Gender Differences After COVID-19-Related Hospitalization: A Longitudinal Examination of Health-Related Quality of Life

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September 14th, 2024

Abstract

Background: As of April 2024, there were 775 million confirmed cases of COVID-19, with negative health impacts that can still be present 12 months after the initial infection, and negatively affect HRQOL. This impact is differently pronounced for men and women. Moreover, pre-existing medical conditions enhance the likelihood of developing Long-COVID. This study aimed to investigate (1) potential gender differences in the course of physical and psychological HRQOL, and (2) the impact of the number of pre-existing medical conditions on physical and psychological HRQOL over time. **Methods:** Data from an observational longitudinal cohort study was analyzed to describe the course of HRQOL over 12 months post-hospital discharge at four measurement points in people hospitalized and diagnosed with SARS-CoV-2. For this purpose, demographic information, clinical data, and HRQOL measurements of 687 participants were analyzed using linear mixed model analyses. **Results:** Men displayed significantly higher HRQOL scores than women 3 months after hospitalization, but both genders showed a similar recovery course over time. Moreover, the number of pre-existing medical conditions did not impact the course of HRQOL scores or interact with gender over time in this context. **Discussion:** Men and women experienced a similar course of recovery of physical and psychological HRQOL over 12 months, independent of gender or the number of pre-existing medical conditions. However, early recovery programs (≤ 3 months) like cognitive rehabilitation measures, physiotherapy, or psychological support should consider the initially observed gender differences and provide tailored support for women.

Keywords: Health-Related Quality of Life, Long COVID-19, Gender Differences, Physical Role Functioning, Psychological Role Functioning

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COVID-19 and Long COVID

The Corona Virus Disease 2019 (COVID-19) was first recorded in Wuhan, China in December 2019 (Zhou, et al., 2020; Wu et al. 2020) and declared a pandemic by the World Health Organization (WHO) in March 2020 (WHO, 2020). In April 2024 there were 775 million confirmed cases of COVID-19 and 7 million deaths linked to the disease worldwide (WHO, 2024). Although various scientists have been working to identify, diagnose, treat, and prevent COVID-19 (Lopez-Leon et al., 2021), gender differences regarding the impact of ongoing COVID-19 sequelae on individuals' physical and psychological health-related quality of life (HRQOL) have not been widely researched. In addition, there is also a lack of observations about a possible interaction between the number of pre-existing medical conditions and gender on the physical and psychological HRQOL of previously hospitalized COVID-19 patients.

COVID-19 is caused by severe acute respiratory syndrome coronavirus 2, in short SARS-CoV-2 (Gupta et al., 2020). Indications of infection usually start 4-5 days after exposure and typically include fever, sore throat, cough, muscle or body pain, loss of taste or smell, and diarrhea (Docherty et al., 2020) and range from mild to severe (Wang et al., 2020). Moreover, COVID-19 can be divided into three stages. The first stage is called acute COVID-19 and includes having symptoms of COVID-19 for a maximum of four weeks. If symptoms continue for four to twelve weeks, the next illness stage is categorized as ongoing symptomatic COVID-19. If symptoms persist for longer than 12 weeks and cannot be explained by an alternative diagnosis, patients enter a third phase referred to as post-COVID-19 syndrome (NICE, SIGN & RCGP, 2020) or Long COVID (LC) (Shah et al., 2021). People affected by LC are tested negative by polymerase-chain-reaction testing (PCR) and therefore recovered on a microbiological level but not symptom-free or, in case of an asymptomatic illness course, clinically recovered yet (Garg et al., 2021). While most people affected by COVID-19 completely recover, around 40% develop LC symptoms (Chen et al., 2022; Whitaker et al., 2022). Furthermore, the prevalence of remaining symptoms for more than twelve weeks is significantly higher in hospitalized patients at 87% compared to patients treated without hospitalization where only 35% develop LC (Carfì et al., 2020; Tenforde et al., 2020).

Symptoms of Long COVID

LC can either include symptoms of earlier stages, thus acute COVID-19 or new symptoms that develop subsequently (Garg et al., 2021). According to the guideline from the

National Institute for Health and Care Excellence (2020), typical symptoms encompass cardiovascular (e.g., chest tightness, heart race), pulmonary (e.g., shortness of breath, cough), neurological (e.g., stroke, headache), gastrointestinal (e.g., abdominal pain, diarrhea), musculoskeletal (e.g., joint pain, muscle pain), inflammatory (e.g., fatigue, fever) or general and non-specific (e.g., rash on the skin, missing taste or smell) complaints. In addition, LC patients frequently report problems with mastering daily tasks, mental health issues, and an overall decreased HRQOL (Carfì et al., 2020). The most commonly reported symptoms include fatigue, bodily pain, shortness of breath, post-exertional malaise, muscle weakness, sleep disorders, anxiety, depression, and cognitive problems (Global Burden of Disease Long COVID Collaborators, 2022; Kuodi et al., 2023). The average length of LC symptom duration varies from 4 months among patients without hospitalization to 9 months for hospitalized patients (Global Burden of Disease Long COVID Collaborators, 2022). In addition, among patients with ongoing sequelae who tested positive for COVID-19 a total of 15.1% still had symptoms one year after the first positive PCR test (Global Burden of Disease Long COVID Collaborators, 2022).

Risk Factors of Long COVID

Several factors increase the risk of developing LC with gender being one of them. Women have twice the risk compared to men (Nabavi, 2020). An investigation by Global Burden of Disease Long COVID Collaborators (2022) found that 63.2% of LC patients worldwide were female. In addition, age can affect the risk of developing LC. Individuals with LC are on average four years older than people who recover after acute COVID-19, making advanced age a further influential factor (Nabavi, 2020). Moreover, an elevated body mass index (BMI) (Sudre et al., 2021) and having more than five symptoms in the initial week of the disease are linked to an enhanced risk of developing LC (Sudre et al., 2021). Lastly, patients with other medical conditions are at a higher risk for developing persistent sequelae (Al-Aly et al., 2021; Maamar et al., 2021).

Two risk factors are of particular interest in the context of this study: gender and hospitalization. Research demonstrated that gender affects the development and symptoms of different diseases (Ballering et al., 2020) and the individual assessment of HRQOL during an illness (Garay et al., 2020; Mrus et al., 2005). However, there is a lack of research on gender differences regarding the impact of COVID-19 sequelae on HRQOL. Consequently, further research among this target group thus men and women hospitalized and diagnosed with COVID-19 is necessary. Furthermore, previous findings showed that LC is more prevalent in hospitalized COVID-19 patients than in non-hospitalized patients (Carfì et al., 2020; Tenforde et al., 2020). Study outcomes about differences in the course of HRQOL can be used to improve or redesign existing health programs and treatment options to support men and women in regaining their former physical and psychological HRQOL. In addition, study results on the course of COVID-19 in men and women post-hospitalization may also be useful from a patient perspective. The information might help draw realistic predictions about the impact of the disease on HRQOL and choose the most effective recovery measure according to time since hospitalization and gender.

Health-Related Quality of Life

According to the WHO, health is the state of total psychological, mental, and social well-being rather than just the absence of illness (WHO, 1958). These elements are included in the concept of quality of life, which considers people's viewpoints thus their current stage of life along with their goals, norms, expectations, and concerns about the culture and value systems in which they live (WHO, 1996). In summary, quality of life is the gap between individuals' plans and wishes and their practical experiences (Sousa & Kwok, 2006). In addition, HRQOL is usually referred to as people's evaluation of their current functional level in comparison to their ideal state (Megari, 2013). HRQOL describes the functional status of an individual and therefore the level at which a person can function in assigned roles without physical or mental restrictions (Bowling et al., 2003). HRQOL as a multidimensional term includes the subjective assessment of an individual's physical health, psychological health, and social functioning and the effects of an illness or medical care on these spectrums (Sawyer et al., 2001; Gill & Feinstein, 1994; Sprangers, 2002). Physical HRQOL includes the ability to carry out daily tasks and is linked to physical signs and symptoms caused by an illness or its treatment. Psychological HRQOL encompasses every state from psychological stress to positive well-being including people's cognitive functioning. Social HRQOL is based on quantitative and qualitative components of social interactions, relationships, and societal involvement (Sprangers, 2002). However, even though HRQOL is multidimensional, many studies concentrate on HRQOL as an overall construct, instead of examining the two main components physical and psychological HRQOL as separate elements. Physical and psychological health issues may impact HRQOL aspects differently and thus might call for different interventions, which highlights the importance of analyzing the impact of both elements independently of one another (Schaap et al., 2024).

The average HRQOL of the Dutch population ranges from 76.3 for physical to 77.9 for psychological health with higher scores (0-100) indicating better health (Aaronson et al., 1998). As symptoms and the course of a disease worsen in long-term illnesses, HRQOL often decreases over time (Fischer et al., 2010). Nevertheless, patients can adjust to the effects of the disease, for example, due to access to new treatment options or stabilizing symptoms, which can result in improvements in HRQOL throughout the illness course (Fischer et al., 2010; Stewart & Yuen, 2011; Xu et al., 2010). Study findings about the relationship between the duration of illness and HRQOL are mixed. For certain diseases, for example, stroke (Dayapoglu & Tan, 2010), diabetes (Sparring et al., 2013), or chronic skin conditions (van Rhijn, 2014), a longer course of the disease is linked to a decline in HRQOL, while the duration of other diseases like osteoarthritis (Kuriyama et al., 2008) or inflammatory bowel disease (Rini et al., 2008) do not negatively affect HRQOL. Consequently, diagnosis and continuation of a long-term illness are not necessarily predictors for decreased HRQOL. Whether the length of an illness negatively influences HRQOL depends on the type of illness, which is why it is important to evaluate how long-term COVID-19 consequences affect HRQOL over time. However, research on LC has shown that the associated prevalence and suffering of ongoing LC sequalae negatively influence HRQOL in LC patients and interfere with the capacity to fulfill daily tasks, for example, the ability to work (Fischer et al., 2022; Malik et al., 2022; Brus et al., 2023; Davis et al., 2021). This can have a temporary impact on the health status of people suffering from LC sequelae and thus impair their HRQOL. For instance, the average HRQOL scores of LC patients typically range between 60.4 and 84.4 and are strongly influenced by additional aspects like age and comorbidities (Poudel et al., 2021).

