Who is at risk of poor mental health following COVID-19 outpatient management?

Figures and Tables

Health after COVID-19 in Tyrol study team

2022-02-03

# Tables

**Table 1:** Baseline characteristic of the study cohorts.

| **Variable** | **AT1** | **IT1** | **Test2** | **pFDR3** | **Effect size4** |
| --- | --- | --- | --- | --- | --- |
| Survey completion | fall 2020: 63% (734) winter/spring 2021: 37% (423) Complete: n = 1157 | fall 2020: 4.4% (39) winter/spring 2021: 96% (854) Complete: n = 893 | χ² | p < 0.001 | V = 0.6 |
| Time between survey and diagnosis | Median = 79 [IQR: 40 - 180] Range: 28 - 400 Complete: n = 1157 | Median = 96 [IQR: 60 - 140] Range: 28 - 390 Complete: n = 893 | Mann-Whitney | p < 0.001 | r = 0.12 |
| Sex | female: 65% (753) male: 35% (404) Complete: n = 1157 | female: 68% (610) male: 32% (283) Complete: n = 893 | χ² | ns (p = 0.19) | V = 0.034 |
| Age | Median = 43 [IQR: 31 - 53] Range: 16 - 94 Complete: n = 1156 | Median = 45 [IQR: 35 - 55] Range: 18 - 95 Complete: n = 891 | Mann-Whitney | p = 0.0041 | r = 0.069 |
| up to 30 years: 22% (259) 31 - 65 years: 72% (831) > 65 years: 5.7% (66) Complete: n = 1156 | up to 30 years: 17% (148) 31 - 65 years: 78% (693) > 65 years: 5.6% (50) Complete: n = 891 | χ² | p = 0.0082 | V = 0.073 |
| Education | secondary: 44% (505) apprenticeship: 14% (164) elementary: 3.6% (41) tertiary: 38% (444) Complete: n = 1154 | secondary: 64% (575) apprenticeship: 0% (0) elementary: 0.22% (2) tertiary: 35% (315) Complete: n = 892 | χ² | p < 0.001 | V = 0.31 |
| Employment status | employed: 81% (939) unemployed: 9.4% (109) leave: 1.9% (22) retired: 7.5% (87) Complete: n = 1157 | employed: 82% (728) unemployed: 8.5% (76) leave: 1.8% (16) retired: 8.2% (73) Complete: n = 893 | χ² | ns (p = 0.88) | V = 0.02 |
| Smoking history | never: 60% (690) former: 31% (361) active: 9.2% (106) Complete: n = 1157 | never: 66% (588) former: 24% (215) active: 10% (90) Complete: n = 893 | χ² | p = 0.004 | V = 0.079 |
| Number of co-morbidities | absent: 50% (582) 1: 29% (332) 2: 12% (142) 3 and more: 8.7% (101) Complete: n = 1157 | absent: 59% (525) 1: 25% (219) 2: 11% (102) 3 and more: 5.3% (47) Complete: n = 893 | χ² | p < 0.001 | V = 0.095 |
| Daily medication | absent: 59% (688) 1 - 4 drugs: 38% (440) 5 drugs and more: 2.5% (29) Complete: n = 1157 | absent: 73% (649) 1 - 4 drugs: 26% (231) 5 drugs and more: 1.5% (13) Complete: n = 893 | χ² | p < 0.001 | V = 0.14 |
| Depression/anxiety before COVID-19 | DA-: 94% (1088) DA+: 6% (69) Complete: n = 1157 | DA-: 95% (852) DA+: 4.6% (41) Complete: n = 893 | χ² | ns (p = 0.27) | V = 0.03 |
| Sleep disorders before COVID-19 | 4.6% (53) Complete: n = 1157 | 4% (36) Complete: n = 893 | χ² | ns (p = 0.66) | V = 0.013 |
| Bruxism | 7.2% (83) Complete: n = 1157 | 5.3% (47) Complete: n = 893 | χ² | ns (p = 0.14) | V = 0.039 |
| BMI before COVID-19 | normal: 56% (648) overweigth: 28% (327) obesity: 15% (175) Complete: n = 1150 | normal: 65% (570) overweigth: 26% (231) obesity: 9.1% (80) Complete: n = 881 | χ² | p < 0.001 | V = 0.1 |
| Hypertension | 11% (130) Complete: n = 1157 | 9.4% (84) Complete: n = 893 | χ² | ns (p = 0.27) | V = 0.03 |
| Cardiovascular disease | 2.9% (34) Complete: n = 1157 | 2.9% (26) Complete: n = 893 | χ² | ns (p = 1) | V = 8e-04 |
| Pulmonary disease | 4.1% (48) Complete: n = 1157 | 2.6% (23) Complete: n = 893 | χ² | ns (p = 0.12) | V = 0.043 |
| Hay fever/allergy | 18% (208) Complete: n = 1157 | 11% (102) Complete: n = 893 | χ² | p < 0.001 | V = 0.091 |
| > 2 respiratory infections per year | 4.4% (51) Complete: n = 1157 | 2.9% (26) Complete: n = 893 | χ² | ns (p = 0.14) | V = 0.039 |
| > 2 bacterial infections per year | 3.9% (45) Complete: n = 1157 | 1.3% (12) Complete: n = 893 | χ² | p = 0.0021 | V = 0.077 |
| 1For categorical variables: percentage of the complete answers (n individuals). AT: Austria/Tyrol cohort, IT: Italy/South Tyrol cohort. | | | | | |
| 2Statistical test used for the AT vs IT comparison. | | | | | |
| 3Test p value corrected for multiple comparisons with Benjamini-Hochberg (FDR) method | | | | | |
| 4Effect size: Wilcoxon r or Cramer's V. | | | | | |

