**Effectiveness of REGEN-COV Antibody Combination in Preventing Severe COVID-19 Outcomes – A retrospective cohort study**

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**Supplemental Table 1: Outcomes associated with REGEN-COV treatment effectiveness, by age group**

|  |  |
| --- | --- |
|  | REGEN-COV effectiveness 95%CI  |
|  | Age ≥60 years old | Age <60 years old |
| Hospitalization due to COVID-19  | 55.3% (16.0%-75.7%) | 91.5%(28.2-99.0%) |
| Severe COVID-19  | 59.4% (20.2%-79.4%) | 86.3%(-147.2-99.2%) |
| Death due to COVID-19  | 93.8% (54.4%-99.2%) | N/A |

**Note:** Treatment effectiveness was measured as 1-Hazard ratio (HR), derived from the adjusted cox –proportional model that was applied after the matching. Patients were matched for: Age, population sector, sex, SES, BMI, immunosuppression status, pregnancy, and first vaccination dose status (vaccinated vs. unvaccinated; those who were vaccinated were treated as the number of weeks from the beginning of the COVID-19 national vaccination campaign until the first vaccination as an indication for health seeking behavior). The model was then further adjusted for: Age, population sector, sex, SES, BMI, number of flu vaccines received in the 5 years prior to COVID-19 infection, smoking status, number of vaccine doses, recent full vaccination status, first vaccination dose, and chronic diseases (cancer, chronic kidney disease, respiratory diseases, cardiovascular diseases, diabetes, hypertension, immunosuppression, neurological conditions, and liver diseases). Complete variable definitions are found in Supplemental Table 1.

Abbreviation: CI, confidence interval. NA, Not applicable due to rare outcome among the treated patients