Gender Differences

Gender is an important determinant within health research (Springer et al., 2012) and is referred to as the roles constructed by social norms, behavior, and identity in a specific context and society that can affect the development and sequelae of disease (Smith & Koehoorn, 2016). For instance, a study by Ballering et al. (2020) found that female gender is linked to increased physical symptoms and higher rates of chronic diseases over a lifetime. In addition, the symptoms and ways a disease is presented can differ between men and women (Heidari et al., 2020). This is also relevant in the context of LC where gender is an influential factor regarding the development and health outcomes of the disease (Heidari et al., 2020). While the severity of acute COVID-19, intensive care admission rates, and the mortality caused by the illness are higher in men, women are more prone to develop LC (Lancet, 2020; Sylvester et al., 2022).

Moreover, even though studies found similarities in the most frequently reported LC symptoms between men and women, for example, muscle- and joint pain or fatigue (Marcilla-Toribio et al., 2024), the general likelihood for a broad spectrum of LC symptoms was found to be significantly higher in women. This includes mental health and mood changes, neurological aspects (e.g., memory impairment, confusion), dermatological aspects (e.g., rash, hair loss), and other symptoms like fatigue or muscle weakness, chest pain, infective complications, rheumatologic complications, fever, pain/discomfort, problems with usual activity, problems with personal care and decreased appetite (Sylvester et al., 2022). In addition, women have a higher number of symptoms. A study from 2022 that investigated gender differences in LC sequelae between men and women found that the number of LC symptoms was 2.25 for women, whereas the number of symptoms reported by men totaled 1.5 (Fernández-de-las-Peñas et al., 2022). Consequently, it can be assumed that gender influences the symptom prevalence and intensity of LC and therefore also the course of physical and psychological HRQOL.

In addition, gender differences were also found regarding the impact of the duration of an illness and its impact on HRQOL. A study on type 1 Diabetes patients showed that HRQOL in female diabetes patients decreases strongly as the disease progresses, whereas only a slight decline in HRQOL was observed in men over the same length of time (Sparring et al., 2013). Consequently, the same illness of the same duration can have a different impact on the perception of HRQOL in men and women. Regarding LC, a recent study by Marcilla-Toribio et al. (2024) observed that the impact of LC symptoms on HRQOL is viewed differently by male and female patients with lower HRQOL in women due to an unequal distribution of care responsibilities. This means that the type and number of social roles an individual has to carry out can affect the way they rate their HRQOL. Consequently, role functioning, one of the eight aspects of HRQOL, seems to be particularly interesting for the investigation of HRQOL. Especially since COVID-19 patients often rated the two categories, physical and psychological role functioning, lower than other subscales of HRQOL (Chen et al., 2020; Temperoni et al., 2021).

Lastly, studies found that women reported poorer HRQOL during and after an illness compared to men affected by the same illness. One example is a study of male and female HIV/AIDS patients undergoing 40 weeks of antiretroviral medication, which revealed poorer HRQOL in women across several HRQOL domains (Mrus et al., 2005). A further study, looking at people diagnosed with systolic heart failure who were treated in a specialized outpatient clinic, found that among all patients with systolic heart failure, HRQOL was significantly worse in women in all areas of self-assessed health status (Garay et al., 2020). Similar observations were made in a study by Oreel et al. (2020) where female patients reported poorer HRQOL and showed slower improvements in physical health compared to men after treatment for coronary artery disease. This indicates that the impact of LC sequelae on HRQOL might be assessed differently by men and women.

Different underlying mechanisms could explain these gender differences regarding the number of symptoms, the impact and duration of diseases, and the poorer HRQOL. One reason lies in biological deviations, for example, variations in the immune system function between men and women. Women have faster and more resilient adaptive immune responses that can shield them better from initial infections and major illnesses. However, this also means that women are more sensitive to prolonged autoimmune diseases (Klein & Flanagan, 2016; Sharma et al., 2020). Another biological explanation lies in the fact that the risk and course of LC are influenced by gender-specific hormones, such as hormones responsible for perimenopause and menopause in women, which can overlap with LC sequelae (Stewart et al., 2021). In addition, women might experience worse health due to underlying immunological differences from men (Marcilla-Toribio et al., 2024; Bwire, 2020) or a greater pain sensitivity that was found in women (Osborne & Davis, 2022; Fillingim et al., 2009). Lastly, impaired health in women often results from sociocultural factors like an unequal care burden between men and women, as unequal sociocultural circumstances create different challenges for both genders and thus influence the perception of HRQOL (del Río et al., 2017).

Pre-Existing Medical Conditions

Several pre-existing medical conditions have been shown to increase the risk of COVID-19 regarding hospitalization, intensive care admittance, or death. This includes cardiovascular diseases, cancer, chronic kidney diseases, liver diseases, metabolic diseases, hypertension (Aggarwal et al., 2020; Biswas et al., 2020), obesity or having a state of immunodeficiency (Clark et al., 2020; Chu et al., 2020; Figliozzi et al., 2020), diabetes, chronic obstructive pulmonary disease, fibromyalgia, multiple sclerosis, migraine, depression, anxiety (Subramanian et al., 2022; Sudre et al., 2021; Galal et al., 2021). A study conducted in the USA showed that 71% of all patients hospitalized due to COVID-19 and 94% of patients dying from COVID-19 had at least one underlying condition (CDC COVID-19 Response

Team, 2020). In terms of LC, existing pre-existing medical conditions can significantly increase the risk of developing persistent symptoms (Al-Aly et al., 2021; Maamar et al., 2021; Jacobs et al., 2023).

In addition to these exclusively surveyed conditions, obesity is an additional condition that can affect the course of COVID-19. According to the WHO (2022), obesity is on the rise in many countries, with 16.9% of the Dutch population affected in 2022. Obesity can lead to a worse disease progression due to a greater viral load and a weaker antiviral response in comparison to normal-weight people (Dicker et al., 2020). A study by Gao et al. (2021) showed that people with obesity had longer hospital stays compared to people with normal weight and suffered more often from a more severe COVID-19 progression. For this reason, obesity was included as a further pre-existing medical condition in this study.

Research Questions

Gender Differences in Health-Related Quality of Life

The first research question examines which subscales of physical and psychological HRQOL show the most prominent longitudinal course, hence the greatest score variation between 3 and 12 months, to determine which subscales are most interesting for further investigation of gender differences. This selection is dictated by the time constraints of this project, as including all subscales would exceed the feasibility of this study. Compared to other aspects of HRQOL, low scores were most frequently found in aspects of physical and psychological role limitations (Chen et al., 2020; Temperoni et al., 2021). Impairment of physical or psychological role functioning includes problems with work or daily activities caused by reduced physical or emotional well-being (Ware et al., 1993). Low initial values, as they were found in physical and psychological role functioning, offer the potential to observe the most pronounced upward development between the first and last measurement on these subscales. This allows the hypothesis, that the subscales of physical and psychological role functioning will prove most interesting for the subsequent investigation of gender differences.

RQ 1: Which subscales of physical and psychological HRQOL show the most prominent longitudinal increase in scores between 3 and 12 months in previously hospitalized COVID-19 patients?

H1: Of all subscales of physical HRQOL "role limitations due to physical problems" demonstrates the most striking score development between 3 and 12 months in previously hospitalized COVID-19 patients.

H2: Of all subscales of psychological HRQOL "role limitations due to psychological problems" demonstrates the most striking score development between 3 and 12 months in previously hospitalized COVID-19 patients.

The second research question examines whether time and gender are linked to the course of physical and psychological HRQOL in previously hospitalized COVID-19 patients. Therefore, this research question aims to get insight into the interaction between the longitudinal course of COVID-19 and gender on physical and psychological HRQOL. Existing research supports the hypothesis that there will be gender differences regarding the course of physical and psychological HRQOL over time in this target group, with women having lower physical and psychological HRQOL scores (Marcilla-Toribio et al., 2024).

RQ 2: Are there gender differences in the course of physical and psychological HRQOL at 3, 6, 9, and 12 months in previously hospitalized COVID-19 patients?

H3: Women score lower in "role limitations due to physical health problems" over 3, 6, 9, and 12 months in previously hospitalized COVID-19 patients.

H4: Women score lower in "role limitations due to emotional problems" over 3, 6, 9, and 12 months in previously hospitalized COVID-19 patients.

The third research question explores the point of greatest divergence between men and women regarding the course of physical and psychological HRQOL. The greatest difference is expected to be found 3 months after hospital discharge based on findings of striking differences in frequency and overall number of LC symptoms in men and women at that time (Fernández-de-las-Peñas et al., 2022; Sylvester et al., 2022).

RQ 3: When (3, 6, 9, or 12 months) does the course of physical and psychological HRQOL show the greatest divergence between men and women in previously hospitalized COVID-19 patients?

H5: The divergence in physical HRQOL between men and women is the strongest 3 months after hospital discharge based on one aspect of physical HRQOL (role limitations due to physical health problems).

H6: The divergence in psychological HRQOL between men and women is the strongest 3 months after hospital discharge based on one aspect of psychological HRQOL (role limitations due to emotional problems).

Information on gender differences in the course of COVID-19 post-hospitalization might improve available health programs and treatment options and support men and women in recovering. Furthermore, information about gender-typical COVID-19 progression can help future COVID-19 patients by providing them with the necessary knowledge to develop realistic expectations for the recovery of physical and psychological HRQOL. This information can also help them avoid setting unrealistic goals that may lead to frustration, which is linked to impaired health (Linton & Shaw, 2011).

