# COVID-19 olfactory dysfunction: associations between coping, quality of life, and mental health

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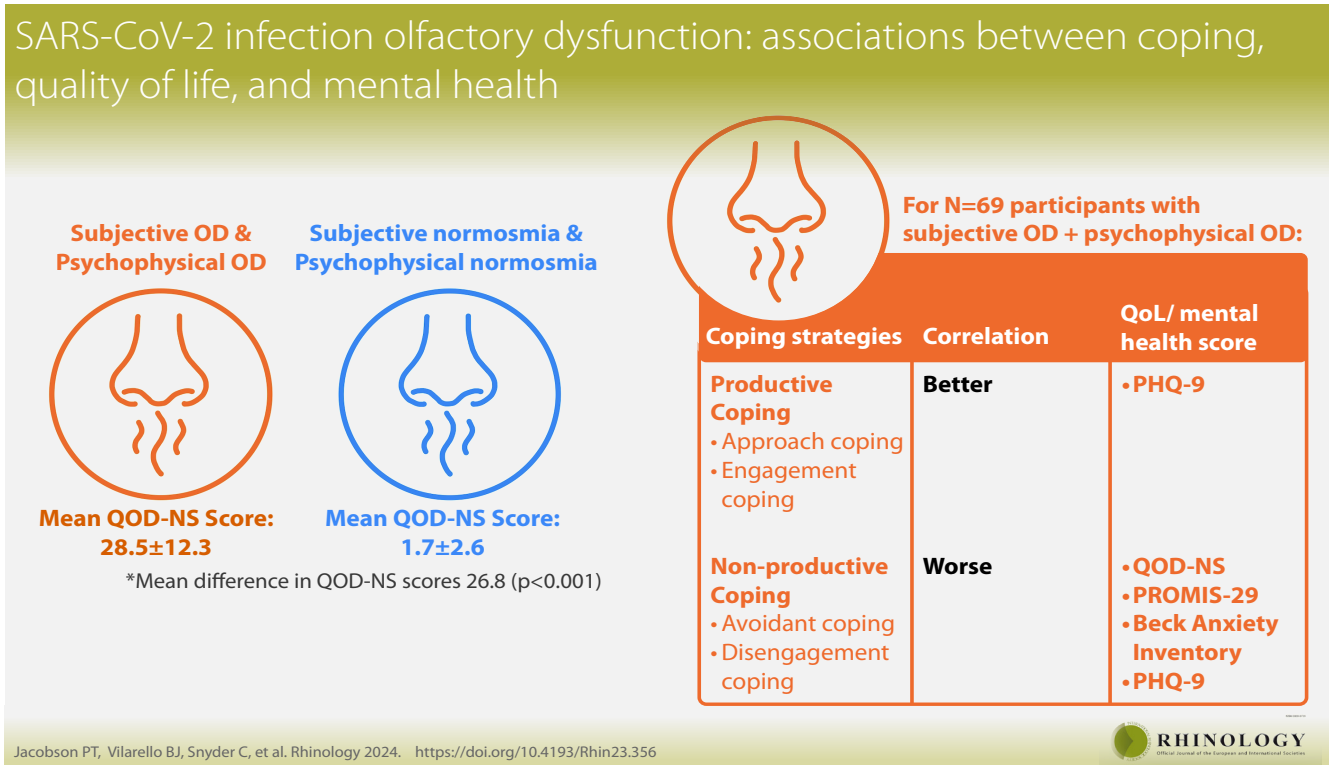


## Abstract

**Background**: Persistent olfactory dysfunction (OD) is a common symptom following SARS-CoV-2 infection that can greatly impact quality of life (QoL). Because coping strategies have been shown to moderate the effect of disease symptoms on functional and affective outcomes, this study aims to determine whether specific coping strategies are associated with and moderate QoL outcomes. **Methodology**: Participants with prior SARS-CoV-2 infection underwent psychophysical olfactory testing with Sniffin' Sticks and completed questionnaires to elicit subjective olfactory function, coping strategies, olfactory-specific QoL, general QoL, and mental health. **Results**: There were 93 participants included in the study. Olfactory specific QoL scores were significantly worse among individuals with subjective and psychophysically measured OD compared to those with subjective and psychophysically confirmed normosmia. Olfactory-specific QoL, general QoL, and anxiety symptom scores were positively correlated with avoidant and disengagement coping among individuals with subjective and psychophysically measured OD. Depression symptom scores were positively correlated with avoidant and disengagement coping and negatively correlated with approach and engagement coping. There were no significant moderating effects on the association between olfactory performance and QoL or mental health screening assessment. **Conclusions**: Approach and engagement coping mechanisms are associated with improved depression, whereas avoidant and disengagement coping tracks with worse QoL and mental health screening assessment, offering an opportunity to counsel patients accordingly.

**Key words**: COVID-19, SARS-CoV-2 infection, olfaction disorders, smell, psychological adaptation, quality of life

## Introduction

Infection with the SARS-CoV-2 virus has affected millions of people globally and can result in numerous neurological symptoms[1], including olfactory dysfunction (OD), which is reported present in approximately half of infected individuals[2,3]. Among those who develop OD acutely, it is estimated that 5.6% experience persistent OD that is present for more than three months[4]. Additionally, individuals with post-viral OD can frequently present with olfactory distortions, especially parosmia[5].

