**Suppl 1.** Characteristics of the Studies Included in the Systematic Review With the Main Findings and Summary of Key Findings (n = 11)

| **Name of the study and author** | **Type of study** | **Publication year** | **Setting** | **Sample size** | **Analysis** | **Major confounders** | **Main findings** | **Summary of findings** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Khunti et al, 2021 [29]  | Nationwide population-based observational cohort study | 2021 | UK |  2.85 million | Cox regression | Age, ethnicity, sex, duration of diabetes, smoking status, body mass index, and comorbidity | There was no evidence to support a protective effect of DDP4 inhibitors on the outcomes among diabetic patients with COVID-19. The authors studied 2,851,465 people with type 2 DM and the findings revealed a negligible evidence of association between DDP4 inhibitors and COVID-related mortality (hazard ratio: 1.07; 95% confidence interval: 1.01 - 1.13). These differences in the hazard ratio of mortality are minute and are probably due to confounding by indication because these are less likely to be used on older or frail people. | There was a negligible effect of DDP4 inhibitors on the COVID-related mortality among diabetic patients. No effect on morbidity was assessed. |
| Wander et al, 2021 [28] | Retrospective study | 2021 | USA | 35,879 | Logistic and Cox regression models | Heart failure, renal disease, and myocardial infarction or cardiovascular disease, statin use, hypertension, and chronic kidney disease. Other confounders were age, sex, race, body mass index, race/ethnicity, smoking, and urban or rural status. | Among diabetic individuals, there was a positive association with prior sulfonylurea or insulin use and adverse outcomes such as hospitalization, ICU admissions, and death at 30 days. However, there was no significant association between DDP4 inhibitors and other antidiabetic medications such as GLP-1 receptor agonists/SGLT-2 inhibitors and the same adverse outcomes. | In summary, there was no effect of DPP4 inhibitors on the hospitalizations, admissions in the ICU, and death at 30 days. Hence there was no effect of DPP4 inhibitors treatment on diabetic patients on either morbidity or mortality. |
| Solerte et al [27] | Case-control retrospective observational study | 2020 | In patient setting | 338 | Cox-regression model | Age and sex | All-cause mortality was reduced among DDP4 inhibitor users than non-users. More specifically, treatment with highly selective DDP4 inhibitors at the time of hospitalization was related with decreased mortality (P-value: 0.0001), with a significant progress in clinical outcomes (P-value: 0.0001) that revealed reduced mortality and with more hospital discharges (P-value: 0.0008) compared with patients not receiving DDP4 inhibitors. | There was a positive effect of DDP4 inhibitor users on all-cause mortality and there was substantial improvement in other clinical outcomes, which shows a positive effect of DDP4 inhibitors on mortality.  |
| Rhee et al [20] | Population-based study  | 2020 | In patient setting | 67,850 but 832 were analyzed | Chi-square, Fisher exact test, one-way analysis of variance, and logistic regression | Age, sex, comorbidity, and medications | This study primarily found a lower risk of severe COVID-19 among DDP4 inhibitor users than non-users after adjusting for diverse confounders, thus highlighting the benefit of DDP4 inhibitor users among diabetic and patients with COVID-19. The proportion of those who were admitted to ICU with higher morbidity or mortality was 3.42% among those who were using DDP4 inhibitors as compared to those (4.39%) who were DDP4 inhibitors.  | The risk of severe COVID (morbidity) was reduced among DDP4 inhibitor users. There was also reduction in the hospital admissions. Hence, they proved effective in improving morbidity related to COVID-19. However, effect on mortality was not assessed. |
| Montastruc et al [26] | Case series | 2020 | In patient setting | 96 | No regression analysis was performed due to small sample size. | Age, gender, and comorbidity | The study findings revealed that patients admitted to ICU were overweight or obese men suffering from arterial hypertension and treated by antidiabetic drugs and medicines for heart disease. Further, a lower rate of intubation was found in DPP4 inhibitor users when compared to the non-users. | DPP4 inhibitors were found effective in lowering the morbidity; however, their effect on mortality was not assessed.  |