Influence of Pre-Existing Medical Conditions

In addition, an exploratory research question examines the extent to which the number of pre-existing medical conditions affects physical and psychological HRQOL in men and women. Pre-existing medical conditions can increase the risk of a severe course of COVID-19, developing LC (Carfi et al., 2020), and experiencing persistent LC symptoms (Al-Aly et al., 2021; Maamar et al., 2021; Jacobs et al., 2023). In combination with other factors that have been found to affect the course and perception of an illness, such as gender, COVID-19 could result in an overall worse course of HRQOL in patients with multiple pre-existing medical conditions compared to people with few or no comorbidities. The above-described study outcomes support the hypothesis that physical and psychological HRQOL is modified by the relationship between the number of pre-existing medical conditions and gender in previously hospitalized COVID-19 patients, resulting in worse HRQOL scores among patients with a high number of comorbidities.

RQ 4: Is there a significant interaction between the number of pre-existing medical conditions and gender in the course of physical and psychological HRQOL at 3, 6, 9, and 12 months in previously hospitalized COVID-19 patients?

H7: There is a significant interaction between the number of pre-existing medical conditions and gender in the course of physical HRQOL at 3, 6, 9, and 12 months in previously hospitalized COVID-19 patients based on one aspect of physical HRQOL (role limitations due to physical health problems) with increasing numbers of pre-existing medical conditions negatively affecting the recovery of physical HRQOL.

H8: There is a significant interaction between the number of pre-existing medical conditions and gender in the course of psychological HRQOL at 3, 6, 9, and 12 months in previously hospitalized COVID-19 patients based on one aspect of psychological HRQOL (role limitations due to emotional problems) with increasing numbers of pre-existing medical conditions negatively affecting the recovery of psychological HRQOL.

Identifying a potential interaction between the number of pre-existing medical conditions and gender concerning the course of physical and psychological HRQOL over time can help healthcare providers recognize risk factors and improve personalized treatment and rehabilitation. By addressing the unique needs of patients with certain numbers of pre-existing medical conditions, more effective interventions might be possible to develop.

Methods

An observational longitudinal cohort research with non-probability sampling was used to analyze the course of HRQOL in people previously hospitalized and diagnosed with COVID-19 over 12 months.

Research Materials

This study is integrated into a larger ongoing longitudinal research project by *Medisch Spectrum Twente* in the Netherlands (Clinical Trials NCT05813574) concerning the long-term impact of COVID-19. Consequently, a wide range of research materials was included to measure HRQOL among hospitalized people who were PCR positive and therefore diagnosed with COVID-19. This study focuses on collected demographic information, patient reports about pre-existing medical conditions, and collected data from the *Short-Form Health Survey 36* (SF-36) evaluating HRQOL.

Sociodemographic Data

At the beginning of this study, participants had to fill in questions about their socio-demographic background assessing age, gender, height, weight, the highest level of education, income, living situation and pet ownership. A detailed overview of the response categories can be found in Appendix 1.

For a better overview, certain sociodemographic data was organized into groups according to the following structure. BMI was calculated as $\frac{weight\ (kg)}{height\ m^2}$ and classified into "underweight (<18.5)", "normal weight (18.5-24.9)", "overweight (25.0-29.9)" and "obesity (≥30)" following the standardized categories of the WHO (2000). In addition, the level of education was divided into "low education" (1= none; 2= lower general education; 3 = lower vocational education), "medium education" (4 = secondary general education; 5 = secondary vocational education; 6 = higher general and preparatory scientific education) and "higher education" (7 = higher vocational education (HBO); 8 = scientific education) according to the division of the Dutch education system by the European Commission (2024).

Health-Related Quality of Life

Gender differences in HRQOL were investigated based on data from the SF-36, a questionnaire used to survey different subscales of HRQOL namely physical functioning (PF), role limitations due to physical health problems (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE), and mental health (MH) (Ware et al., 1993). The SF-36 Measurement Model by Ware et al. (1993), allocates all questions of the SF-36 to one of the eight aspects of HRQOL. Physical health is analyzed by questions about PF, RP, BP, and GH while VT, SF, RE, and MH give insight into an individual's psychological health (Ware et al., 1993). The score ranges from 0 to 100. High scores were achieved if there were no restrictions, no limitations in social or ordinary activities, and a high level of well-being alongside a positive assessment of personal health (Ware et al., 1993). As a self-report measure, the outcomes refer to patients' perceptions of HRQOL.

Based on a study by Gandek et al. (2004) with 177,714 participants the internal consistency of the SF-36 was rated from good to excellent ranging between .89 and .94 for all subscales with an internal consistency of .94 for physical and .89 for psychological components. In the context of this analysis, two subscales were selected for further investigations based on the outcomes of research question one. RP was selected to represent physical HRQOL while RE was chosen for the assessment of psychological HRQOL.

Pre-Existing Medical Conditions

Pre-existing medical conditions were measured by twelve individual questions, one for each disease. The twelve questions were designed to assess the following illnesses: cardiovascular condition, hypertension, lung condition, diabetes, gastrointestinal condition, kidney disease, liver disease, blood condition or anemia, cancer, depression, rheumatic condition, and neurological condition. Participants could answer the following question for each of the twelve diseases "Have you been diagnosed with any other conditions [in addition to COVID-19] at this time?" on a dichotomous scale with either "Not applicable" or "Yes". The study focused on the above-mentioned twelve pre-existing medical conditions as they are clearly defined clinical conditions in the medical field. All "other conditions" were excluded from the analysis. In addition to pre-defined illnesses, obesity defined as having a BMI ≥30 was considered an additional pre-existing medical condition due to the link between obesity and negative disease progression, more severe COVID-19, and increased length of hospitalization (FAO, 2018; Dicker et al., 2020; Gao et al., 2021)

Participants

The long-term course of COVID-19 was investigated among hospital patients in the Netherlands who were subsequently diagnosed with SARS-CoV-2. Therefore, although hospitalization is an important factor to properly describe the study sample, patients have not been hospitalized because of COVID-19. Participants had to meet the following inclusion criteria: Dutch proficiency, being 18 years or older, and being hospitalized in one of the following hospitals: *Medisch Spectrum Twente* (MST) in Enschede or the *Ziekenhuisgroep Twente* (ZGT) in Almelo and Hengelo. In addition, participants had to test positive for SARS-CoV-2 via PCR testing at the time of hospitalization. Before the start of the study, all participants received an e-mail containing a patient information form educating them about the purpose and procedure of the study as well as their legal rights as participants.

Procedure

After receiving ethical permission from the MST's institutional review board (correspondence number K20-30), data collection began in September 2020. The initial step was recruiting study participants among people infected with COVID-19 who met the above-mentioned inclusion criteria allowing them to participate in this study. After filling out an informed consent form, participants could either fill in the questionnaires via a digital or paper-based application. If questionnaires were answered on paper, data was later converted into a digital database. Alongside the questionnaires used in this study, participants' sociodemographic data was assessed once. The target group had to fill in the questionnaires in three-month intervals 3, 6, 9, and 12 months after hospital discharge. All digital data was stored on Qualtrics while paper-based data was collected at the rheumatology department of the MST. By filling in the last questionnaire at 12 months the study ended. The general data collection ended in November 2023.

Data Analysis

Data Preparation

As this research is linked to a larger longitudinal study, data from paper questionnaires and Qualtrics was already merged into one coherent data set and thus could be imported into *IBM SPSS Statistics* Version 29.0.1.0. without further preparation. Afterward, the inserted data was examined for missing values among the eight subscales of the SF-36 as well as the demographical information. This step was conducted since missing values can decrease the effectiveness of statistical interference (Little & Rubin, 2019). Participants who did not specify their gender were excluded, as this information was deemed essential to analyze gender differences. Based on the distribution of the missing values, it was assumed that they were missing randomly.

Statistical Analyses

All analyses were performed in *IBM SPSS Statistics* Version 29.0.1.0. A significance level of $\alpha = .05$ was chosen to indicate statistical significance.

Research Question 1. To answer the first research question "Which subscales of physical and psychological HRQOL show the most prominent longitudinal increase in scores between 3 and 12 months in previously hospitalized COVID-19 patients?" a linear mixed model (LMM) analysis for each subscale (PF, RP, BP, GH, VT, SF, RE, MH) of physical and psychological HRQOL was performed. The model was constructed with a first-order autoregressive covariance structure AR(1) to account for correlations between repeated measurements. The variable time was included as a fixed effect to capture the influence of time on the dependent variables thus the subscales of physical and psychological HRQOL. Within this analysis, estimated marginal means (EMM) for all subscales at each time point were calculated. In addition, two post hoc LMM analyses on the effect of RP on general physical HRQOL and RE on general psychological HRQOL were conducted. Missing data was addressed using maximum likelihood estimation (MLE) which was selected in favor of fixed effects. MLE allows accounting for missing values throughout the measurements maximizing the available data, and reducing possible biases (Guo & Zhao, 2000).

Research Questions 2 and 3. To answer the following research questions "Are there gender differences in the course of physical and psychological HRQOL at 3, 6, 9, and 12 months in previously hospitalized COVID-19 patients?" and "When (3, 6, 9, or 12 months) does the course of physical and psychological HRQOL show the greatest divergence between men and women in previously hospitalized COVID-19 patients?" two LMM analyses with time, gender, and time*gender as fixed factors were executed. The dependent variable for the first analysis of physical HRQOL was RP while RE was the dependent variable for the second analysis of psychological HRQOL. In addition, EMMs were assessed to compare gender differences at each time point.

Research Question 4. To explore the influence of pre-existing medical conditions via the following research question "Is there a significant interaction between the number of pre-existing medical conditions and gender in the course of physical and psychological HRQOL at 3, 6, 9, and 12 months in previously hospitalized COVID-19 patients?" two LMM analyses were performed. The fixed effects in this model included time, gender, the number of pre-existing medical conditions, and the interactions between time*gender, time*number of pre-existing conditions as well as the three-way interaction between time*gender*number of pre-existing conditions. The dependent variables were again RP and RE to evaluate physical and psychological HRQOL.

