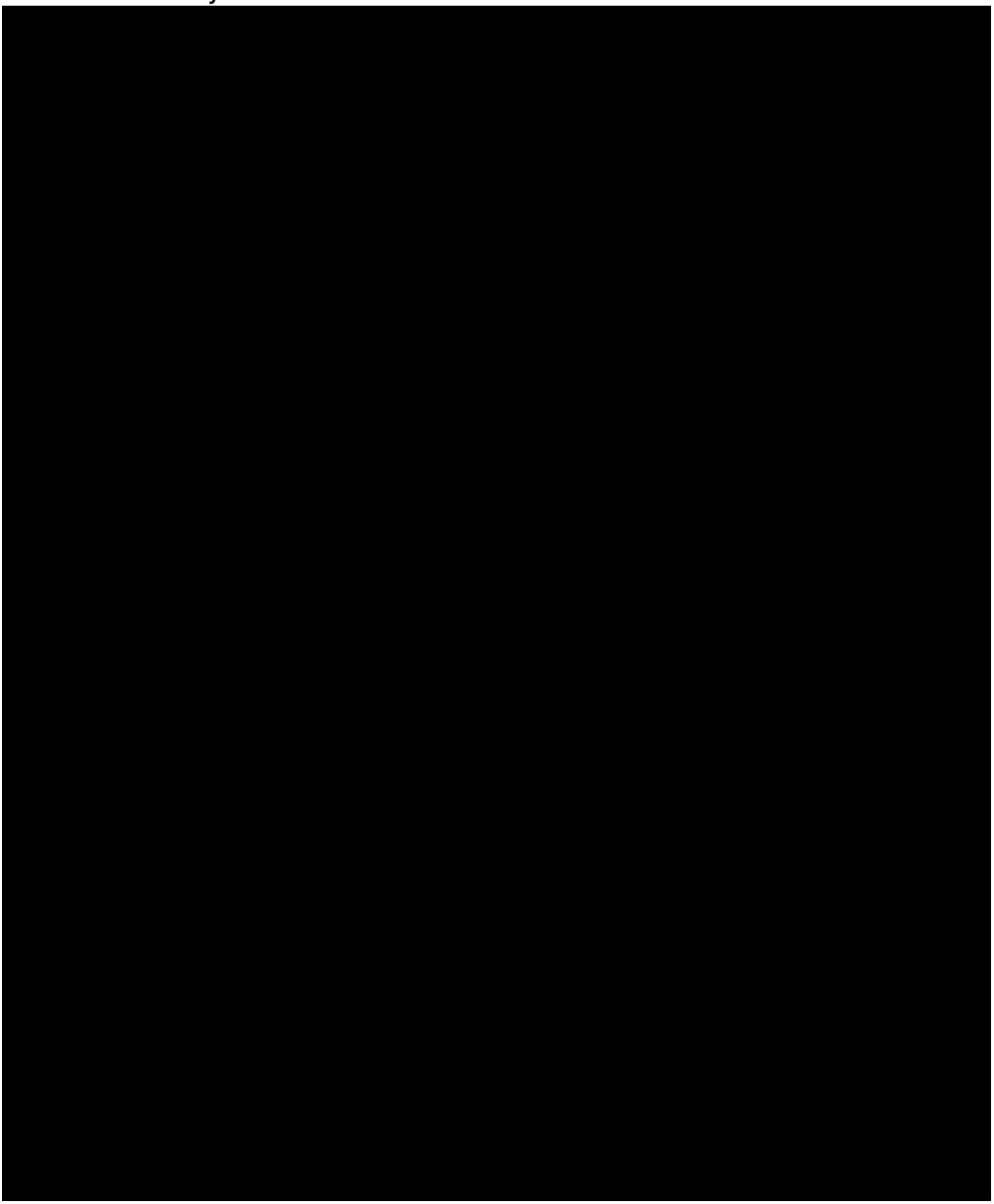
Results from both cohort and pharmacovigilance studies are shown in Table 23.

