The study found a significant correlation between depression and a higher probability of initiating insulin treatment, with an initial hazard ratio of 1.38.

*The association between comorbid depression and insulin initiation in type 2 diabetes: A cohort OHDSI study*

**Background:** Individuals diagnosed with type 2 diabetes have a higher risk of experiencing depression compared to those without the condition. Hyperglycemia-induced neurochemical dysregulation promotes the progression of type 2 diabetes. Furthermore, depression can lead to poor outcomes and may cause insulin resistance. This comorbidity may fail diabetes oral medications, and insulin therapy may be required.

**Result:** We analyzed data from 35,589 patients, and after PS matching (1:4), we obtained 1903 patients for the target group and 5857 patients for the comparator group. We examined the association between depression comorbidity with the outcome of insulin initiation. Depression was found to be significantly associated with insulin initiation, with a hazard ratio of 1.38 (95% CI: 1.11, 1.71).

**Methods**

**Figure 1.** The Kaplan Meier plot shows the estimated incidence of first initiation of insulin use. Patients with type 2 diabetes and depression are on the target curve (blue line), while those with type 2 diabetes are on the comparator curve (red line).

**Figure 2.** Empirical calibration plots where estimates below the dashed line are statistically significant (alpha = 0.05) different from the true effect size. There are two images in the picture, the below showing uncalibrated estimates and the above depicting calibrated estimates.

**Cohort Entry**

- Type 2 diabetes patients and having at least 1-year database history.

**Event**

- Start antidiabetic therapy (non insulin)
- The target group consisted of diabetes patients who had depression or depression medication after the first DM medication. For the comparative group, the same criteria were applied, but without depression or depression medication.

**One year**

- Initiation of insulin therapy
- We considered only insulins with a pen dosage form and a minimum use period of 60 days.

**End of the observation period**

**Limitation:** Furthermore, after refining the findings using negative controls, the effect size estimates were recalibrated, revealing no significant difference in the hazard of insulin initiation after calibration. This recalibrated outcome indicates a hazard ratio of 0.92, suggesting that the observed connection between depression and insulin initiation may be more complex than initially thought, possibly influenced by unmeasured confounding factors.

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