Assumptions for Linear Mixed Model Analyses. Model assumptions, including linearity, normality of residuals, homoscedasticity, and independence of residuals, were tested to validate the appropriateness of the LMM approach. Scatter plots were used to investigate linearity. RP and RE scores were distributed across the entire range (0 to 100) at each time point for all variables indicating a violation of linearity (Appendix 2). Normality for the residuals was analyzed using histograms and Q-Q plots. Both indicated deviations from normality (Appendix 3). Homoscedasticity was assessed using scatter plots of residuals which revealed a clear pattern of increasing spread of residuals with higher RP and RE scores, indicating a violation of homoscedasticity (Appendix 4). Lastly, independence for the residuals was assessed using scatter plots which revealed that residuals were randomly scattered around zero with no visible patterns or trends thus showing independence (Appendix 5). Given the nature of the data, linear mixed modeling was still perceived as the best-fitting analysis to capture all important patterns despite these violations. Based on careful consideration, no adaptations to the data were made which is further discussed in the limitations of this study.

Results

Study Sample

In total, data from 687 participants, 431 men (62.7%) and 256 women (37.3%), aged between 26 and 89 (μ = 63.76, SD = 11.33) was used in the current analysis. A noticeable trend was the high proportion of overweight (n = 308, 44.8%) and obese (n = 215, 31.3%) people with a BMI above 24.9. For detailed sample characteristics and an overview of missing values, see Table 2.

Table 2

Descriptive Statistics of the Study Sample (N=687)

Characteristics	*n*	%
Body Mass Index (BMI)		
Underweight (BMI <18.5)	2	0.3
Normal weight (BMI 18.5 - 24.9)	138	20.1
Overweight (BMI 25.0 - 29.9)	308	44.8

Obesity (BMI ≥30)	215	31.3
Missing Values	24	3.5
Level of Education		
Low	147	21.4
Medium	314	45.7
High	217	31.6
Missing Values	9	1.3
Level of Income		
< €1.000	68	9.9
€1.000 - €2.500	279	40.6
€2.500 - €5.000	184	26.8
> €5.000	21	3.1
I'd rather not say	124	18.0
Missing Values	11	1.6
Living Situation		
Living alone	116	16.9
Living with partner without kid	340	49.5
Living with partner and kids	198	28.8
Living without partner with kids	11	1.6
Other	10	1.5
Missing Values	12	1.7
Pet Ownership		
No	443	64.5
Yes	233	33.9
Missing Values	11	1.6
Number of Pre-Existing Medical Conditions		
0	192	27.9
1	257	37.4
2	127	18.5
3	66	9.6
4	23	3.3
5	11	1.6
6	2	0.3

7	1	0.1
Missing Values	8	1.2
Frequency of Occurrence for Each Pre-Existing Medical Condition		
Obesity	215	31.3
Hypertension	176	25.6
Lung condition	163	24.0
Cerebrovascular Condition	147	21.4
Diabetes	119	17.3
Rheumatoid arthritis	88	12.8
Gastrointestinal condition	51	7.4
Cancer	40	5.8
Neurological condition	24	3.5
Depression	22	3.2
Blood condition or anemia	21	3.1
Kidney disease	19	2.8
Liver disease	5	0.7

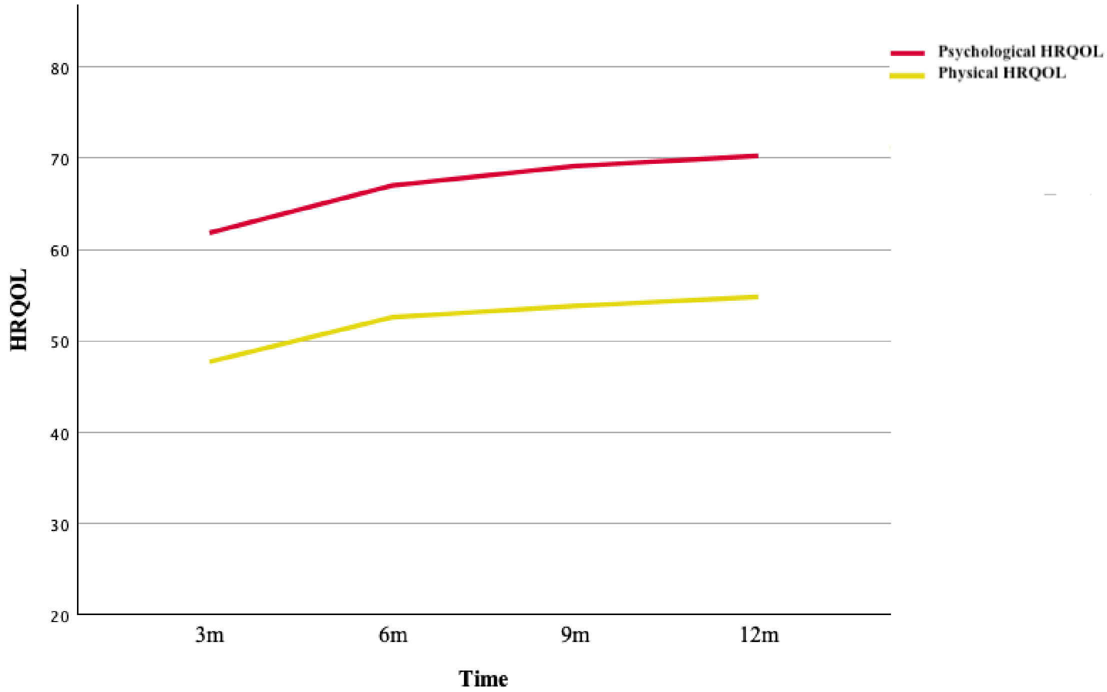
Note. The level of education was classified according to the division of the Dutch education system. Adapted from *Key Features of the Dutch Education System* by the European Commission, 2024.

Research Question 1: Subscales of Physical and Psychological HRQOL with Most Prominent Longitudinal Increase in Scores Between 3 and 12 Months

On average, people scored lower in overall physical HRQOL than in overall psychological HRQOL (see Figure 1). The first stage involved analyzing the general course of physical and psychological HRQOL on each subscale by examining the development of EMMs for the different scales across all four measurement points (see Appendix 6).

Figure 1

Overview of the Average Scores in Physical and Psychological HRQOL over Twelve Months in Previously Hospitalized COVID-19 Patients (N = 687)

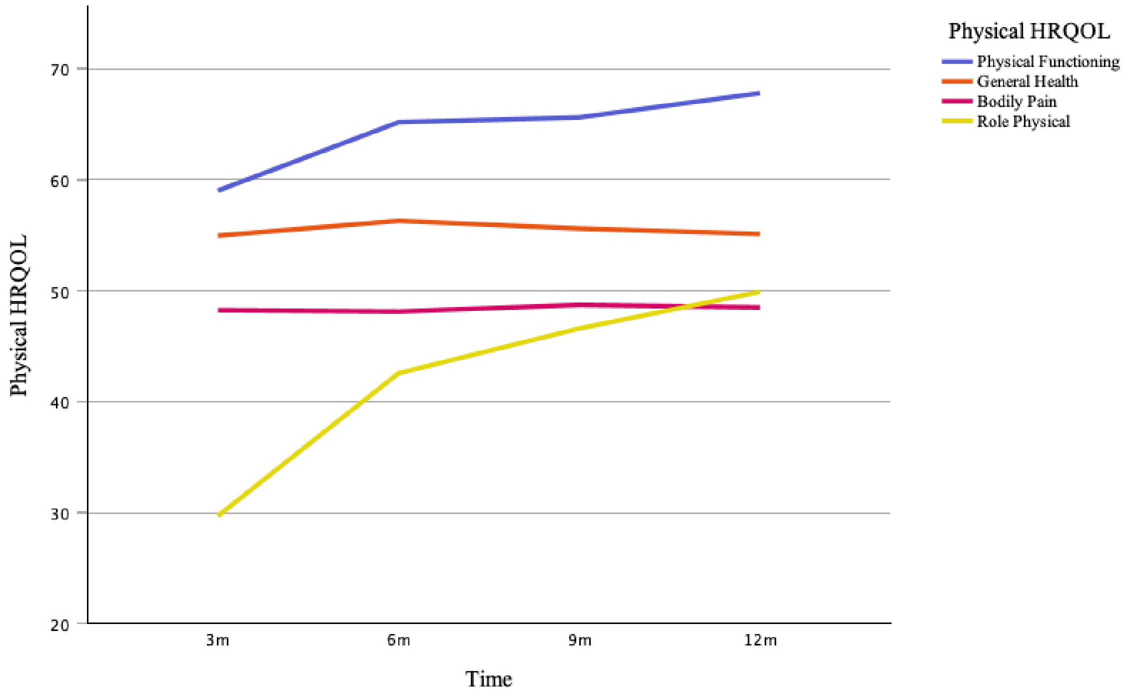


Note. The score ranges from 0 (high perceived restrictions) to 100 (no perceived restrictions).

The calculated EMMS of the first four LMM analyses were used to provide a descriptive overview of the score distribution on the different subscales of physical HRQOL. Figure 2 illustrates the general distribution of scores for the different scales of physical HRQOL at 3, 6, 9, and 12 months in this sample (N = 687). The first analysis showed a general improvement on all subscales of physical HRQOL except for GH which slightly decreased between the first and last measurement. What stands out is a noticeable score increase in average RP scores over 12 months in previously hospitalized COVID-19 patients. 3 months after hospitalization, the average RP value was 29.05 (SE = 1.87). Reaching the 12-month measurement point the average value had increased considerably to 48.33 (SE = 1.86) indicating a strong improvement in RP in the year after hospitalization. This means that the values have come closer to the average RP score of 76.4 in the Dutch population (Aaronson et al., 1998). Based on this great longitudinal score increase, RP was of the most interest for subsequent analyses of physical HRQOL.