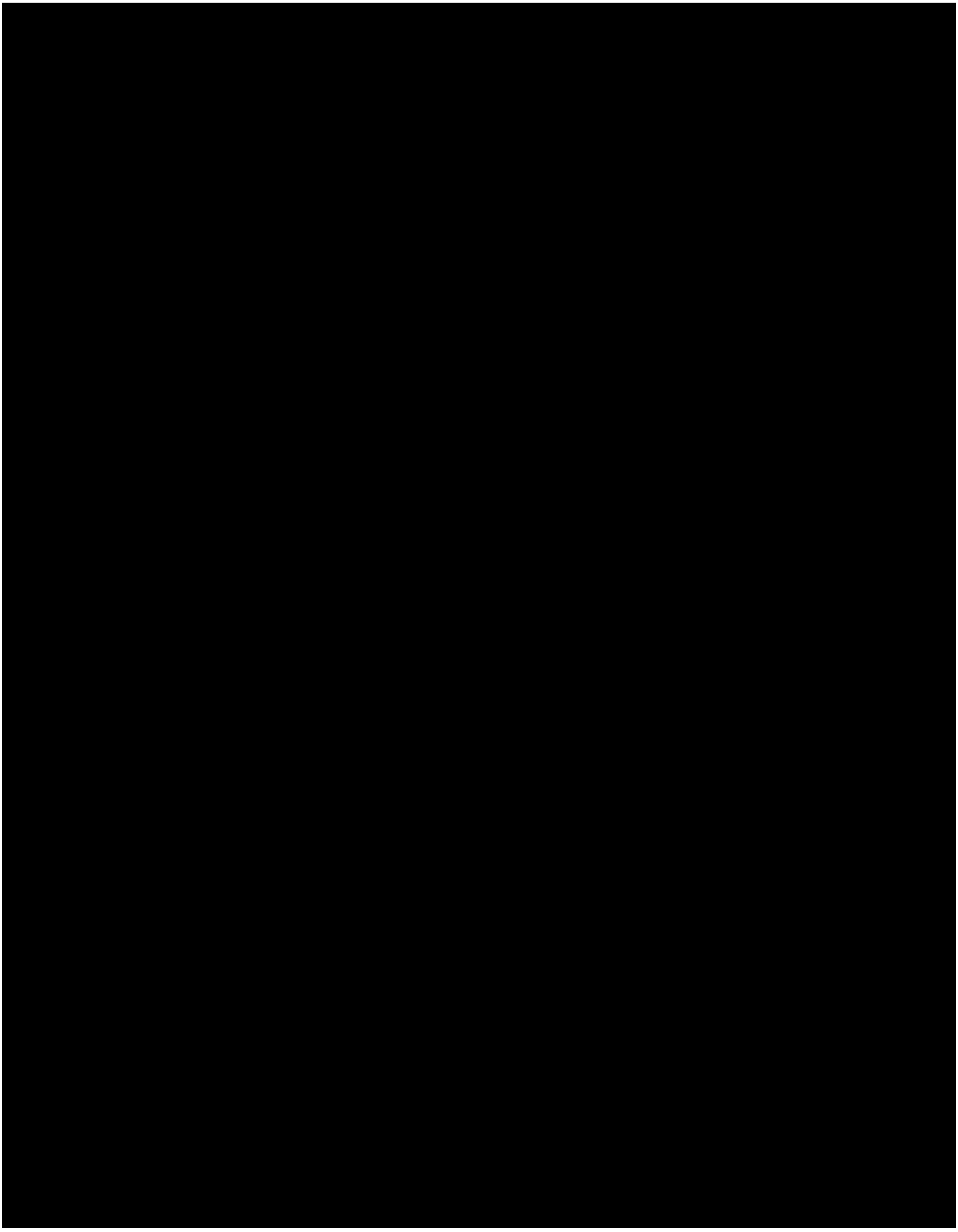
Results – Cohort studies: Most studies calculated hazard ratios (HR) using a comparator medicine to evaluate the association between GLP-1s and suicidality. Dose effects were generally not reported. Taken together, results from cohort studies suggest that GLP-1s are not consistently associated with an increase in any aspect of suicidality; instead some agents are associated with decreased suicide ideation and suicide attempts.