Prior research has demonstrated that persistent OD secondary to causes such as sinonasal disease, traumatic brain injuries, and neurodegenerative diseases can impact one's quality of life (QoL)[6]. Additionally, there have been studies looking specifically at the impact COVID-19-related OD has had on QoL[7–9], with some showing that COVID-19-related OD has a greater impact on olfactory-specific QoL compared to chronic rhinosinusitis-related OD[10]. Lower psychophysical olfactory performance as assessed with Sniffin' Sticks, along with worse subjective assessment of olfaction, younger age, and female sex each has been associated with poorer olfactory-specific QoL[11]. Decreased energy, poor sleep quality, and increased fatigue have been reported by individuals with OD after SARS-CoV-2 infections, as well as increased mental health problems and impaired mood[12–15]. People with COVID-19-related OD have impaired nutrition, poorer social functioning, and an inability to detect environmental dangers such as fires, gas leaks, and spoiled food[12–14]. Individuals who experience parosmia due to SARS-CoV-2 infections may present with normosmia on psychophysical olfaction testing, but will often have more disruption in their activities of daily life and a worse quality of life compared to those who experience solely hyposmia or anosmia[5]. Based on early estimates that SARS-CoV-2 infection causes acute olfactory loss in nearly 50% of cases and that 8% are impacted by parosmia, while 5.6%-34.6% of those individuals suffer from persistent OD[1,4,5,16,17], the potential impact on QoL and diminished mental health is substantial.

Individuals adopt coping strategies after the development of OD, regardless of etiology[18–21]. It has been shown that individuals with congenital anosmia or persistent OD have better QoL compared to those with recent smell loss[19,22], indicating the importance of well-developed coping strategies. The utilization of poor coping mechanisms can have detrimental effects on QoL outcomes[23,24]. Coping strategies have been shown to moderate the effect of various disease symptoms on functional and affective outcomes[25,26], though this has not yet been studied in OD. Therefore, the primary objectives of this study are to determine which coping strategies are associated with better QoL and mental health outcomes and determine whether specific coping strategies can moderate the association between OD and QoL.

The secondary objectives of this study are to determine QoL and mental health outcome differences among individuals with and without smell loss who have previously been diagnosed with SARS-CoV-2 infection.

## Materials and methods

### Study design and participants

In this prospective, observational study, participants were recruited at a tertiary care university teaching hospital through otolaryngology clinic referrals, flyer postings, and an online research study recruitment platform. Individuals with a history of SARS-CoV-2 infection diagnosed by polymerase chain reaction or antibody serology were eligible to enroll. Participants underwent a nasal endoscopy before enrollment in the study to rule out any sinonasal conditions potentially contributing to OD and to assign an Olfactory Cleft Endoscopy Scale (OCES) score. Participants were excluded from analysis if they had any preexisting neurological issue such as stroke, traumatic brain injury, or neurodegenerative disease, rated their sense of smell prior to their SARS-CoV-2 infection as <33.5 on a scale of 0 (no sense of smell) to 100 (excellent sense of smell), had a rhinologic subdomain score greater than 21 on the SNOT-22, answered "problem as bad as it can be" to any of the rhinologic subdomain questions on the SNOT-22, or had an OCES score of 3 or more indicating probable rhinologic disease[27]. All study procedures were approved by the Columbia University Irving Medical Center Institutional Review Board and informed consent was obtained from each participant.

### Data collection

Participants completed a detailed online questionnaire eliciting smell history, SARS-CoV-2 infection history, vaccination status, QoL, mental health, demographics, and coping strategies. Psychophysical olfactory testing was performed during an in-person assessment. Participants' subjective report of olfaction was obtained as part of their smell history. For this study, parosmia was defined as endorsement of parosmia symptoms during rhinologic clinical exam, or answering "often" or "always" to either of the following statements: "food tastes different than it should because of a problem with odors" or "odors that are pleasant to others are unpleasant to me"[28,29]. Individuals endorsing a diminished sense of smell, complete loss of smell, or distorted sense of smell at the time of questionnaire completion were placed in the subjective OD group.

### Olfactory testing

The extended Sniffin' Sticks test was utilized to obtain psychophysical scoring of participants' olfaction. The Sniffin' Sticks test consists of 3 separate subtests including threshold, discrimination, and identification. The highest score possible for each subtest is 16 points, with a total cumulative TDI score of 48 possible

points. Based on normative population data from the validation study[30], normosmia was defined as a score greater than 30.75, hyposmia was defined as a score greater than 16.25 but equal to or less than 30.75, and anosmia was defined as a score equal to or less than 16.25.

Participants were not initially recruited based on subjective or psychophysical olfaction scores, but rather based on a positive history of SARS-CoV-2 infection. After data collection, participants were separated into 2 main groups based on subjective olfaction and 4 subgroups based on subjective olfaction and psychophysical olfaction testing scores. The subgroups were as follows: group A represents individuals with subjective OD and hyposmia or anosmia on olfactory testing, group B includes those with subjective OD and normosmia on olfactory testing, group C represents individuals with subjectively normal smell and normosmia on olfaction testing, and group D includes those who had normal smell subjectively but hyposmia or anosmia on olfaction testing.

### Questionnaires

To examine QoL outcomes in this study, the Questionnaire of Olfactory Disorders – Negative Statements (QOD-NS) was used to measure olfactory-specific QoL, while the Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29) was used to measure general QoL. The QOD-NS is a validated questionnaire[31] that consists of 17 statements specifically relating olfaction to daily life. Scores can range from 0-51 with higher scores representing a higher degree of impairment in olfactory-specific QoL. The PROMIS-29 is another validated questionnaire[32] that consists of 29 questions and statements inquiring about physical function, anxiety, depression, fatigue, sleep disturbance, social functioning, and pain interference. Scores can range from 28-150 points with lower scores representing better QoL.