**Table 2:** Characteristic of the course of SARS-CoV2 infection and convalescence in the study cohorts.

| **Variable** | **AT1** | **IT1** | **Test2** | **pFDR3** | **Effect size4** |
| --- | --- | --- | --- | --- | --- |
| SARS-CoV2 outbreak | spring 2020: 27% (309) summer/fall 2020: 68% (789) winter/spring 2021: 5.1% (59) Complete: n = 1157 | spring 2020: 16% (144) summer/fall 2020: 54% (484) winter/spring 2021: 30% (265) Complete: n = 893 | χ² | p < 0.001 | V = 0.34 |
| Acute COVID-19 symptoms | 92% (1060) Complete: n = 1156 | 88% (782) Complete: n = 892 | χ² | p = 0.0067 | V = 0.066 |
| Number of acute symptoms | Median = 13 [IQR: 9 - 18] Range: 0 - 42 Complete: n = 1156 | Median = 13 [IQR: 7 - 18] Range: 0 - 39 Complete: n = 892 | Mann-Whitney | ns (p = 0.13) | r = 0.038 |
| Number of acute neurocognitive symptoms | Median = 1 [IQR: 0 - 2] Range: 0 - 3 Complete: n = 1157 | Median = 0 [IQR: 0 - 2] Range: 0 - 3 Complete: n = 893 | Mann-Whitney | ns (p = 0.66) | r = 0.011 |
| 0: 50% (574) 1: 20% (236) 2: 17% (197) 3: 13% (150) Complete: n = 1157 | 0: 52% (464) 1: 14% (127) 2: 16% (146) 3: 17% (156) Complete: n = 893 | χ² | p < 0.001 | V = 0.095 |
| Persistent COVID-19 symptoms | 48% (550) Complete: n = 1156 | 49% (440) Complete: n = 892 | χ² | ns (p = 0.52) | V = 0.017 |
| Number of persistent symptoms | Median = 0 [IQR: 0 - 3] Range: 0 - 34 Complete: n = 1156 | Median = 0 [IQR: 0 - 3] Range: 0 - 29 Complete: n = 892 | Mann-Whitney | ns (p = 0.56) | r = 0.015 |
| Number of persistent neurocognitive symptoms | Median = 0 [IQR: 0 - 0] Range: 0 - 3 Complete: n = 1157 | Median = 0 [IQR: 0 - 0] Range: 0 - 3 Complete: n = 893 | Mann-Whitney | p = 0.0067 | r = 0.065 |
| 0: 82% (946) 1: 7.3% (84) 2: 7.8% (90) 3: 3.2% (37) Complete: n = 1157 | 0: 77% (691) 1: 5.6% (50) 2: 9.6% (86) 3: 7.4% (66) Complete: n = 893 | χ² | p < 0.001 | V = 0.11 |
| Physical performance loss | Median = 13 [IQR: 1 - 26] Range: 0 - 100 Complete: n = 1151 | Median = 11 [IQR: 0 - 25] Range: 0 - 100 Complete: n = 884 | Mann-Whitney | ns (p = 0.35) | r = 0.024 |
| Complete convalescence | 54% (624) Complete: n = 1155 | 63% (563) Complete: n = 889 | χ² | p < 0.001 | V = 0.093 |
| 1Percentage of the complete answers (n individuals). AT: Austria/Tyrol cohort, IT: Italy/South Tyrol cohort. | | | | | |
| 2Statistical test used for the AT vs IT comparison. | | | | | |
| 3Test p value corrected for multiple comparisons with Benjamini-Hochberg (FDR) method | | | | | |
| 4Effect size: Wilcoxon r or Cramer's V. | | | | | |

