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

## Figures and Tables

#### Health after COVID-19 in Tyrol study team

#### 2021-09-20

## Contents

Tables	2
Figures	6

#### **Tables**

Table 1: Baseline characteristic of the study cohorts.

AT: Austria/Tyrol cohort, IT: Italy/South Tyrol cohort, Test: statistical test used for the AT vs IT comparison, Significance: test p value corrected for multiple comparisons with Benjamini-Hochberg method.

Variable	AT	IT	Test	Significance
Sex	female: 65.1% (753) male: 34.9% (404) n = 1157	female: 68.3% (610) male: 31.7% (283) n = 893	$\chi^2$	ns
	median(IQR) = $43 (31 - 53)$ range = $16 - 94$ n = $1156$	median(IQR) = 45 (35 - 55) range = 18 - 95 n = 891	U	p = 0.0044
Age	up to 30 y: 22.4% (259) 31 - 65 y: 71.9% (831) 65 y and more: 5.71% (66) n = 1156	up to 30 y: 16.6% (148) 31 - 65 y: 77.8% (693) 65 y and more: 5.61% (50) n = 891	$\chi^2$	p = 0.0088
Education	secondary: 43.8% (505) apprenticeship: 14.2% (164) elementary: 3.55% (41) tertiary: 38.5% (444) n = 1154	secondary: 64.5% (575) elementary: 0.224% (2) tertiary: 35.3% (315) n = 892	$\chi^2$	p = 6.4e-41
Employment status	employed: 81.2% (939) unemployed: 9.42% (109) leave: 1.9% (22) retired: 7.52% (87) n = 1157	employed: 81.5% (728) unemployed: 8.51% (76) leave: 1.79% (16) retired: 8.17% (73) n = 893	$\chi^2$	ns
Smoking history	never: 59.6% (690) former: 31.2% (361) active: 9.16% (106) n = 1157	never: 65.8% (588) former: 24.1% (215) active: 10.1% (90) n = 893	$\chi^2$	p = 0.0044
Number of co-morbidities	absent: 50.3% (582) 1: 28.7% (332) 2: 12.3% (142) 3 and more: 8.73% (101) n = 1157	absent: 58.8% (525) 1: 24.5% (219) 2: 11.4% (102) 3 and more: 5.26% (47) n = 893	$\chi^2$	p = 0.001
Daily medication	absent: 59.5% (688) 1 - 4 drugs: 38% (440) 5 drugs and more: 2.51% (29) n = 1157	absent: 72.7% (649) 1 - 4 drugs: 25.9% (231) 5 drugs and more: 1.46% (13) n = 893	$\chi^2$	p = 2.7e-08
Depression/anxiety before COVID-19	5.96% (69) n = 1157	4.59% (41) n = 893	$\chi^2$	ns
Sleep disorders before COVID-19	4.58% (53) n = 1157	4.03% (36) n = 893	$\chi^2$	ns

Table 1: Baseline characteristic of the study cohorts.

AT: Austria/Tyrol cohort, IT: Italy/South Tyrol cohort, Test: statistical test used for the AT vs IT comparison, Significance: test p value corrected for multiple comparisons with Benjamini-Hochberg method. (continued)

Variable	AT	IT	Test	Significance
Bruxism	7.17% (83) n = 1157	5.26% (47) n = 893	$\chi^2$	ns
BMI before COVID-19	normal: 56.3% (648) overweigth: 28.4% (327) obesity: 15.2% (175) n = 1150	normal: 64.7% (570) overweigth: 26.2% (231) obesity: 9.08% (80) n = 881	$\chi^2$	p = 0.00011
Hypertension	11.2% (130) n = 1157	9.41% (84) n = 893	$\chi^2$	ns
Cardiovascular disease	2.94% (34) n = 1157	2.91% (26) n = 893	$\chi^2$	ns
Pulmonary disease	4.15% (48) n = 1157	2.58% (23) n = 893	$\chi^2$	ns
Hay fever/allergy	18% (208) n = 1157	11.4% (102) n = 893	$\chi^2$	p = 0.00021

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

AT: Austria/Tyrol cohort, IT: Italy/South Tyrol cohort, Test: statistical test used for the AT vs IT comparison, Significance: test p value corrected for multiple comparisons with Benjamini-Hochberg method.