Mental health outcomes were examined using the Patient Health Questionnaire-9 (PHQ-9) to screen for depression and the Beck Anxiety Inventory (BAI) to screen for anxiety. The PHQ-9 is a quick and effective screening tool that can be used for the detection of depression by utilizing 9 statements that inquire about the frequency of depression symptoms[33,34]. PHQ-9 scores greater than or equal to 10 have a sensitivity and specificity of 88% for major depressive disorder[33]. The BAI is a 21-symptom screening measurement tool where participants can select how bothered they have been by each symptom of anxiety[35]. Scores range from 0-63 with lower scores representing fewer symptoms of anxiety and higher scores indicating more symptoms of anxiety[36]. BAI scores of 8 or greater have a sensitivity and specificity of 75% for identifying individuals with an anxiety disorder[37].

To assess coping strategies used among individuals with smell loss, the Coping Strategies Inventory Short Form (CSI-SF) and Brief-COPE questionnaires were administered. The CSI-SF[38] is a 16-item questionnaire that allows participants to rate how frequently they use the specified coping strategy. The CSI-SF can be broken down into the following subscales: engagement vs. disengagement coping or emotion-focused coping vs. problem-focused coping[38,39] with 8 questions being assigned to each factor for a total range of 8-40 points per factor where higher scores are associated with increased use of that specified coping strategy. The Brief-COPE[40] is a 28-item instrument, that solicits responses about the frequency of coping mechanism utilization, with coping strategies that can be grouped into approach or avoidant coping[41]. There are 12 items in each subscale of approach and avoidant coping, therefore scores for each subscale can range from 12-48 with higher scores representing increased use of that coping strategy[26].

### Statistical analysis

Descriptive statistics were summarized as frequencies and proportions for categorical variables and means and standard deviations, or median and interquartile range for continuous variables. Differences between groups were tested with ANOVA or Kruskal-Wallis tests for continuous variables (specific test utilized for each comparison is specified in the table footnotes for Tables 1 and 2) and with Fisher's exact test for categorical variables. Spearman correlations were analyzed between coping mechanism scores and QoL and mental health outcomes (QOD-NS, PROMIS-29, PHQ-9, Beck Anxiety). Partial Spearman correlations were also examined while adjusting for age and sex. Due to the positive skewness of the distributions for the PROMIS-29, PHQ-9, and Beck Anxiety scores, natural log transformations were applied to these variables before analysis.

Linear regression models were utilized to examine the associations between pairs of coping mechanism scores and QoL and mental health measurements in subjects that had both subjective and psychophysically measured OD. The pairs of coping mechanisms scores were approach and avoidant coping, engagement and disengagement coping, and emotion-focused and problem-focused coping. Models were initially run controlling only for the pair of coping mechanisms, and then again adjusting for age and sex. A moderation analysis was then conducted to identify whether or not the association between TDI total score and QoL and mental health measurements was moderated by any of the coping mechanism scores. The distribution of the residuals for each model was used to identify any potential outliers and assess model fit. No influential outliers were identified. All analyses were carried out using SAS version 9.4. All statistical tests were two-sided with a pre-selected level of significance of 5%.

## Results

A total of 93 participants were eligible to be included in the

Table 1. Demographic and clinical characteristics.

| Variable | Group A (n=69) | Group B (n=13) | Group C (n=7) | Group D (n=4) | Pairwise p-values | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Overall p-value | A vs B | A vs C | A vs D | B vs C | B vs D | C vs D |
| Demographics | | | | | | | | | | | |
| Age - years | 42.5 ± 15.8 | 39.5 ± 11.5 | 34.0 ± 9.7 | 41.5 ± 14.5 | 0.517 | 0.524 | 0.170 | 0.903 | 0.294 | 0.781 | 0.327 |
| Sex | | | | | 0.868 | 0.497 | 1.000 | 1.000 | 0.587 | 1.000 | 1.000 |
| Male | 20 (29.0%) | 2 (15.4%) | 2 (28.6%) | 1 (25.0%) | | | | | | | |
| Female | 48 (69.6%) | 11 (84.6%) | 5 (71.4%) | 3 (75.0%) | | | | | | | |
| Not Reported | 1 (1.4%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | | | | | | | |
| Race | | | | | 0.051 | **0.029** | 0.433 | 0.217 | 0.233 | 0.446 | 0.394 |
| Black or African American | 8 (11.6%) | 0 (0%) | 2 (28.6%) | 0 (0%) | | | | | | | |
| Native American or Alaskan Native | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | | | | | | | |
| Native Hawaiian or Other Pacific Islander | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | | | | | | | |
| Asian or Asian American | 2 (2.9%) | 3 (23.1%) | 0 (0%) | 0 (0%) | | | | | | | |
| White | 41 (59.4%) | 5 (38.5%) | 3 (42.9%) | 1 (25%) | | | | | | | |
| Other or Mixed Race | 15 (21.7%) | 4 (30.8%) | 2 (28.6%) | 3 (75.0%) | | | | | | | |
| Declined or Unknown | 3 (4.3%) | 1 (7.7%) | 0 (0%) | 0 (0%) | | | | | | | |
| Hispanic | | | | | 0.655 | 1.000 | 1.000 | 0.243 | 1.000 | 0.518 | 0.500 |
| No | 47 (68.1%) | 9 (69.2%) | 5 (71.4%) | 1 (25.0%) | | | | | | | |
| Yes | 21 (30.4%) | 4 (30.8%) | 2 (28.6%) | 2 (50.0%) | | | | | | | |
| Declined or Unknown | 1 (1.4%) | 0 (0%) | 0 (0%) | 1 (25.0%) | | | | | | | |
| Smoking status | | | | | 0.621 | 0.427 | 0.664 | 0.616 | 1.000 | 0.579 | 0.364 |
| Never | 55 (79.7%) | 11 (84.6%) | 7 (100.0%) | 3 (75.0%) | | | | | | | |
| Former | 12 (17.4%) | 1 (7.7%) | 0 (0.0%) | 1 (25.0%) | | | | | | | |
| Current | 2 (2.9%) | 1 (7.7%) | 0 (0.0%) | 0 (0.0%) | | | | | | | |
| Education | | | | | 0.493 | 0.244 | 1.000 | 0.453 | 0.751 | 0.181 | 0.697 |
| High school | 7 (10.3%) | 1 (7.7%) | 0 (0.0%) | 1 (25.0%) | | | | | | | |
| College | 31 (45.6%) | 3 (23.1%) | 3 (42.9%) | 2 (50.0%) | | | | | | | |
| Advanced degree | 30 (44.1%) | 9 (69.2%) | 4 (57.1%) | 1 (25.0%) | | | | | | | |
| Vaccination status at time of infection | | | | | **0.002** | 1.000 | **0.001** | 0.416 | **0.007** | 0.427 | 0.242 |
| Not vaccinated | 61 (88.4%) | 12 (92.3%) | 2 (28.6%) | 3 (75.0%) | | | | | | | |
| Vaccinated | 8 (11.6%) | 1 (7.7%) | 5 (71.4%) | 1 (25.0%) | | | | | | | |
| Hospitalized due to COVID | | | | | 0.696 | 0.487 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| No | 59 (85.5%) | 10 (76.9%%) | 6 (85.7%) | 4 (100.0%) | | | | | | | |
| Yes | 3 (4.3%) | 1 (7.7%) | 0 (0.0%) | 0 (0.0%) | | | | | | | |
| Not Reported | 7 (10.1%) | 2 (15.4%) | 1 (14.3%) | 0 (0.0%) | | | | | | | |