**Table 3:** Rating of the mental health following COVID-19 in the study cohorts.

| **Variable** | **AT1** | **IT1** | **Test2** | **pFDR3** | **Effect size4** |
| --- | --- | --- | --- | --- | --- |
| Overall Mental Health | poor: 3.5% (40) fair: 18% (212) good: 49% (562) excellent: 30% (343) Complete: n = 1157 | poor: 2.9% (26) fair: 21% (189) good: 48% (430) excellent: 28% (248) Complete: n = 893 | χ² | ns (p = 0.44) | V = 0.039 |
| Overall Mental Health Score | Median = 1 [IQR: 0 - 1] Range: 0 - 3 Complete: n = 1157 | Median = 1 [IQR: 0 - 1] Range: 0 - 3 Complete: n = 893 | Mann-Whitney | ns (p = 0.29) | r = 0.027 |
| Quality of Life | poor: 4.3% (50) fair: 16% (185) good: 51% (590) excellent: 29% (332) Complete: n = 1157 | poor: 3.4% (30) fair: 23% (201) good: 54% (485) excellent: 20% (177) Complete: n = 893 | χ² | p < 0.001 | V = 0.12 |
| Quality of Life Score | Median = 1 [IQR: 0 - 1] Range: 0 - 3 Complete: n = 1157 | Median = 1 [IQR: 1 - 2] Range: 0 - 3 Complete: n = 893 | Mann-Whitney | p < 0.001 | r = 0.1 |
| Depression Score | Median = 1 [IQR: 0 - 2] Range: 0 - 6 Complete: n = 1154 | Median = 1 [IQR: 0 - 2] Range: 0 - 6 Complete: n = 892 | Mann-Whitney | p = 0.0082 | r = 0.063 |
| Depression Screening-positive | 17% (200) Complete: n = 1154 | 23% (207) Complete: n = 892 | χ² | p = 0.0028 | V = 0.073 |
| Anxiety score | Median = 0 [IQR: 0 - 2] Range: 0 - 6 Complete: n = 1151 | Median = 1 [IQR: 0 - 2] Range: 0 - 6 Complete: n = 893 | Mann-Whitney | p < 0.001 | r = 0.14 |
| Anxiety Screening-positive | 12% (143) Complete: n = 1151 | 19% (172) Complete: n = 893 | χ² | p < 0.001 | V = 0.094 |
| Psychosocial Stress Score | Median = 4 [IQR: 2 - 6] Range: 0 - 19 Complete: n = 1153 | Median = 4 [IQR: 2 - 7] Range: 0 - 19 Complete: n = 890 | Mann-Whitney | ns (p = 0.47) | r = 0.019 |
| Substantial psychosocial stress | 21% (246) Complete: n = 1153 | 26% (228) Complete: n = 890 | χ² | p = 0.045 | V = 0.05 |
| 1Percentage of the complete answers (n individuals). AT: Austria/Tyrol cohort, IT: Italy/South Tyrol cohort. | | | | | |
| 2Statistical test used for the AT vs IT comparison. | | | | | |
| 3Test p value corrected for multiple comparisons with Benjamini-Hochberg (FDR) method | | | | | |
| 4Effect size: Wilcoxon r or Cramer's V | | | | | |

# Figures

![Figure 1: Study inclusion flow diagram.](data:application/pdf;base64,)

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![Figure 2: Random Forest modeling of the mental health and quality of life scoring during COVID-19 convalescence.](data:application/pdf;base64,)

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**Figure 2. Random Forest modeling of the mental health and quality of life scoring during COVID-19 convalescence.**

The effects of 201 demographic, clinical, socioeconomic and psychosocial factors (**Supplementary Table S1**) on the anxiety (ANX), depression (DPR), overall mental health (OMH) and quality of life (QoL) scoring were modeled with Random Forest technique. Numeric variables were minimum/maximum normalized prior to modeling. The models were trained and calibrated in the Austria (AT) cohort, 10-fold cross-validated (CV) and their predictions validated in the Italy (IT) cohort. The top 20 most influential explanatory variables were identified in the AT cohort for each mental health and life quality score by unbiased MSE statistic (**Supplementary Figures S6 - S9** ). Numbers of complete observations are indicated in (**A**).

**(A)** Random Forest model performance measured by root mean squared error (RMSE) and the fraction of explained variance in mental health and quality of life scoring expressed as R2.

**(B)** Identification of common influential explanatory variables. Left: overlap in the top 20 most influential explanatory variables presented in a quasi-proportional Venn plot. Right: MSE statistics for the most influential explanatory statistics shared by all responses, point size and color corresponds to the MSE value.

NC: neurocognitive symptoms, imp. conc.: impaired concentration, phys.: physical, #: number of.