Variable	AT	IT	Test	Significance
Acute COVID-19 symptoms	91.7% (1060) n = 1156	87.7% (782) n = 892	$\chi^2$	p = 0.0068
Number of acute symptoms	median(IQR) = 13 (9 - 18) range = 0 - 42 n = 1156	median(IQR) = 13 (7 - 18) range = 0 - 39 n = 892	U	ns
Number of acute	median(IQR) = 1 (0 - 2) range = 0 - 3 n = 1157	median(IQR) = 0 (0 - 2) range = 0 - 3 n = 893	U	ns
neurocognitive symptoms	0: 49.6% (574) 1: 20.4% (236) 2: 17% (197) 3: 13% (150) n = 1157	0: 52% (464) 1: 14.2% (127) 2: 16.3% (146) 3: 17.5% (156) n = 893	$\chi^2$	p = 0.0015
Persistent COVID-19 symptoms	47.6% (550) n = 1156	49.3% (440) n = 892	$\chi^2$	ns
Number of persistent symptoms	median(IQR) = 0 (0 - 3) range = 0 - 34 n = 1156	median(IQR) = 0 (0 - 3) range = 0 - 29 n = 892	U	ns
Number of persistent neurocognitive symptoms	median(IQR) = 0 (0 - 0) range = 0 - 3 n = 1157	median(IQR) = 0 (0 - 0) range = 0 - 3 n = 893	U	p = 0.0068
	0: 81.8% (946) 1: 7.26% (84) 2: 7.78% (90) 3: 3.2% (37) n = 1157	0: 77.4% (691) 1: 5.6% (50) 2: 9.63% (86) 3: 7.39% (66) n = 893	$\chi^2$	p = 0.00032

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

AT: Austria/Tyrol cohort, IT: Italy/South Tyrol cohort, Test: statistical test used for the AT vs IT comparison, Significance: test p value corrected for multiple comparisons with Benjamini-Hochberg method.

Variable	AT	IT	Test	Significance
Overall Mental Health	poor: 3.46% (40) fair: 18.3% (212) good: 48.6% (562) excellent: 29.6% (343) n = 1157	poor: 2.91% (26) fair: 21.2% (189) good: 48.2% (430) excellent: 27.8% (248) n = 893	$\chi^2$	ns
Overall Mental Health Score	$\begin{aligned} & mean(SD) = 0.956 \\ & (0.785) \\ & median(IQR) = 1 \; (0 - 1) \\ & range = 0 - 3 \\ & n = 1157 \end{aligned}$	mean(SD) = 0.992 (0.779) median(IQR) = 1 (0 - 1) range = 0 - 3 n = 893	U	ns
Quality of Life	poor: 4.32% (50) fair: 16% (185) good: 51% (590) excellent: 28.7% (332) n = 1157	poor: 3.36% (30) fair: 22.5% (201) good: 54.3% (485) excellent: 19.8% (177) n = 893	$\chi^2$	p = 8.3e-06
Quality of Life Score	mean(SD) = 0.959 (0.787) median(IQR) = 1 (0 - 1) range = 0 - 3 n = 1157	mean(SD) = 1.09 (0.741) median(IQR) = 1 (1 - 2) range = 0 - 3 n = 893	U	p = 2.1e-05
DPR score	mean(SD) = 1.39 (1.58) median(IQR) = 1 (0 - 2) range = 0 - 6 n = 1154	mean(SD) = 1.61 (1.68) median(IQR) = 1 (0 - 2) range = 0 - 6 n = 892	U	p = 0.0076
Depression Screening-positive	17.3% (200) n = 1154	23.2% (207) n = 892	$\chi^2$	p = 0.0023
Anxiety score	mean(SD) = 0.949 (1.33) median(IQR) = 0 (0 - 2) range = 0 - 6 n = 1151	mean(SD) = 1.35 (1.57) median(IQR) = 1 (0 - 2) range = 0 - 6 n = 893	U	p = 5.2e-09
Anxiety Screening-positive	12.4% (143) n = 1151	19.3% (172) n = 893	$\chi^2$	p = 7.1e-05
Psychosocial Stress Score	mean(SD) = $4.28 (3.53)$ median(IQR) = $4 (2 - 6)$ range = $0 - 19$ n = $1153$	mean(SD) = $4.4 (3.54)$ median(IQR) = $4 (2 - 7)$ range = $0 - 19$ n = $890$	U	ns
Substantial psychosocial stress	21.3% (246) n = 1153	25.6% (228) n = 890	$\chi^2$	p = 0.038