Continuous variables are reported as mean ± (SD), or median [IQR]. Categorical variables are reported as n (%). * Kruskal-Wallis test was used due to non-normal distributions.

analysis. Among those included, 72% were female, and the average age was 41.4 years. Based on Sniffin' Sticks psychophysical characterization of olfaction, there were 20 normosmics, 69 hyposmics, and 6 ansomics. Of all participants, 82 participants endorsed subjective OD, while 11 participants reported having a normal sense of smell subjectively. Of those with subjective OD, there were 69 participants in group A and 13 in group B. Of those with subjective normosmia, there were 7 participants in

Table 2. Olfaction, coping, QoL, and mental health scores.

| Variable | Group A (n=69) | Group B (n=13) | Group C (n=7) | Group D (n=4) | Overall p-value | A vs B | A vs C | A vs D | B vs C | B vs D | C vs D |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Olfaction Scores** | | | | | | | | | | | |
| TDI Score | 24.3 ± 5.0 | 34.1 ± 2.2 | 35.5 ± 3.2 | 25.6 ± 2.1 | **<.001** | **<.001** | **<.001** | **<.001** | 0.594 | 0.265 | **<.001** |
| **Coping Scores** | | | | | | | | | | | |
| Avoidant coping | 22.6 ± 6.0 | 20.0 ± 3.5 | 22.7 ± 2.9 | 22.0 ± 8.0 | 0.522 | 0.145 | 0.976 | 0.839 | 0.099 | 0.659 | 0.831 |
| Approach coping | 31.9 ± 8.0 | 33.6 ± 6.7 | 35.6 ± 5.5 | 31.8 ± 6.9 | 0.609 | 0.486 | 0.237 | 0.979 | 0.517 | 0.646 | 0.335 |
| Engagement coping | 26.6 ± 5.5 | 27.7 ± 5.5 | 28.6 ± 5.2 | 29.0 ± 6.6 | 0.639 | 0.505 | 0.362 | 0.400 | 0.731 | 0.694 | 0.907 |
| Disengagement coping | 23.6 ± 5.9 | 22.8 ± 5.7 | 23.3 ± 2.9 | 21.0 ± 4.1 | 0.805 | 0.632 | 0.882 | 0.384 | 0.827 | 0.578 | 0.306 |
| Emotion-focused coping | 24.1 ± 5.4 | 24.2 ± 4.5 | 26.4 ± 2.3 | 25.0 ± 2.9 | 0.701 | 0.929 | 0.264 | 0.741 | 0.163 | 0.753 | 0.392 |
| Problem-focused coping | 26.1 ± 4.4 | 26.2 ± 4.1 | 25.4 ± 2.3 | 25.0 ± 2.2 | 0.932 | 0.931 | 0.688 | 0.620 | 0.638 | 0.576 | 0.768 |
| **Quality of Life Scores** | | | | | | | | | | | |
| QOD-NS score | 28.5 ± 12.3 | 21.0 ± 9.9 | 1.7 ± 2.6 | 2.7 ± 2.1 | **<.001** | **0.044** | **<.001** | **0.006** | **0.002** | **0.024** | 0.371 |
| PROMIS-29 score | 55.0 [44.0 -74.0] | 44.5 [39.5 - 64.5] | 37.0 [37.0 -57.0] | 68.5 [43.0 -94.0] | 0.166* | 0.170 | 0.078 | 0.819 | 0.385 | 0.333 | 0.271 |
| **Mental Health Scores** | | | | | | | | | | | |
| PHQ-9 score | 4.0 [1.0 - 10.0] | 4.0 [0.0 - 9.0] | 2.0 [0.0 - 7.0] | 4.0 [2.0 - 7.0] | 0.442* | 0.371 | 0.154 | 0.990 | 0.675 | 0.743 | 0.361 |
| BAI score | 5.0 [2.0 - 13.0] | 3.0 [2.0 - 7.0] | 2.0 [1.0 - 6.0] | 1.5 [0.5 - 5.0] | 0.272* | 0.514 | 0.156 | 0.170 | 0.555 | 0.404 | 0.709 |

Continuous variables are reported as mean ± (SD), or median [IQR]. Categorical variables are reported as n (%). *Kruskal-Wallis test was used due to non-normal distributions.