| Dalan et al [25] | Retrospective, observational cohort study | 2020 | In patients admitted to the hospital | 717 | Poisson regression and multiple linear regression models | Age, gender, ethnicity, anti-hypertensive drugs, diabetes drugs, body mass index, and statins | Results revealed a four times higher risk of being admitted in the ICU among the users of DDP4 inhibitors than those who did not use DDP4 inhibitors. They also found a higher association between DDP4 inhibitors and the risk of admission in ICU. Further, the findings revealed a significant association between comorbidity such as diabetes and hypertension with hypoxia and admission to ICU (P < 0.05) indicating the morbidity. Among diabetics, those who were receiving DDP4 inhibitors were at higher risk of being admitted into the hospital than those who were not with statistically significant results (P < 0.05). | DDP4 inhibitors users were more likely to be admitted in the hospitals and in ICUs. Hence there was a negative effect of DDP4 inhibitors users on the morbidity.  |
| Fadini et al [24] | Case-control study | 2020 | Hospitalized patients | 85 | Logistic regression analysis | Age, sex, smoking, dyspnea, hypertension, dyslipidemia, cardiovascular disease, cancer, and COPD | The study findings did not support the hypothesis about the prevention of DPP4 inhibitors against COVID-19. | There was no preventive effect of DDP4 inhibitors on the COVID-19.  |
| Wargny et al [23] | Multicenter observational study | 2020 | In patients admitted to the hospital  | 2,796 | Multivariable logistic regression analysis | Age, sex, body mass index, and lymphocyte count, fever, dyspnea, hypertension, dyslipidemia, smoking, heart failure, COPD, and cirrhosis | 20.6% of the patients experienced mortality on 28 days of the follow-up. The final multivariable analysis revealed that factors such as younger people who were on routine medications such as metformin therapy with a longer duration of symptoms at the time of admission were less likely to die in the hospital and more likely to discharge from the hospital. In addition, patients with microvascular complications, who were on anti-coagulation therapy, had dyspnea at the time of admission, with higher levels of white cell count, C-reactive protein, and higher levels of aspartate aminotransferase were less likely to be discharged and within 28 days than their counterparts with a P-value of < 0.001 for these factors. | The authors did not clearly describe the role of DDP4 inhibitors users in the morbidity and mortality. |
| Cariou et al [22] | A nationwide multicenter observational study  | 2020 | Admitted into the hospitals  | 1,317 | Multivariable logistic regression analysis | Age, sex, body mass index, and lymphocyte count | Around 10.6% of the patients in this cohort experienced mortality; however 18.0% were discharged on the day 7. The final model adjusted for age and sex revealed that body mass index, patients’ age, lymphocyte count, obstructive sleep apnea, micro- and macrovascular complications related to DM were found to be independent risk factors of mortality on day 7 with a P-value < 0.05 for all these variables. | The findings revealed that among patients with diabetes who were positive for COVID-19, only body mass index was found to be positively associated with morbidity (tracheal intubation) and death within a week; however, there was no association between DDP4 inhibitors with morbidity and mortality among the same patients.  |
| Izzi-Engbeaya et al [30] | Retrospective cohort study | 2020 | In patients admitted in the hospital  | 889 | Multivariable logistic regression analysis, factors significantly associated with morbidity and mortality at P-value of < 0.05  | Age, gender, comorbidity, platelet count, ethnicity, anemia, temperature, respiratory rate, heart rate, systolic and diastolic blood pressures | In older males with heart disease, ischemic heart disease with low platelet count and several morbidities were found to be important risk factors for the poor outcomes such as higher mortality (death) and morbidity (indicated by admission to ICU) among COVID-19 patients with DM adjusting for confounders such as ethnicity, anemia, temperature, respiratory rate, heart rate, systolic and diastolic blood pressures. | The authors did not clearly describe the role of DDP4 inhibitors users in the morbidity and mortality. |
| Chen et al [21] | Retrospective cohort study  | 2020 | In patients admitted in the hospital  | 904  | Logistic regression analysis, a significant P-value for all the factors was < 0.05 | Age, sex type of medications, comorbidities such as hypertension and diabetes | Older diabetic patients had a higher tendency to die from COVID-19 than younger patients. Patients having diabetes and COVID and who were using insulin had higher mortality than those who were not using, therefore they need more attention. There was no significant difference in mortality related to COVID between those who were using ACE inhibitors or angiotensin receptor blockers.  | The authors did not clearly describe the role of DDP4 inhibitors users in the morbidity and mortality. |

DPP4: dipeptidyl peptidase-4; COVID-19: coronavirus disease 2019; DM: diabetes mellitus; ICU: intensive care unit; GLP-1: glucagon-like peptide-1; SGLT-2: sodium-glucose co-transporter-2; COPD: chronic obstructive pulmonary disease; ACE: angiotensin-converting enzyme.