#### **Figures**

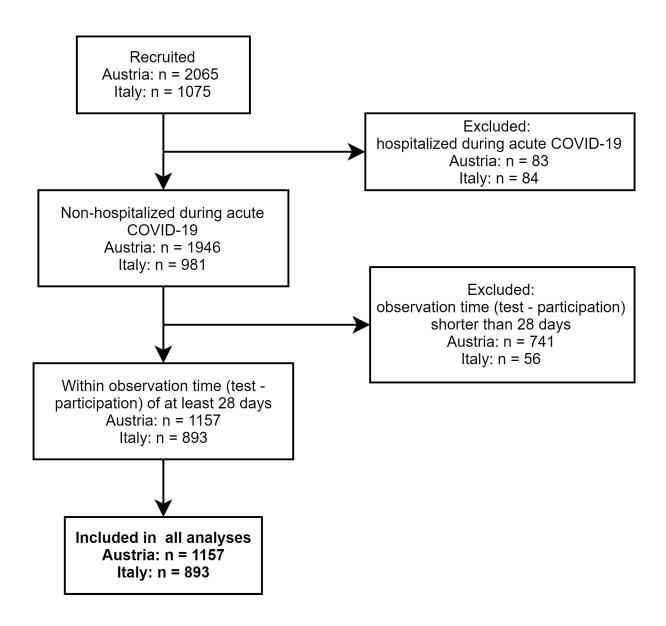


Figure 1: CONSORT flow diagram for the study cohorts.

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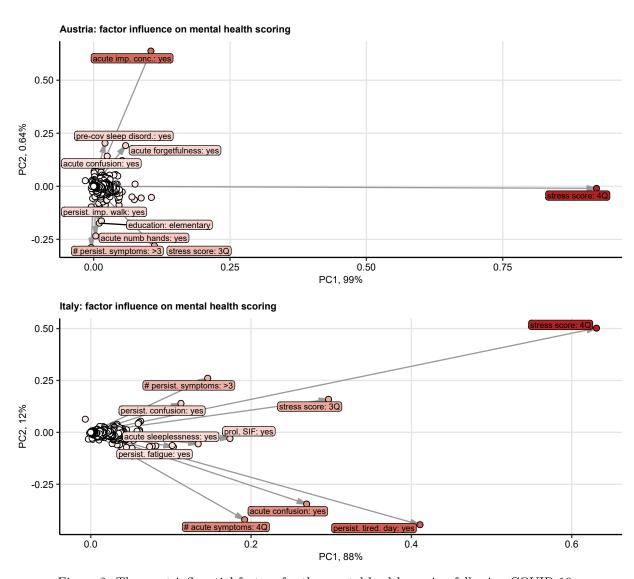


Figure 2: The most influential factors for the mental health scoring following COVID-19.

#### Figure 2. The most influential factors for the mental health scoring following COVID-19.

The effects of 144 demographic, clinical, socioeconomic and psychosocial factors (**Supplementary Table S3**) on the overall mental health, quality of life and depression scoring (**Supplementary Table S1**) was modeled with random forest technique (**Supplementary Figures S1 - S4**) and the impacts of each candidate factors on the model fits calculated and subjected to two-dimensional centered principal component analysis. Factors' loadings in respect to the principal components (PC) are presented in the plots, percent variance is shown in the axes. Top 10 factors with the largest loadings vectors as a measure of net mental scoring influence were labeled, point color corresponds to the vector length.

prol.: prolonged, SIF: severe illness feeling, imp.: impaired, conc.: concentration, #: number, tired.day.: tiredness at day, pre-cov sleep disord.: sleep disorder before COVID-19, 3Q, 4Q:  $3^{\rm rd}$  and  $4^{\rm th}$  quartile, persist.: persistent.