Table 3. Spearman correlations between coping mechanism and QoL and mental health outcomes.

| | QOD-NS | | | PROMIS-29 | | | PHQ-9 | | | BAI | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Coping Variable** | **n** | **Spearman r** | **p-value** | **n** | **Spearman r** | **p-value** | **n** | **Spearman r** | **p-value** | **n** | **Spearman r** | **p-value** |
| Avoidant coping | 61 | 0.353 | **0.006** | 52 | 0.417 | **0.003** | 60 | 0.496 | **<.001** | 61 | 0.413 | **0.001** |
| Approach coping | 62 | -0.150 | 0.252 | 52 | -0.238 | 0.095 | 61 | -0.265 | **0.042** | 62 | -0.172 | 0.188 |
| Engagement coping | 68 | -0.113 | 0.365 | 56 | -0.240 | 0.081 | 66 | -0.252 | **0.044** | 68 | -0.196 | 0.115 |
| Disengagement coping | 68 | 0.373 | **0.002** | 56 | 0.383 | **0.004** | 66 | 0.480 | **<.001** | 68 | 0.368 | **0.002** |
| Problem-focused coping | 68 | 0.123 | 0.326 | 56 | 0.059 | 0.669 | 66 | 0.029 | 0.818 | 68 | 0.003 | 0.983 |
| Emotion-focused coping | 68 | 0.179 | 0.150 | 56 | 0.214 | 0.121 | 66 | 0.277 | **0.027** | 68 | 0.261 | **0.034** |

Analyses performed only on Group A. All analyses adjusted for age and sex.

group C and 4 in group D. There were 63 (67.7%) participants that endorsed symptoms of parosmia, with 9 of those individuals in group B (having normosmia) and 54 in group A (49 having hyposmia and 5 having ansomia). Demographics including race, ethnicity, education, smoking history, vaccination status, and hospitalization with SARS-CoV-2 infection can be found in Table 1. There were no significant differences between groups for any demographic variables, except for vaccination status (p=0.002). Groups A and B had significantly more individuals vaccinated than Group C (p=0.001 and p=0.007, respectively).

Olfaction, coping strategy, QoL, and mental health questionnaire average scores can be seen in Table 2. Among QoL and mental health screening outcome measures, only the QOD-NS score was significantly different between the 4 groups (p<0.001). Group A had an average QOD-NS score of 28.5, which was significantly higher than the average scores of groups B, C, and D (p=0.044, p<0.001 and p=0.006, respectively). Additionally, group B had a significantly higher average QOD-NS score compared to group C (p=0.002) and group D (p=0.024). There were no statistically significant differences in median scores

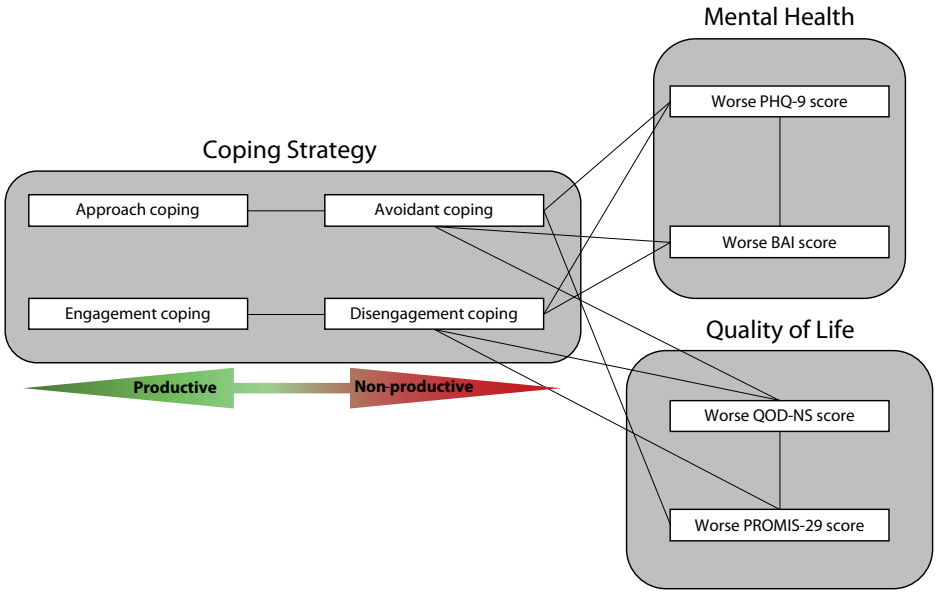


Figure 1. Keygraph showing the main result of our study that avoidant and disengagement coping are associated with worse quality of life and mental health outcomes.