![Figure 3: Association of the most influential factors with the mental health readouts investigated by univariable modeling.](data:application/pdf;base64,)

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Association of the most influential factors for the mental health and quality of life scoring (**Figure 2B**) with the anxiety (ANX) (**A**), depression (DPR) (**B**), overall mental health (OMH) (**C**) and quality of life (QoL) (**D**) rating was investigated by univariable, age- and sex-weighted Poisson regression (**Supplementary Table S2**). Numeric variables were minimum/maximum normalized prior to modeling. Exponent estimate values with 95 confidence intervals presented as Forest plots. Explained variance fraction estimated by adjusted R2 is presented in adjunct bar plots. Numbers of complete observations are shown under the plots. AT: Austria, IT: Italy.

NC: neurocognitive symptoms, imp. conc.: impaired concentration, phys.: physical, #: number of.

![Figure 4: Clustering of the study participants by the most influential factors affecting the mental health and quality of life scoring.](data:application/pdf;base64,)

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**Figure 4. Clustering of the study participants by the most influential factors affecting the mental health and quality of life scoring.**

Study participants were assigned to the Low Risk (LR), Intermediate Risk (IR) and High Risk (HR) subsets by clustering in respect to the most influential factors for the mental health and quality of life scoring (**Figure 2B**). Numeric variables were minimum/maximum normalized prior to modeling. The procedure in the training Austria (AT) cohort involved the self-organizing map (SOM, 13 13 hexagonal grid, Manhattan distance between participants) and the hierarchical clustering (Ward D2 method, Manhattan distance between the SOM nodes) algorithms. Assignment of the Italy (IT) cohort participants to the clusters was accomplished by the k-nearest neighbors classification. Numbers of participants assigned to the clusters are presented in (**B**).

**(A)** Cluster assignment of the participants in the 3-dimensional principal component (PC) analysis score plot. First two components are shown. Percentages of the data set variance associated with the particular PC are presented in the plot axes.

**(B)** Heat map of the minimum/maximum-normalized clustering features.

NC: neurocognitive symptoms, imp. conc.: impaired concentration, phys.: physical, #: number of.

![Figure 5: Mental health and quality of life scoring, depression and anxiety prevalence in the mental disorder risk clusters.](data:application/pdf;base64,)

Figure 5: Mental health and quality of life scoring, depression and anxiety prevalence in the mental disorder risk clusters.

**Figure 5. Mental health and quality of life scoring, depression and anxiety prevalence in the mental disorder risk clusters.**

Study participants were assigned to the Low Risk (LR), Intermediate Risk (IR) and High Risk (HR) subsets as presented in **Figure 4**. Numbers of participants assigned to the clusters are presented in (**E**).

**(A - D)** Rating of anxiety (ANX) (**A**), depression (DPR) (**B**), overall mental health (OMH) (**C**) and quality of life (QoL) (**D**) in the clusters presented as violin plots, diamonds with whiskers represent medians with IQRs. Statistical significance was assessed by Kruskal-Wallis test. P values corrected for multiple testing with Benjamini-Hochberg method and effect size statistic values are shown in the plot captions

**(B)** Frequency of positive depression (DPR+) and anxiety (ANX+) screening in the clusters. Statistical significance was assessed by Benjamini-Hochberg-corrected test, effect size was expressed as Cramer’s V.

![Figure 6: Characteristic of baseline features, COVID-19 course and recovery in participants with pre-existing depression or anxiety.](data:application/pdf;base64,)

Figure 6: Characteristic of baseline features, COVID-19 course and recovery in participants with pre-existing depression or anxiety.

**Figure 6. Characteristic of baseline features, COVID-19 course and recovery in participants with pre-existing depression or anxiety.**

Differences in baseline characteristic, COVID-19 course, recovery, mental health and quality of life scoring between the participants with pre-existing depression or anxiety (DA+) and the subjects without mental disorder history (DA-) were assessed by or Mann-Whitney test in the Austria (AT) and Italy (IT) cohort. The testing results were corrected form multiple testing with Benjamini-Hochberg method (FDR: False Discovery Rate). Numbers of DA+ and DA- participants are shown in (**A**).

**(A)** Multiple testing-adjusted significance (pFDR) and effect size (categorical: Cramer’s V for categorical factors, numeric features: Wilcoxon r) for the investigated variables. Variables significantly different between DA+ and DA- are highlighted in red.

**(B)** Values of the features significantly different between DA+ and DA- participants in both AT and IT collectives presented in violin plots. The numeric features were minimum/maximum normalized. Orange diamonds represent mode (categorical variables) or median values (numeric variables).

pre-CoV: before COVID-19, sleep disord.: sleep disorder, freq. resp. inf.: > 2 respiratory infections per yes before COVID-19, daily medic.: number of drugs taken daily, comorb.: comorbidities, #: number of, QoL: quality of life, OMH: overall mental health, ANX: anxiety, NC: neurocognitive symptoms.

![Figure 7: Summary of the study results.](data:application/pdf;base64,)

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