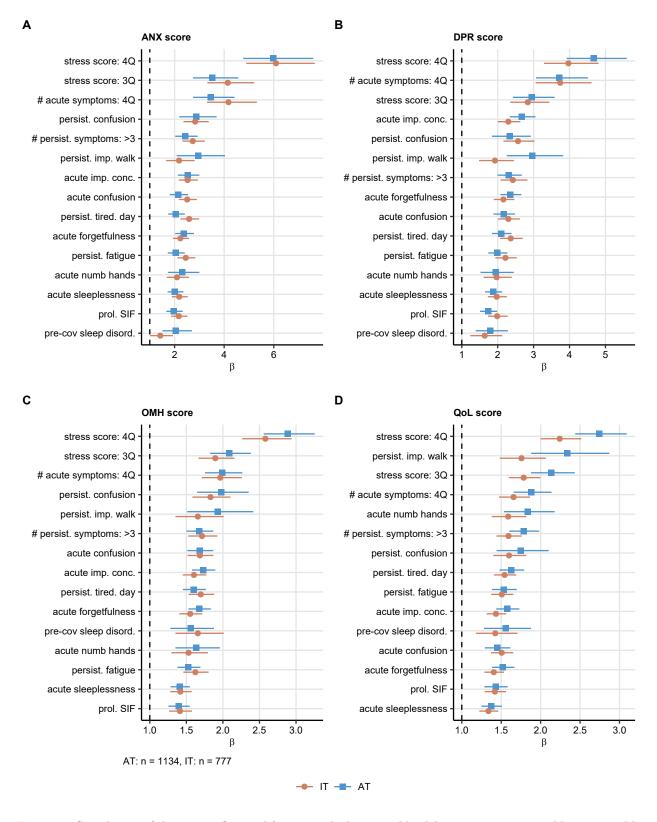


Figure 3: Correlation of the most influential factors with the mental health scoring investigated by univariable modeling.

## Figure 3. Correlation of the most influential factors with the mental health scoring investigated by univariable modeling.

Correlation of the 10 most influential factors affecting the net mental health scoring (**Figure 2**) with the anxiety (ANX) (**A**), depression (DPR) (**B**), overall mental health (OMH) (**C**) and quality of life (QoL) (**D**) rating was investigated by a series of univariable, age- and sex-weighted Poisson linear models (see: **Supplementary Table S5** for the full modeling results). Estimate values ( $\beta$ , points) with 95% confidence intervals (whiskers) for the significant correlations in both the Austria/Tyrol (AT) and Italy/South Tyrol (IT) cohort are presented as forest plots.

prol.: prolonged, SIF: severe illness feeling, imp.: impaired, conc.: concentration, #: number, tired.day.: tiredness at day, pre-cov sleep disord.: sleep disorder before COVID-19, 3Q, 4Q:  $3^{\rm rd}$  and  $4^{\rm th}$  quartile, persist.: persistent.

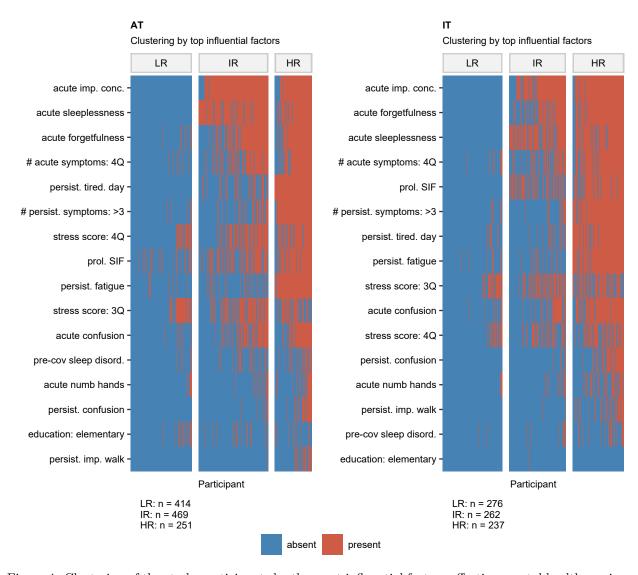


Figure 4: Clustering of the study participants by the most infleuntial factors affecting mental health scoring.

# Figure 4. Clustering of the study participants by the most influential factors affecting mental health scoring.

Study participants were assigned to the Low Risk (LR), Intermediate Risk (IR) and High Risk (HR) subsets by clustering analysis of the most influential factors affecting the net mental health scoring (**Figure 2**) with the self-organizing map (SOM,  $11 \times 11$  hexagonal grid, Jaccard distance between participants) and the hierarchical clustering (Ward D2 method, Euclidean distance between the SOM nodes) algorithms. Presence/absence of the features is presented as heat maps. N numbers of individuals assigned to the clusters are presented next to the plots.

prol.: prolonged, SIF: severe illness feeling, imp.: impaired, conc.: concentration, #: number, tired.day.: tiredness at day, pre-cov sleep disord.: sleep disorder before COVID-19, 3Q, 4Q: 3<sup>rd</sup> and 4<sup>th</sup> quartile, persist.: persistent.