Table 4. Estimated mean change for approach and avoidant coping mechanisms on QoL and mental health measures.

| Outcome | Coping Mechanism | N | Partially Adjusted Means (95% CIs) | p-value | N | Fully Adjusted Means (95% CIs)* | p-value |
|---|---|---|---|---|---|---|---|
| QOD-NS Total Score | Approach Coping | 59 | -0.33 (-0.71, 0.06) | 0.093 | 58 | -0.32 (-0.72, 0.09) | 0.121 |
| | Avoidant Coping | 59 | 0.84 (0.34, 1.34) | 0.001 | 58 | 0.82 (0.31, 1.34) | 0.002 |
| Promis-29 Total Score (ln-transformed) | Approach Coping | 51 | -0.01 (-0.02, 0.01) | 0.280 | 50 | -0.01 (-0.02, 0.00) | 0.194 |
| | Avoidant Coping | 51 | 0.03 (0.01, 0.04) | <.001 | 50 | 0.03 (0.01, 0.05) | <.001 |
| PHQ-9 Total Score (ln-transformed) | Approach Coping | 57 | -0.05 (-0.07, -0.02) | <.001 | 57 | -0.05 (-0.07, -0.02) | 0.001 |
| | Avoidant Coping | 57 | 0.08 (0.05, 0.12) | <.001 | 57 | 0.09 (0.06, 0.13) | <.001 |
| BAI Total Score (ln-transformed) | Approach Coping | 59 | -0.03 (-0.07, 0.00) | 0.050 | 58 | -0.04 (-0.07, -0.00) | 0.041 |
| | Avoidant Coping | 59 | 0.07 (0.03, 0.11) | 0.002 | 58 | 0.07 (0.03, 0.12) | 0.002 |

*Model is adjusted for age, and sex. Analyses performed only on Group A. The first model is partially adjusted because it included both types of coping mechanisms, while the fully adjusted model also contained both types of coping mechanisms, but also included age and sex as covariates.

Table 5. Estimated mean change for engagement and disengagement coping mechanisms on QoL and mental health measures.

| Outcome | Coping Mechanism | N | Partially Adjusted Means (95% CIs) | p-value | N | Fully Adjusted Means (95% CIs)* | p-value |
|---|---|---|---|---|---|---|---|
| QOD-NS Total Score | Engagement Coping | 69 | -0.34 (-0.83, 0.16) | 0.178 | 68 | -0.35 (-0.88, 0.18) | 0.189 |
| | Disengagement Coping | 69 | 0.92 (0.46, 1.38) | **<.001** | 68 | 0.85 (0.38, 1.33) | **<.001** |
| Promis-29 Total Score (ln-transformed) | Engagement Coping | 57 | -0.01 (-0.02, 0.01) | 0.439 | 56 | -0.01 (-0.03, 0.01) | 0.205 |
| | Disengagement Coping | 57 | 0.02 (0.01, 0.04) | **0.007** | 56 | 0.02 (0.01, 0.04) | **0.006** |
| PHQ-9 Total Score (ln-transformed) | Engagement Coping | 66 | -0.04 (-0.08, -0.01) | **0.024** | 66 | -0.04 (-0.08, -0.00) | **0.032** |
| | Disengagement Coping | 66 | 0.09 (0.06, 0.12) | **<.001** | 66 | 0.09 (0.05, 0.13) | **<.001** |
| BAI Total Score (ln-transformed) | Engagement Coping | 69 | -0.04 (-0.08, 0.01) | 0.114 | 68 | -0.04 (-0.09, 0.01) | **0.097** |
| | Disengagement Coping | 69 | 0.07 (0.03, 0.11) | **<.001** | 68 | 0.07 (0.03, 0.12) | **<.001** |

*Model is adjusted for age, and sex. Analyses performed only on Group A. The first model is partially adjusted because it included both types of coping mechanisms, while the fully adjusted model also contained both types of coping mechanisms, but also included age and sex as covariates.

Table 6. Estimated mean change for problem-focused and emotion-focused coping mechanisms on QoL and mental health measures.

| Outcome | Coping Mechanism | N | Partially Adjusted Means (95% CIs) | p-value | N | Fully Adjusted Means (95% CIs)* | p-value |
|---|---|---|---|---|---|---|---|
| QOD-NS Total Score | Problem-focused Coping | 69 | 0.12 (-0.63, 0.87) | 0.748 | 68 | 0.10 (-0.68, 0.87) | 0.806 |
| | Emotion-Focused Coping | 69 | 0.49 (-0.12, 1.10) | 0.116 | 68 | 0.47 (-0.15, 1.09) | 0.135 |
| Promis-29 Total Score (ln-transformed) | Problem-focused Coping | 57 | -0.00 (-0.03, 0.02) | 0.870 | 56 | -0.00 (-0.03, 0.02) | 0.826 |
| | Emotion-Focused Coping | 57 | 0.02 (-0.00, 0.04) | 0.081 | 56 | 0.02 (-0.00, 0.04) | 0.106 |
| PHQ-9 Total Score (ln-transformed) | Problem-focused Coping | 66 | -0.02 (-0.08, 0.04) | 0.494 | 66 | -0.02 (-0.08, 0.05) | 0.585 |
| | Emotion-Focused Coping | 66 | 0.06 (0.01, 0.11) | **0.013** | 66 | 0.06 (0.01, 0.11) | **0.012** |
| BAI Total Score (ln-transformed) | Problem-focused Coping | 69 | -0.03 (-0.10, 0.03) | 0.298 | 68 | -0.04 (-0.10, 0.03) | 0.307 |
| | Emotion-Focused Coping | 69 | 0.06 (0.01, 0.12) | **0.017** | 68 | 0.06 (0.01, 0.12) | **0.021** |

*Model is adjusted for age, and sex. Analyses performed only on Group A. The first model is partially adjusted because it included both types of coping mechanisms, while the fully adjusted model also contained both types of coping mechanisms, but also included age and sex as covariates.

on the PROMIS-29, PHQ-9, and BAI between groups. Likewise, there were no significant differences in coping strategy scores between groups.