Figure 2

Overview of the Average Course of Physical HRQOL over Twelve Months in Previously Hospitalized COVID-19 Patients (N = 687)

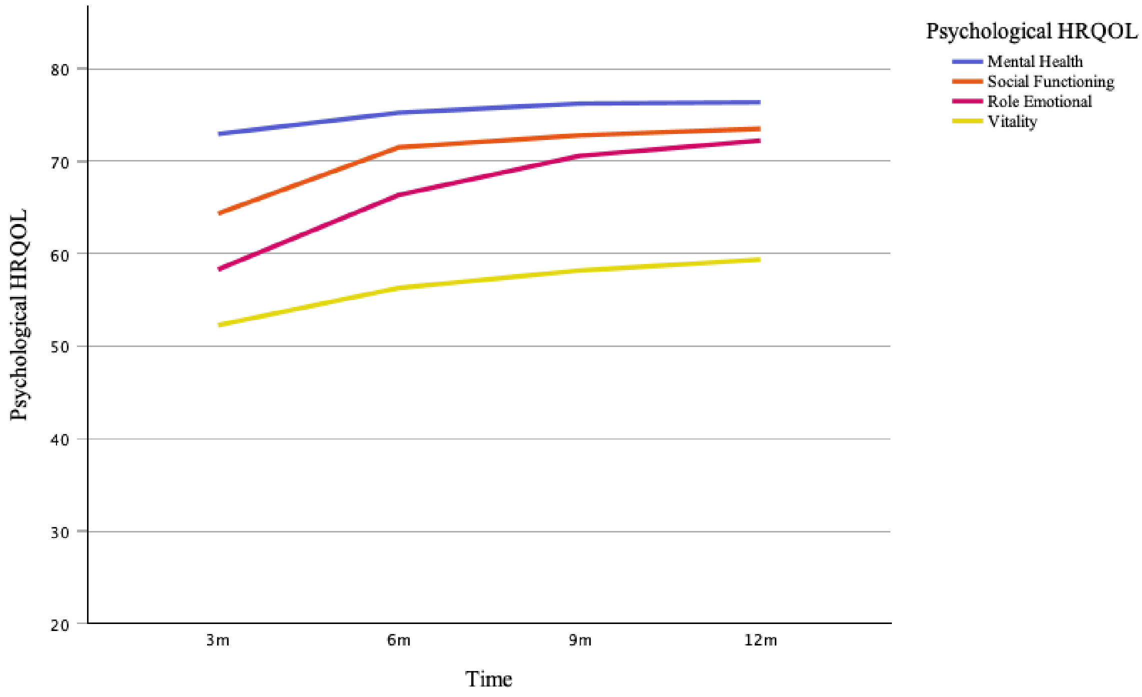


Note. The score ranges from 0 (high perceived restrictions of RP) to 100 (no perceived restrictions of RP).

Afterward, the calculated EMMs of the following four LMM analyses were used to provide a descriptive overview of the score distribution on the different scales of psychological HRQOL. Figure 3 illustrates the general distribution of scores for the different scales of psychological HRQOL at 3, 6, 9, and 12 months in this sample ($N = 687$). The average scores of psychological HRQOL in previously hospitalized COVID-19 patients showed steady improvements over 12 months on all subscales. However, the most interesting course over 12 months was found in RE. Starting at 3 months, the mean RE score was 58.25 ($SE = 1.86$) which is low compared to the average RE score in the Dutch population of 82.3 (Aaronson et al., 1998). RE scores increased to 72.20 ($SE = 1.83$) at 12 months, which indicates the strongest score improvement among all psychological subscales. Based on this great longitudinal score increase, RE was of most interest for subsequent analyses of psychological HRQOL.

Figure 3

Overview of the Average Course of Psychological HRQOL over Twelve Months in Previously Hospitalized COVID-19 Patients (N = 687)



Note. The score ranges from 0 (high perceived restrictions of RE) to 100 (no perceived restrictions of RE).

Following this pre-selection of subscales, the significance between time and RP and time and RE ($N = 687$) was analyzed in two separate models. Significant main effects of time on RP were found ($B = 6.152$, $SE = 0.79$, $t = 7.75$, $p < .001$), indicating that RP scores increased by an average of 6.152 points every 3 months post-hospitalization. This suggests a consistent improvement of RP over the 12-month follow-up period. In addition, the main effect of time on RE was also highly significant ($B = 4.595$, $SE = 0.82$, $t = 5.62$, $p < .001$), indicating that RE scores increased by an average of 4.595 points every 3 months post-hospitalization. This result suggests a consistent improvement in RE in the year after hospitalization. These analyses highlight that both RP and RE subscales show significant positive trends over time.

Research Question 2: Gender Differences in the Development of Physical and Psychological HRQOL at 3, 6, 9, and 12 Months

Second, it was investigated whether there were gender differences in the course of physical and psychological HRQOL at 3, 6, 9, and 12 months in previously hospitalized COVID-19 patients. The results of the first LMM ($N = 687$) with RP as the dependent variable revealed no significant interaction between time and gender ($B = -1.719$, $SE = 1.64$, $t = -1.05$, $p = .295$), suggesting that the rate of improvement in RP scores over time did not significantly differ between men and women. This implies that although there is a gender difference in RP at 3 months, the course of improvement over the subsequent measurements at 6, 9, and 12 months is similar for both genders. Overall, these results indicate that while both time and gender independently influence RP, the lack of a significant interaction effect suggests that the pattern of recovery over time is comparable between men and women. For an overview of the results of the interaction effect between time and gender on RP see Appendix 7.

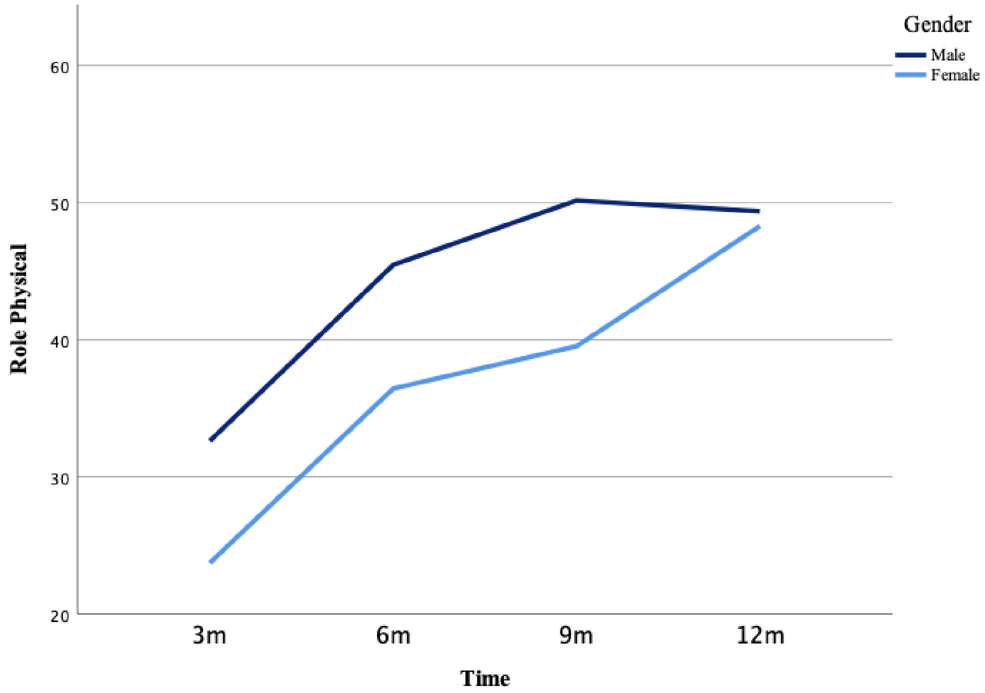
A further analysis ($N = 687$) with RE as the dependent variable revealed no significant interaction effect between time and gender ($B = -3.262$, $SE = 1.69$, $t = -1.93$, $p = .054$), suggesting that the rate of improvement in RE scores over time did not significantly differ between men and women. Overall, these results indicate that while both time and gender independently influence RE, the pattern of recovery over time shows no notable gender difference in the course of recovery between genders. For an overview of the results of the interaction effect between time and gender on RE see Appendix 8.

Research Question 3: Time Point with the Greatest Divergence in Physical and Psychological HRQOL Between Men and Women

In the next step, this study investigated the measurement point with the greatest divergence in RP and RE between men and women ($N = 687$). As illustrated in Figure 4, the greatest divergence in physical HRQOL measured by RP between men and women occurred 3 months after hospital discharge with men ranking RP higher than women. For a detailed overview of the estimated mean scores and the standard error of RP in men and women at each time point, see Appendix 9.