**Supplemental table 2: Variable defintion**

|  |  |  |
| --- | --- | --- |
| **Variable name**  | **Defintion**  | **Timing**  |
| Exposure  | REGEN-COV (Yes/No)  | September 19, 2021 -December 8, 2021  |
| Outcome | Three different outcomes: 1. Hospitalization due to COVID-19. Defined as hospitalization that was reported to the Israeli MOH as a hospitalization of a SARS-CoV-2 infected individuals.
2. Severe COVID-19 based on the Israeli Ministry of Health definition. As defined by the hospitalizing institution per the Israeli MOH guidelines, consistent with the The first date during the hospitalization in which the individual was flagged as being NIH criteria for severe illness or critical illness: Individuals who have SpO2 30 breaths/min, or lung infiltrates >50%. Critical Illness: Individuals who have respiratory failure, septic shock, and/or
3. Death due to COVID-19. A death of a SARS-CoV-2 infected individual reported to the Israeli MOH.
 |  1. The start date of the hospitalization
2. The first date during the hospitalization in which the individual was flagged as being in a severe or critical state
3. The reported date of death
 |
| Age  | Age at infection date. Defined as continuous and categorical.Age group:  (1) 20-39; (2) 40-49; (3) 50-59; (4) 60-69; (5) 70-74; (6) ≥75 | Current  |
| Gender  | Male/Female  | Current  |
| Socio-economic status | For matching – we used it as as a catigorical variable with 20 level. For table 1 we categorized it into 3 levels: Low, medium , and high | Current  |
| Population group  | Jewish, Arab, Ultra-Orthodox Jewish  | Current  |
| Flu vaccination in the last 5 years | Number of influenza vaccination in the last 5 yeas prior to the index date. It is categorical variable that ranges between 0 –doses up to at least 5 doses of flu vaccine in the last 5 years prior to the index date  | Last 5 years  |
| BMI | Body Mass Index :Under weight <18.5Normal weight –BMI: 18.5-25.0 Overweight- BMI: >25-30 Obesity – BMI: >30  | Latest measurement in last 5 years not taken during pregnancy |
| Smoking status  | Categorical variable. Current smoker, past smoker, non-smoker  |  |
| Recent full vaccination status | Defined as two or more vaccination doses, and fewer than 150 days from the most recent vaccination dose until the first positive PCR test |  |
| First vaccination dose  | the number of weeks from the beginning of the COVID-19 national vaccination campaign until the first vaccination dose  |  |
| Hypertension  | ICD9 Code 401\*ICD9 Code 402\*ICD9 Code 403\*ICD9 Code 404\*ICD9 Code 405\* | Ever |
| Cardiovascular disease | ICD9 Code 410\*ICD9 Code 411\*ICD9 Code 412ICD9 Code 413\*ICD9 Code 414\*ICD9 Code 429.2, 429.7\*ICD9 Code V45.81, V45.82ICD9 Procedure Code 36.0\*ICD9 Procedure Code 36.1\*ICD9 Code 428\*ICD9 Code 398.91ICD9 Code 402.\_1ICD9 Code 404.\_1, ICD9 Code404.\_3ICD9 Code 416.9ICD9 Code 514ICD9 Code 425\*ICD9 Code 416\* | Ever |
| Respiratory disease  | Having any pulmonary disease (mentioned below) prior to the index date COPD: ICD9 codes: 491.2\*, 492.\* 496.\* Asthma: ICD9 code: 493.\*Other respiratory disease: ICD9 Code 277.0\* ICD9: Code 494\*. ICD9 : Code 515.\* | Ever  |
| Neurological conditions | ICD9 Code 290.\*ICD9 Code 294\*ICD9 Code 310.1ICD9 Code 331\*ATC Codes N06DA02, N06DA03ICD9 Code 358\*ICD9 Code 332.[0,1]ICD9 Code 345\*ICD9 Code 340ATC Codes L03AB07, L03AB08,L04AA07ICD9 Code 343\*ICD9 Code 333.4ICD9 Code 334\*ICD9 Code 356\*ICD9 Code 138ICD9 Code 335\*ICD9 Code 730.7\*ICD9 V12.02ICD9 Code 228.02ICD9 Code 307.23ICD9 Code 330.9ICD9 Code 331.3\*ICD9 Code 331.4ICD9 Code 333\*ICD9 Code 334\*ICD9 Code 336\*ICD9 Code 337ICD9 Code 335.1\*ICD9 Code 359.0ICD9 Code 359.21ICD9 Code 357.0ICD9 Code 237.7\*ICD9 Code 742.8[1,2] | For diagnosis codes, Ever For drugs, 4 or more dispensed in last 12 months |
| Cancer  | ICD9 Code 174\*ICD9 Code 175\*ICD9 Code 233.0ICD9 Code V10.3ICD9 Procedure Code 85.4\*ICD9 Code 153\*ICD9 Code 154\*ICD9 Code V10.5\*ICD9 Code V10.6\*ICD9 Code 185ICD9 Code V10.46ICD9 Code 162\*ICD9 Code V10.1\*ICD9 Code 188\*ICD9 Code V10.51ICD9 Code 183\*ICD9 Code V10.43ICD9 Code 179ICD9 Code 182\*ICD9 Code V10.42ICD9 Code 157\*ICD9 Code 191\*ICD9 Code 192\*ICD9 Code V10.85ICD9 Code 151\*ICD9 Code V10.04ICD9 Code 172\*ICD9 Code V10.82ICD9 Code 201\*ICD9 Code 200\*ICD9 Code 202.4\*ICD9 Code 204\*ICD9 Code 205\*ICD9 Code 206\*ICD9 Code 207.1\*ICD9 Code 208.1\*ICD9 Code 189\*ICD9 Code V10.52ICD9 Code 160\*ICD9 Code 161\*ICD9 Code 164.0ICD9 Code 195.0ICD9 Code V10.21ICD9 Code V10.22ICD9 Code 180\*ICD9 Code V10.41ICD9 Code 140\*ICD9 Code 141\*ICD9 Code 142\*ICD9 Code 143\*ICD9 Code 144\*ICD9 Code 145\*ICD9 Code 150\*ICD9 Code V10.03ICD9 Code 155\*ICD9 Code 156\*ICD9 Code V10.07ICD9 Code 170\*ICD9 Code V10.81ICD9 Code 193ICD9 Code V10.87ICD9 Code 171\*ICD9 Code 176\*ICD9 Code 184\*ICD9 Code 186\*ICD9 Code 187\*ICD9 Code V10.4\*ICD9 Code 203\*ICD9 Code 273.3ICD9 Code 152\*ICD9 Code 158\*ICD9 Code 159\*ICD9 Code 163\*ICD9 Code 164\*ICD9 Code 165\*ICD9 Code 181ICD9 Code 190\*ICD9 Code 192.8ICD9 Code 196\*ICD9 Code 197\*ICD9 Code 198\* | Last 5 years  |
| Chronic kidney disease | ICD Procedure Code 39.95ICD Procedure Code 54.98ICD9 Code 996.81ICD9 Code V42.0ICD Procedure Code 55.6\*ICD9 Code 403.\_1ICD9 Code 404.\_2ICD9 Code 404.\_3ICD9 Code 585\*ICD9 Code 586ICD9 Code 250.4\*ICD9 Code 274.1\*ICD9 Code 440.1ICD9 Code 581\*ICD9 Code 582\*ICD9 Code 583\*ICD9 Code 587ICD9 Code 588\*ICD9 Code 589\* | Ever  |
| Pregnancy  | Internal Clalit Registry | Current  |
| Diabetes | Having type 2 Diabetes or having Type 1 diabetes.Type 2 diabetes (T2DM): HbA1C > 6.5ATC Codes A10[A,B]ICD9 Code 250\*ICD9 Code 357.2ICD9 Code 362.0\*And not:ICD9 Code 250.\_1, 250.\_3Type 1 diabetes (T1DM): ICD9 Code 250.\_1, 250.\_3 | T2DM: For diagnosis codes, Ever For drugs, 4 or more dispensed in last 12 monthsT1DM: Ever  |
| Hypertension  | ICD9 Code 401\*ICD9 Code 402\*ICD9 Code 403\*ICD9 Code 404\*ICD9 Code 405\* | Ever  |
| Immunosuppression  | Any of:ICD9 Code 042\*ICD9 Code 043\*ICD9 Code 044\*ICD9 Code 795.71ICD9 Code V08ICD9 Code V42.8\*ICD9 Proc Code 41.0\*Or at least 2 of:ATC4 Code H02ABATC4 Code H02BXATC4 Code M01BAOr at least 2 of:ATC2 Code L04 | For diagnosis codes,EverFor drugs, 4 or moredispensed in last 12months |
| Liver disease | ICD9 Code 070.22ICD9 Code 070.23ICD9 Code 070.32ICD9 Code 070.33ICD9 Code 070.44ICD9 Code 070.54ICD9 Code V02.61ICD9 Code V02.62ICD9 Code 571\*ICD9 Code 275.1ICD9 Code 277.4ICD9 Code 452ICD9 Code 453.0ICD9 Code 571.8ICD9 Code 571.9 | Ever |

**Notes:** Additional confirmation of the diagnostic codes was done by checking the matching of the free text within the diagnosis description field.

Abbreviations: CHS: Clalit Health Services; ICD, International Classification of Disease. ATC, Anatomic therapeutic chemical; NDC, National drug code

**Supplemental figure 1: Flow chart for study participants**

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**Supplemental Figure 2: Love Plot for the Covariate Balance**

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**Legend :** A covariate balance plot showing the difference in the means for the different matched variables. A strict balance cut-off was set at 0.1.