To examine the correlations between coping strategies and QoL and mental health outcomes (Table 3), only group A was examined, as these were individuals with both subjective and psychophysically measured OD who were most likely utilizing coping strategies to deal with their smell loss. When adjusting for age and sex, there was a weak correlation between QOD-NS scores and avoidant coping (r=0.353, p=0.006) and disengagement coping (r=0.373, p=0.002). Likewise, there was a correlation between PROMIS-29 scores and avoidant coping (r=0.417, p=0.003) and disengagement coping (r=0.383, p=0.004). PHQ-9 had a moderately positive correlation with avoidant coping (r=0.496, p<0.001) and disengagement coping (r=0.480, p<0.001), a weak negative correlation with approach coping (r=–0.265, r=0.042) and engagement coping (r=–0.252, p=0.044), and a weak positive correlation with emotion-focused coping (r=0.277, p=0.027). The BAI scores were moderately correlated with avoidant coping (r=0.413, p=0.001) and weakly correlated with disengagement coping (r=0.368, p=0.002) and emotion-focused coping (r=0.261, p=0.034). Figure 1 uses a keygraph to depict the findings that avoidant and disengagement coping are correlated with worse QOD-NS, PROMIS-29, PHQ-9, and BAI scores.

Tables 4, 5, and 6 show the estimated mean change effect that each coping mechanism had on the QoL and mental health screening assessments. Again, the estimated mean change analyses were performed only on group A. On average, when adjusting for age, sex, and approach coping, with each additional point to one's avoidant coping score, their QOD-NS score also increased by 0.82 points (95% CI: 0.31, 1.34; p=0.002). A similar pattern can be seen with PROMIS-29, PHQ-9, and BAI scores, where an additional point in one's avoidant coping score increased their PROMIS-29 score by 3%, PHQ-9 score by 9.4%, and BAI score by 7.3% (adjusting for natural logarithm transformation). Approach coping was negatively associated with mental health screening scores PHQ-9 (β= –0.05; 95% CI: –0.07, –0.02; p=0.001) and BAI (β= –0.04; 95% CI: –0.07, 0.00; p=0.041) scores. When adjusting for age, sex, and engagement coping, participants had an increase in their QOD-NS scores by 0.85 (95% CI: 0.38, 1.33) points on average with each 1-point increase in disengagement coping score (p<0.001). Similarly, with each 1-point increase in disengagement coping score, participants also demonstrated a 2.0%, 9.4%, and 7.3% increase in PROMIS-29, PHQ-9, and BAI scores, respectively. A 1-point increase in engagement coping was significantly associated with a 3.9% decrease in PHQ-9 scores, on average. Lastly, a 1-point increase in emotion-focused coping was associated with 6.2% increases in PHQ-9 and BAI scores when adjusting for problem-focused coping, age, and sex.

There were no significant interaction p-values when examining the moderating effects of each coping mechanism on the association between TDI and QoL and mental health outcomes.

## Discussion

### Smell loss, QoL, and mental health

The findings from this study indicate that individuals with subjective OD and hyposmia or anosmia on psychophysical testing have significantly worse olfactory-specific QoL than individuals with subjectively normal sense of smell. Among those with psychophysically measured normal smell scores, those with subjectively normal smell (group C) had significantly better olfactory-specific scores than those with subjective OD (group B), indicating that an individual's perception of their olfactory

status is an important factor in olfactory QoL. This is an expected finding based on prior research using the QOD-NS questionnaire and the impact that subjective smell loss has on an individual's QoL related to their olfaction[42]. Likewise, other studies have found a similar association between COVID-19-related smell loss and worse olfactory-specific QoL[8,22]. Similar to our findings in group B, Otte et. al.[8] found that even with recovered smell in the normosmia range on psychophysical testing these individuals still exhibited significantly worse QoL. Additionally, because the majority of individuals (69%) in group B experienced symptoms of parosmia, this olfactory distortion could be a likely cause of diminished QoL with QOD-NS scores significantly worse than those with subjectively normal smell even though group B individuals have psychophysically measured normosmia.

Prior research has shown that individuals with OD suffer from worse overall QoL, depression, and anxiety at significantly higher rates than individuals with normal smell[6,18,20]. Interestingly, our findings show mixed results among the 4 groups for general QoL and mental health questionnaire scores with no statistically significant differences between groups. Studies have shown that the COVID-19 pandemic itself has affected QoL and increased levels of depression and anxiety among the general public due to the uncertainty, social isolation, emotional strain, and financial difficulties that it has caused[43]. Because all participants in our study endured the pandemic hardships, it is possible that this caused no major differences in general QoL and mental health symptom outcomes between groups, especially when observing that individuals in group D (subjective normal smell; psychophysically measured smell dysfunction) had the worst PROMIS-29 mean score and an equivalent PHQ-9 median score as those with subjective OD.

**Smell loss and coping strategies**

Avoidant coping and disengagement coping were each significantly correlated with worse QOD-NS, PROMIS-29, PHQ-9, and BAI scores, while approach coping and engagement coping were associated with better PHQ-9 scores among individuals with smell loss subjectively and on psychophysical testing. Although it is known that individuals with smell loss utilize coping mechanisms[18,20,21], the relationship between coping strategies and QoL or mental health has not yet been studied in those with smell loss. Among studies that have examined coping strategies and QoL outcomes in other disorders and diseases, they have found similar findings to ours. In a study examining approach versus avoidant coping mechanisms and their association with depressive symptoms, it was found that depressive symptoms were most prevalent among avoidant copers, and individuals who changed from approach to avoidant coping strategies over time worsened their depressive symptoms[44]. It has also been shown that individuals utilizing disengagement coping strategies are more likely to have poor psychological well-being, while the use of engagement coping was associated with higher psychological well-being[45].