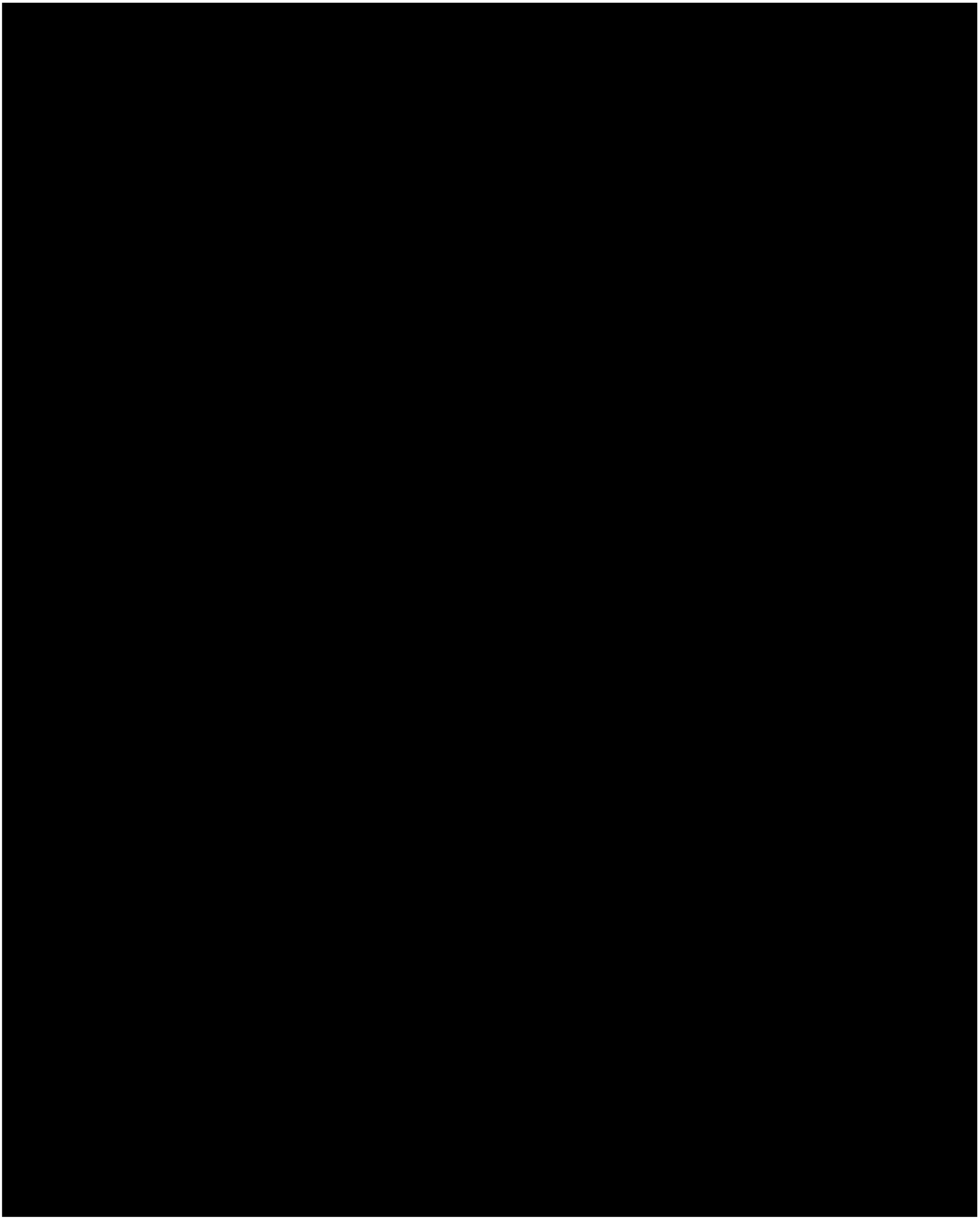
Results – Pharmacovigilance studies: Most calculated reporting odds ratios (ROR) to identify disproportionality. Databases used include EudraVigilance, FAERS, and WHO Vigibase.

Discussion: There is inadequate information to ascertain whether causality exists linking GLP-1s to suicidality. Ongoing vigilance and further information is required to inform whether the possibility of causality exists. Practitioners prescribing GLP-1s should be vigilant for the possibility of the emergence of suicide ideation and be aware of the higher risk of mental illness in persons who would be candidates for GLP-1s.

Table 23: Summary of results from included studies







5 SUMMARY OF FINDINGS

Table 24 contains a summary of findings from the studies specifically mentioned in the EMA's review and US FDA's review, and the meta-analyses presented in section 4.1 of this paper.