Figure 4

Visual Representation of the Relationship Between Time and the Course of RP

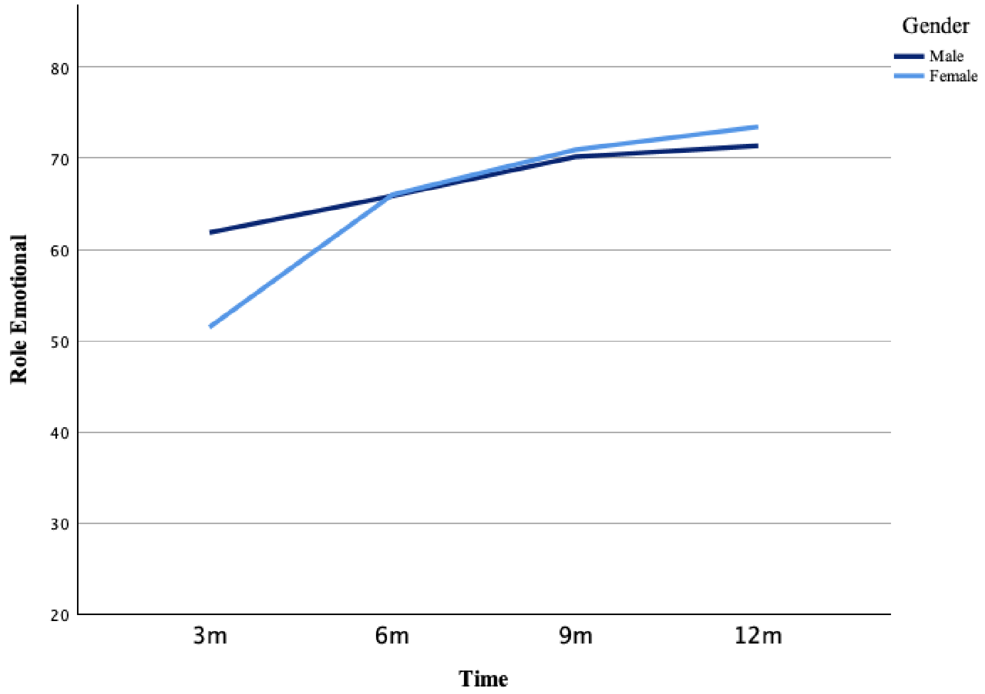


Note. The score ranges from 0 (high perceived restrictions of RP) to 100 (no perceived restrictions of RP).

In model two, RE served as the dependent variable. As illustrated in Figure 5, the greatest divergence in psychological HRQOL measured by RE between men and women occurred 3 months after hospital discharge with men ranking higher in RE than women. For a detailed overview of the mean scores and the standard error of RE in men and women at each time point see Appendix 10.

Figure 5

Visual Representation of the Relationship Between Gender and the Course of RE



Note. The score ranges from 0 (high perceived restrictions of RE) to 100 (no perceived restrictions of RE).

Research Question 4: Interaction Between the Number of Pre-Existing Medical Conditions and Gender in the Development of Physical and Psychological HRQOL at 3, 6, 9, and 12 months

Lastly, it was analyzed whether there is an interaction between the number of pre-existing medical conditions and gender in the course of physical and psychological HRQOL over 12 months. The first analysis (N = 679) focused on RP as a dependent variable. This analysis showed a significant interaction effect between time and the number of pre-existing medical conditions on the course of RP over 12 months (B = −3.461, SE = 1.08, t = -3.20, p < .001), indicating that the negative impact on RP of one or more pre-existing medical conditions increases over time. However, no further significant effects have been found. Thus, no significant interaction effect between time, gender, and the number of pre-existing medical conditions on RP has been found (B = 1.713, SE = 1.33, t = 1.29, p = .199). For a detailed overview of the results see Appendix 11.

The second analysis (N = 679) focused on RE as a dependent variable. This analysis showed no significant interaction effect between time, gender, and the number of pre-existing medical conditions on RE ($B = .656$, $SE = 1.38$, $t = .475$, $p = .635$). For a detailed overview of the results see Appendix 12.

Discussion

This observational longitudinal cohort study investigated potential gender differences regarding the course of recovery from COVID-19 in previously hospitalized COVID-19 patients with a focus on physical and psychological role functioning. Both subscales showed the most striking divergences of average scores. This aligns with previous studies that observed lower scores in both role functioning scales in comparison to other subscales of physical and psychological health (Chen et al., 2020; Temperoni et al., 2021). H1 and H2 can therefore be accepted.

In summary, a consistent increase in physical and psychological role functioning over time was observed for all patients in this sample. While men displayed higher initial role functioning scores both genders showed a similar course of recovery with the greatest gender difference in physical and psychological role functioning scores 3 months post-hospitalization. Lastly, regarding an interaction between the number of pre-existing medical conditions, time, and gender no negative impact of the number of pre-existing medical conditions on the course of physical and psychological role functioning was noted under consideration of time and gender.

Overall, physical HRQOL was rated worse than psychological HRQOL. However, physical long-term symptoms often dominate psychological long-term symptoms. Studies found that eight of the top ten most persistent symptoms one year after SARS-CoV-2 infection were physical symptoms namely fatigue, aching muscles, physical slowness, poor sleep, breathlessness, joint pain, pain, and limb weakness (PHOSP-COVID Collaborative Group, 2022; Van Wambeke et al., 2023). In addition, in this study sample, 76.1% were either overweight or obese, which is linked to an average physical HRQOL score under 50 (Chen et al., 2020). Therefore, people in this target group had better mental health than physical well-being in the 12-month post-hospitalization and were thus more affected by physical restrictions than psychological issues.

Moreover, physical and psychological role functioning increased over 12 months, indicating a general trend of recovery post-hospitalization. This observation aligns with findings from other studies, such as Iqbal et al. (2021). In the context of this study, recovery refers to increased physical and psychological well-being measured by an upward development in points toward the normal range of the average Dutch population hence 76.4

for physical and 82.3 for psychological role functioning (Aaronson et al., 1998) on the subscales of the SF-36. Consequently, the more time has passed since the infection with SARS-CoV-2, the lower the restrictions caused by persistent COVID-19 symptoms, and the higher people's ability to fulfill their social roles either in work- or free-time activities.

Gender Differences

3 months after hospital discharge men had fewer role functioning restrictions caused by physical and psychological health issues, rating physical role function 12.5 points and psychological role function 13.2 points higher than women. Consequently, women are more restricted in fulfilling professional and private roles due to limitations in physical or psychological health during the 12-month post-hospitalization. This is consistent with findings of other studies that observed better physical and psychological well-being in men in the time following a COVID-19 infection (Schröder et al., 2024; Marcilla-Toribio et al., 2024) or COVID-19-related hospitalization (Chen et al., 2020; Qu et al., 2021; PHOSP-COVID Collaborative Group, 2022). It is important to consider, that women in the Netherlands already had lower average physical and psychological role functioning scores of 4.9 and 7.0 points compared to Dutch men (Aaronson et al., 1998). Therefore, gender differences in health status have already been present. Nevertheless, the gender differences in this study were greater than the ones found in the average Dutch population, which could be rooted in different aspects. First, a stronger impairment of physical and psychological well-being in women (Schröder et al., 2024) due to a higher frequency of LC symptoms (Iqbal, 2012; Gebhard et al., 2021). Second, gender inequalities resulting from societal norms and expectations, which pose special challenges for women in general, but also regarding the disease progression of long-term illnesses such as LC (del Río et al., 2017; Gebhard et al., 2021; Roethlisberger et al., 2023; Barr et al., 2024; Marcilla-Toribio et al., 2024). Lastly, the initially described biological variations between men and women like differences in immune reactions (Klein et al., 2016; Sharma et al., 2020), hormones (Stewart et al., 2021), immunological aspects (Marcilla-Toribio et al., 2024; Bwire, 2020), and pain sensitivity (Osborne & Davis, 2022; Fillingim et al., 2009).

A key finding was that time and gender did not influence the course of recovery of physical and psychological role functioning, indicating similar recovery trajectories for both genders. Although men had higher scores at 3 months, the overall recovery courses were comparable, with an average increase of 7.2 points in physical and 6.7 points in psychological role functioning every 3 months. H3 and H4 must therefore be rejected. There is a lack of studies on gender differences in the course of HRQOL after COVID-19-related and non-related hospitalization. However, studies that investigated the average recovery period for COVID-19 found that the general time of recovery is similar for men and women (Zhou et al., 2020; Ejaz et al., 2023). This similarity may be caused by the "post-hospital syndrome". Shared experiences with hospitalization can result in less pronounced gender differences, in this case in comparison to the general Dutch population (Voiriot et al., 2022; Rodríguez Onieva et al., 2024).

The difference in physical and psychological role functioning scores between men and women was the greatest 3 months after hospital discharge. This means, that the differences in the ability to fulfill social roles without physical or psychological health restrictions between men and women were the greatest 3 months post-hospitalization. H5 and H6 can therefore be accepted. This discrepancy can be explained by a higher load of persistent LC symptoms in women leading to increased burdens on physical and psychological well-being (Gebhard et al., 2021; Fernández-de-las-Peñas et al., 2022; Sylvester et al., 2022). Consequently, early recovery programs like occupational therapy, cognitive rehabilitation programs, physiotherapy, or psychological support should especially target women during this critical phase.

Impact of Pre-Existing Medical Conditions

The interaction of gender, time, and the number of pre-existing medical conditions did not have an impact on physical and psychological role functioning scores when considering time and gender. This shows that although scientists found that pre-existing medical conditions increase the risk for a more severe course of COVID-19 (Jacobs et al., 2023) as well as LC (Aggarwal et al., 2020; Biswas et al., 2020), men and women with varying numbers of pre-existing medical conditions experience a similar course in the restoration of physical and psychological role functioning over time. Consequently, H7 and H8 are to be rejected. Two key aspects could have led to this outcome. First, the impact of pre-existing medical conditions on the course of LC is disease-specific and can differ between illnesses (Fernández-de-las-Peñas et al., 2023). However, this study made no distinctions between different comorbidities. In addition, collected information on pre-existing medical conditions was self-reported and did not evaluate details about the nature and severity of the disease or the amount of time that passed since the diagnosis.

Strengths and Limitations

This study has several strengths that highlight its value to current research. First, the large sample of participants increased the statistical power and reliability of the study results and improved the generalisability of the findings to a larger population (Ioannidis, 2005; Faber & Fonseca, 2014). Second, the longitudinal design of this study included four measurement points over a 12-month period, which improved the ability to detect long-term effects and patterns. Third, the use of the SF-36, as a validated measurement instrument, ensured that all HRQOL constructs were measured accurately.