The minimal clinically important difference (MCID) on the QOD-NS is 5.2 points, on average, in patients with chronic rhinosinusitis[46]. Our study found that with each additional point in avoidant coping score or disengagement coping score, the QOD-NS score increased by 0.82 and 0.85 points, respectively. Therefore, decreasing avoidant or disengagement coping scores by 6.3 and 6.1 points, respectively, will create a clinical difference in olfactory-specific QoL. Although there has been no MCID established for the PHQ-9 or BAI in patients with smell loss since these questionnaires are utilized as screening tools, our data suggest that an increase in the utilization of avoidant or disengagement coping strategies is associated with increased depressive and anxiety symptoms. Additionally, an increase in approach or engagement coping mechanisms is associated with fewer screening depressive symptoms[33,47].

Most of the literature examining coping techniques in individuals with smell loss has concentrated on problem-focused and emotion-focused coping, reporting that individuals with OD commonly utilize these coping strategies[18,20,21]. Interestingly, our study results showed significant associations between increased emotion-focused coping resulting in increased PHQ-9 and BAI scores. The lack of associations between problem-focused and emotion-focused coping with QoL outcomes may be due to the inherent nature of these coping strategies. Neither emotion-focused nor problem-focused coping is better or worse than the other, although some argue that emotion-focused coping is maladaptive[41,48]. This ambiguity is in contrast to the universality of engagement and approach coping being recognized as positive coping strategies, whereas disengagement and avoidant coping are negative strategies[45,49]. With the number of significant associations being more prominent among approach, avoidant, engagement, and disengagement coping, it would be worthwhile to conduct additional studies focusing on these coping strategies among those with smell loss.

Our results do not demonstrate a moderating effect of coping strategies on the relationship between smell loss and QoL, likely due to our limited sample size. However, our results demonstrate a significant association between QoL and coping strategies used in individuals with smell loss, highlighting the importance of including counseling on effective and ineffective coping techniques in the management of patients with olfactory dysfunction. Potential counseling points include encouraging individuals to find emotional support, discuss their smell loss with family or friends, and plan and engage in efforts to improve smell loss such as smell training as these are considered approach and

engagement coping mechanisms[39,40,50].

When interpreting the results of coping strategies, it is important to account for the greater likelihood that women may rely on emotional support compared to men[51]. Our participant cohort is predominantly female, which is consistent with other studies investigating persistent OD following SARS-CoV-2 infections[52], reflective of a higher prevalence of OD, increased awareness of olfactory acuity, or a general increased health vigilance among females[52,53]. Understanding the impact of coping strategies on symptoms of anxiety and depression as well as gender-specific differences in coping efficacy is important, as prior studies report that women who rely less on positive reframing as a coping strategy have higher levels of depressive symptoms compared to men, irrespective of their reframing technique[51]. Moreover, women who utilize self-blame as a coping mechanism may have more symptoms of anxiety compared to women who do not utilize self-blame, and yet the same was not reported for men.

### Limitations

This study is not without limitations, including a relatively small sample size of 93 individuals. The small sample size may be contributory to a lack of significant findings when completing the moderation analysis. Likewise, the number of participants included in subgroups A-D is imbalanced, potentially limiting our ability to interpret the result and generalize to the larger population. Other studies that have examined coping strategies among individuals with smell loss on psychophysical testing also had small population sizes between 59 to 135 participants(18,20). Additionally, our study population was racially and ethnically diverse, allowing for generalization of our results. Another limitation of our study was that individuals were recruited to participate in our study over approximately 1.5 years. Individuals therefore were exposed to different variants of SARS-CoV-2 that may in turn have differing effects on smell, were recruited at different stages in the pandemic, and possibly experienced varying durations of smell loss. These are limitations incurred by any longitudinally enrolling study. Participants only had their olfaction tested and questionnaires administered following SARS-CoV-2 infection and therefore lacked a priori baseline olfactory, QoL, and mental health measurements. Regardless, each participant included in this study endorsed a notable change in their sense of smell after their SARS-CoV-2 infection and had their smell results compared to normative population-level data. While the majority of our data are based on questionnaires, which may be affected by priming and contextual influence providing less precise data than experimentally acquired data[54], the selected questionnaires used in this study represent validated measures of patient-reported outcomes.

## Conclusion

While our finding that individuals with COVID-19-related OD have worse olfactory-specific QoL compared to those with normosmia, our results highlight how specific coping mechanisms may ameliorate this impact. Specifically, we identify an important association between approach and engagement coping mechanisms and higher scores on QoL and mental health screening assessments compared to individuals relying on avoidant or disengagement coping. Future studies utilizing larger study cohorts that also examine longitudinal effects of variations in coping strategies will provide additional evidence to understand the effect that coping mechanisms have on QoL and mental health outcomes.

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## Authors' contributions

Study concepts: PTJ, BJV, PVJ, TEG, DPD, JBO; Study design: PTJ, BJV, DAG, PVJ, TEG, DPD, JBO; Data collection: PTJ, BJV, FFC, LWG, JPT, JBG, TMS, JBO; Data analysis and interpretation: PTJ, CS, THC, JBO; Manuscript draft preparation: PTJ, CS, JBO; Manuscript editing, review, and approval: all authors.

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## Conflicts of interest

The authors declare no conflicts of interest.

## Data availability

None to declare.

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