Table 24: Summary of findings from studies included in the EMA review, US FDA review, meta-analyses

Study	Design	Results
Wang 2024	Cohort study using TriNetX health records comparing semaglutide vs. non-GLP-1 medicines. Separate analyses for patients with overweight/obesity, and patients with T2DM.	Incident suicidal ideation Semaglutide vs. non-GLP-1 obesity medicine: HR 0.27 (95% CI 0.20 to 0.36) Semaglutide vs. non-GLP-1 T2DM medicine: HR 0.36 (95% CI 0.25-0.53)
EMA real-world cohort study 2024	Cohort study using an active comparator, new user design to assess GLP-1s vs. SGLT-2s in patients with T2DM.	Incident suicide- and self-harm-related events (ITT analysis) following IPTW adjustment GLP1s vs. SGLT-2s for T2DM: HR 1.10 (95% CI 0.86-1.41)
Kuzucan 2026	Cohort study using an active comparator, new user design to assess GLP-1s vs. SGLT-2s and GLP-1s vs. DPP-4s in patients with T2DM.	Intentional self-harm following IPTW adjustment GLP-1s vs. SGLT-2s for T2DM: HR 0.93 (95% CI 0.81 to 1.08) GLP-1s vs. DPP-4s for T2DM: HR 0.94 (95% CI 0.82 to 1.07)
Alansari 2025	Meta-analysis of RCTs and observational studies.	Suicidal ideation GLP-1s vs. other obesity and diabetes medicines: OR 1.0 (95% CI 1.0 to 1.0) Suicide GLP-1s vs. other obesity and diabetes medicines: OR 1.77 (95% CI 0.80 to 3.91)
Bushi 2025	Meta-analysis of observational studies.	Suicidal outcomes GLP-1s vs. other anti-hyperglycaemic medicines: RR 0.57 (95% CI 0.08 to 4.2)
Chen 2025	Meta-analysis of RCTs.	Suicidal behaviour GLP-1s vs. controls: RR 0.84 (95% CI 0.54 to 1.32)
Choudhury 2026	Meta-analysis of RCTs and observational studies.	Suicidality GLP-1s vs. controls in observational studies: OR 0.34 (95% CI 0.18 to 0.63) GLP-1s vs. controls in RCTs: RR 1.13 (95% CI 0.53 to 2.41)
Ebrahimi 2025	Meta-analysis of RCTs.	Suicide and/or self-harm-related events GLP-1 vs. placebo RR 0.76 (95% CI 0.48 to 1.21).
Han 2026	Meta-analysis of RCTs.	Suicide GLP-1 vs. control RR 0.90 (95% CI 0.59-1.38)

6 DISCUSSION AND CONCLUSIONS

Almost 20 years ago in 2007, the first GLP-1 (exenatide) was approved in New Zealand. Since then, other GLP-1s have been approved and are mostly used in the treatment of T2DM and for weight management. The use of GLP-1 medicines in New Zealand and internationally is expected to continue increasing with time.

Over the last 2 years, a number of studies have been published investigating the association between the use of GLP-1 medicines and suicidality. These range from disproportionality analyses using pharmacovigilance databases, cohort studies using large datasets such as the TriNetX database, and systematic reviews and meta-analyses.

There were 6 meta-analyses presented in this paper and all generally indicate there is no statistically significant association between the use of GLP-1 medicines and suicidality. Of the 6 meta-analyses, 5 included RCTs and it is unlikely that suicide-related events were a primary outcome measure in these RCTs. There was significant heterogeneity in the observational studies included in the meta-analyses and systematic reviews. Studies using pharmacovigilance databases are generally considered hypothesis-generating and causality cannot be inferred from these cases.

The EMA's PRAC was the first regulator to complete a review on suicidal ideation and self-injurious ideation concluding there is insufficient evidence of a causal association. The US FDA's review came to the same conclusion, but they have gone a step further by requesting removal of these warnings from the GLP-1 US data sheets. The TGA has maintained their position that these warnings should remain in the Australian data sheets, and New Zealand has harmonised packaging with Australia. Medsafe is requesting advice from the MARC due to these differing views of whether a warning on suicidality is needed in the GLP-1 data sheets.

7 ADVICE SOUGHT

The Committee is asked to advise:

- On the strength of the evidence for a potential association between the use of GLP-1 medicines and the risk of suicidality.
- Whether the GLP-1 NZ data sheets should contain a warning on the risk of suicidality.

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