However, this research does have limitations that should be considered when evaluating the study results. One of them is the above-described partial violations of the assumption for LMM analyses which could affect the reliability of outcomes in this study. The course of RP and RE scores over time did not follow a linear pattern, indicating that the scores might change in a more complex pattern. For both aspects, gender and the number of pre-existing medical conditions, RP and RE scores varied widely. In addition, there was no linear relationship between the number of conditions and RP and RE scores, indicating variation in scores at each number of conditions. However, it is difficult to obtain perfectly straight-lined scatter plots, as it is almost impossible to specify a model without any bias and LMMs are perceived as relatively stable to slight violations, especially with larger sample sizes (Wang et al., 2022). Moreover, the residuals for RP and RE were not normally distributed and exhibited skewness which could affect the p-values that have been found. This could result in misinterpretations or unreliable conclusions about the study population. However, in certain cases, such as the investigation of diseases, normally distributed data is not always considered useful (Oberg & Mahoney, 2007). In addition, a violation of normally distributed residuals is considered not fatal regarding its effects on standard errors even if the distribution is slightly skewed (Field et al., 2012). The scatter plots regarding homoscedasticity revealed a clear pattern of increasing spread of residuals with higher RP and RE scores, indicating that the variance of the residuals is not constant. However, less severe violations of homoscedasticity were found to only have a minimal influence on the reliability of standard errors (Tabachnick et al., 2013). Flawless adherence to all modeling assumptions is rare (Field et al., 2012). While the model still provides valuable insights, data should be interpreted with caution due to the violation of multiple assumptions and future research should consider alternative models. Generalized linear mixed models are a particularly strong option, as they are robust to many of the violated assumptions identified in this study (Bolker et al., 2009).

In addition, other limitations should be considered while interpreting the results. First, this study did not contain a baseline measurement and is therefore lacking information about the status of HRQOL before the infection with COVID-19. Moreover, the assessment of pre-existing medical conditions was partly flawed. Pre-existing medical conditions were assessed via self-reports which means that the precise time of diagnosis could not be considered, the nature and severity of an illness could not be assessed, and none of them were verified by medical professionals afterward. This means that diagnoses could date back several years, the same diseases could affect people differently or pre-existing medical conditions could be reported incorrectly. Moreover, additional pre-existing medical conditions listed in "other conditions" that were not listed in the pre-defined response options were excluded from the analysis, which may have influenced the total number of comorbidities among people in this target group and thus the study outcomes. Lastly, the sample was collected by non-probability sampling containing people from two hospitals in the Twente region in the Netherlands which may limit the generalizability of these findings.

Conclusion and Recommendations for Future Research

Role functioning—both physical and psychological—improved over time among previously hospitalized COVID-19 patients, indicating recovery over 12 months. While men had higher initial role functioning scores 3 months post-hospitalization, and the scores of physical and psychological role functioning of men and women showed the greatest divergence at this time point, a similar recovery course regarding physical and psychological role functioning suggests that gender differences 3 months post-hospitalization diminish in the longer term. Consequently, as time passes, the impact of COVID-19 on the fulfillment of personal and work-related roles diminishes for both men and women. Moreover, the number of pre-existing medical conditions had no impact on physical and psychological role functioning under consideration of time and gender. This indicates that the recovery pattern of physical and psychological role functioning is similar regardless of the number of underlying pre-existing medical conditions. This finding is reassuring for the treatment of COVID-19 patients with multiple medical conditions as a higher number of comorbidities in men and women is not linked to a stronger impairment of physical or psychological role functioning over time compared to people with fewer comorbidities in this context.

The following conclusions can be made for existing health measures and the design of future recovery programs that aim to restore the physical and psychological HRQOL of previously hospitalized COVID-19 patients in the Netherlands: First, early recovery programs during the first months post-hospitalization should consider providing additional support for women in aspects like self-management and general healthcare by implementing tailored post-COVID-19 interventions, either physical (Nambi et al., 2022) or digital (Fowler-Davis et al., 2021; Rinn et al., 2024). Existing multidisciplinary rehabilitation programs such as the *Recovering from COVID* rehabilitation course could be replicated and tailored to women of this target group to offer support during the first months of recovery (Harenwall et al., 2021). Second, given that initial gender differences diminish with time and the course of recovery becomes more similar, additional recovery programs that start after the critical phase 3 months post-hospital discharge can be uniformly applied for all previously hospitalized COVID-19 patients without the need for gender-specific adjustments. Third, from a long-term and gender-related perspective, no targeted interventions for previously hospitalized COVID-19 patients with multiple pre-existing medical conditions are needed. These study findings could be useful for various areas of post-COVID-19 health interventions, for example, occupational therapy (von Zweck et al., 2023), physiotherapy (Santangelo, L., & Ginestra, 2022), psychological support (Priyamvada et al., 2021) or cognitive rehabilitation programs (Möller et al., 2023).

Future studies alongside larger sample sizes or different models like generalized linear mixed models are required to further investigate gender differences in the course of physical and psychological HRQOL in previously hospitalized COVID-19 patients. Researchers could gain a more holistic understanding of areas most impacted by COVID-19 by investigating other subscales of HRQOL that might be affected by COVID-19 sequel, leading to better-targeted interventions and more comprehensive healthcare strategies, for example, a longitudinal cohort study centered on the HRQOL subscale SF to study the impact of ongoing COVID-19 sequel on social interactions and relationship quality. In addition, future research on gender differences should include non-binary people as they are often neglected in health research (Singh et al., 2022). Lastly, research on the influence of pre-existing medical conditions may be enhanced by improving the data collection, by focusing on the individual impact of specific pre-existing medical conditions, rather than the influence of the number of conditions on COVID-19 recovery, by collecting additional information, like the time of diagnosis and the severity of the illness.

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AI statement

During the preparation of this work, the author used *Grammarly* to check grammar and spelling and enhance the clarity and readability of this Master thesis. Additionally, the author used *Chat GPT* to generate Codes for SPSS. After using these tools/services, the author reviewed and edited the content as needed and is therefore fully responsible for the content of this work.

Appendices

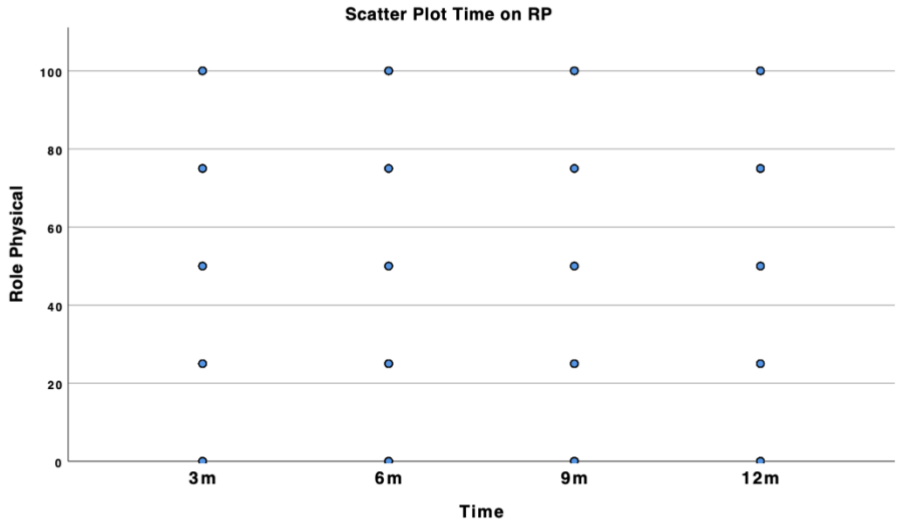
Appendix 1

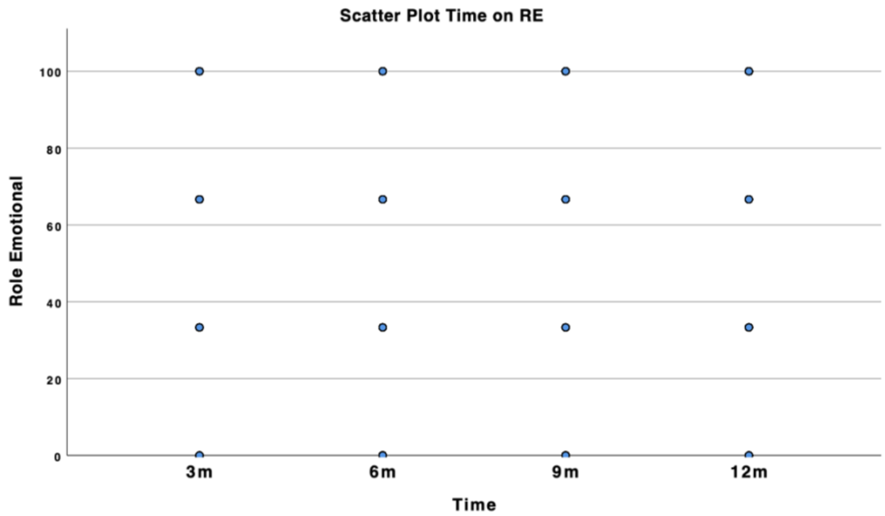
Response Categories for Socio-Demographic Data Collection