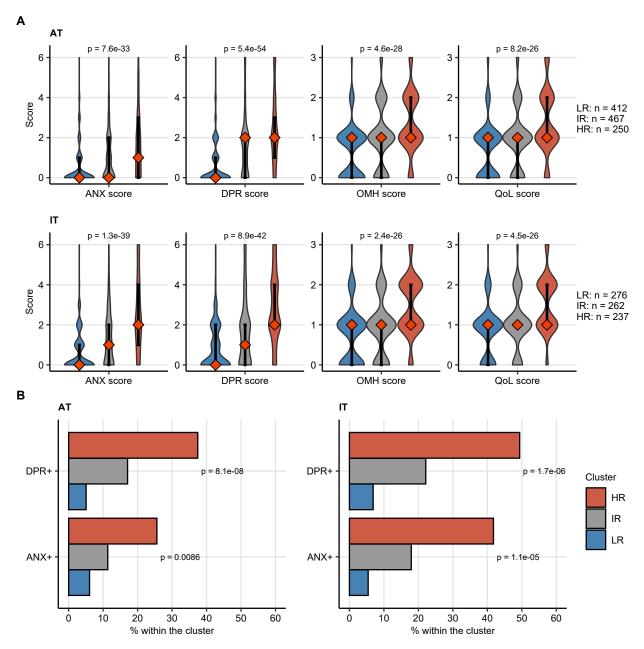


Figure 5: Mental health scoring, depression and anxiety prevalence in the mental health risk clusters

## Figure 5. Mental health 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**.

- (A) Rating of anxiety (ANX), depression (DPR), overall mental health (OMH) and quality of life (QoL) in the clusters presented as violin plots, diamonds with whiskers represent medians with IQRs. Statistical significance was assessed by Kuskal-Wallis test.
- (B) Frequency of positive depression (DPR+) and anxiety (ANX+) screening in the clusters. Statistical significance was assessed by  $\chi^2$  test.

P values corrected for multiple comparisons with Benjamini-Hochberg method are shown in the plots. N

numbers of individuals assigned to the clusters are presented next to the plots.

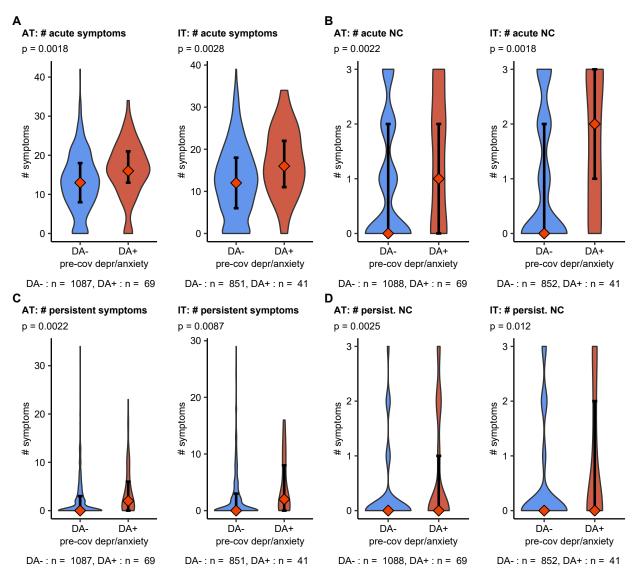


Figure 6: Depression or anxiety before COVID-19 and COVID-19 symptom burden.

#### Figure 6. Depression or anxiety before COVID-19 and COVID-19 symptom burden.

Association of depression or anxiety before COVID-19 with the overall number of acute and persistent COVID-19 symptoms and neurocognitive (NC) COVID-19 symptoms was assessed by Mann-Whitney U test. Symptom numbers are presented as violin plots, diamonds with whiskers represent medians with IQRs. p values corrected for multiple comparisons with Benjamini-Hochberg method are shown in plot sub-headings. N numbers of observations are indicated below the plots.