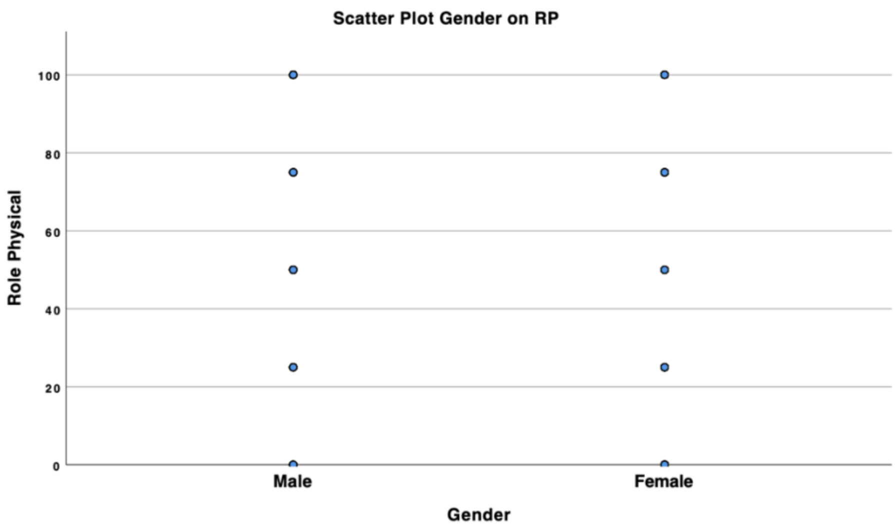
Requested Information	Response Categories
Gender	1= male; 2= female
Height	In cm
Weight	In kg
Highest level of education	1= none
	2= lower general education (primary school, elementary education)
	3 = lower vocational education (e.g. homeschool, LEAO, LTS, VMBO-kader, etc.)
	4 = secondary general education (MAVO, VMBO-theoretisch, IVO, (M)ULO, etc.)
	5 = secondary vocational education (MTS, MEAO, MHNO, INAS, etc.)
	6 = higher general and preparatory scientific education (HAVO, HBS, MMS, VWO, etc.)
	7 = higher vocational education (HBO)
	8 = scientific education (University)
	9 = others
Income	1 = < €1.000
	2 = €1.000 - €2.500
	3 = €2.500 - €5.000
	4 = > €5.000
	5 = I'd rather not say
Living situation	1 = living alone
	2 = living with partner without kid
	3 = living with partner and kids
	4 = living without partner with kids
	5 = others
Pet ownership	1 = no; 2 = yes

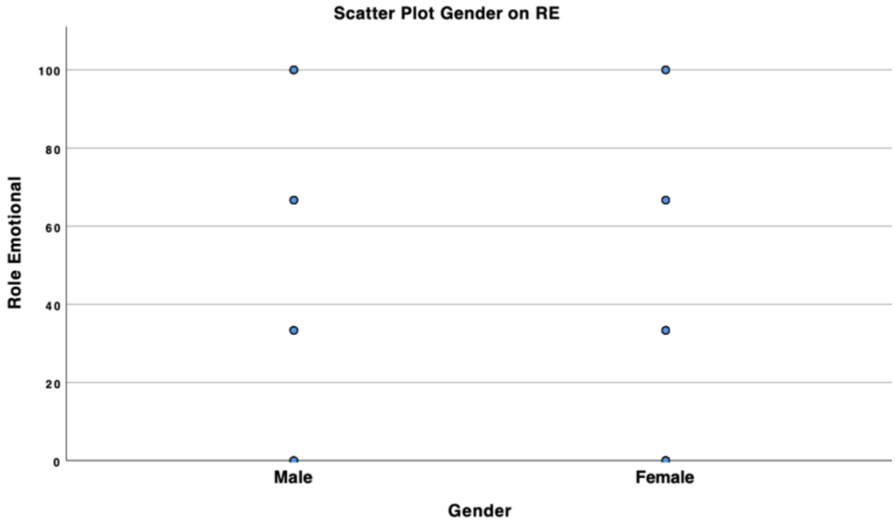
Appendix 2

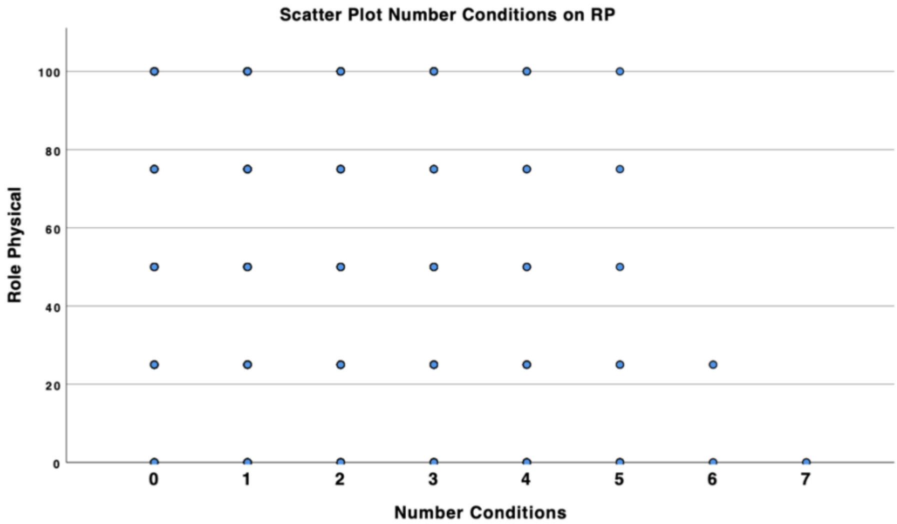
Assumption of Linearity Tested for Linear Mixed Models

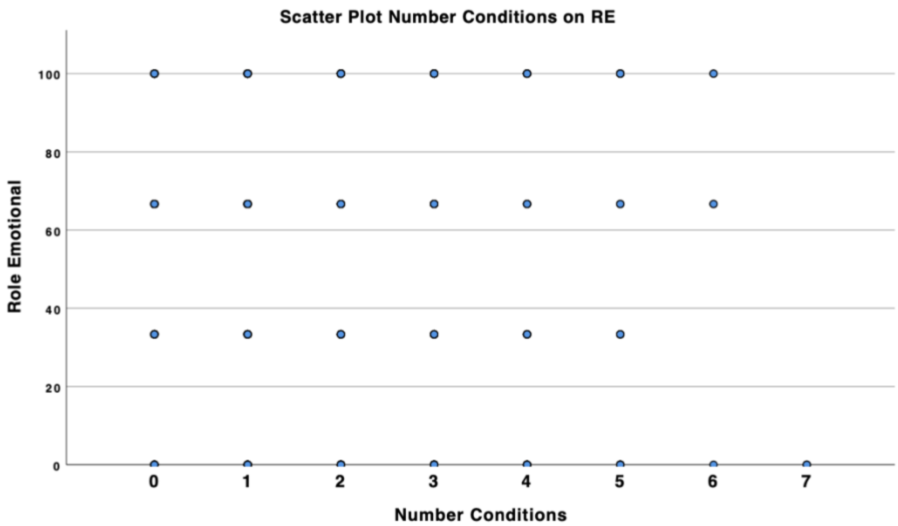






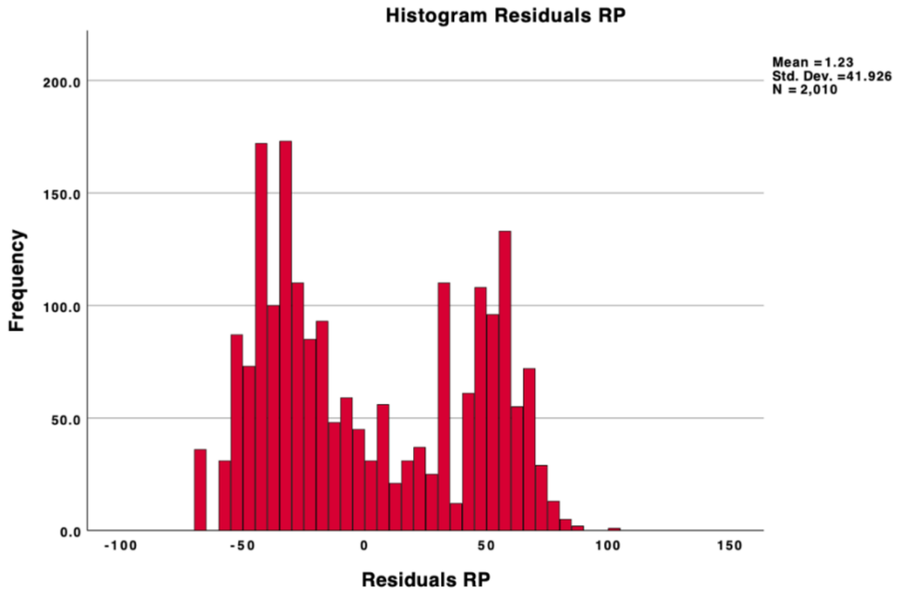

Scatter Plot Gender on RE
Role Emotional
100
80
60
40
20
0
Male
Female
Gender

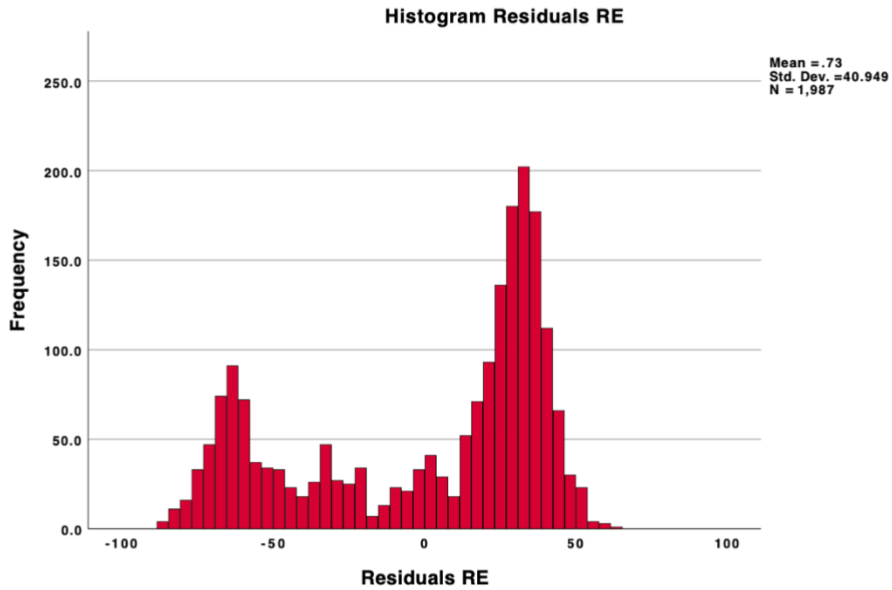

Scatter Plot Number Conditions on RP
Role Physical
100
80
60
40
20
0
0
1
2
3
4
5
6
7
Number Conditions

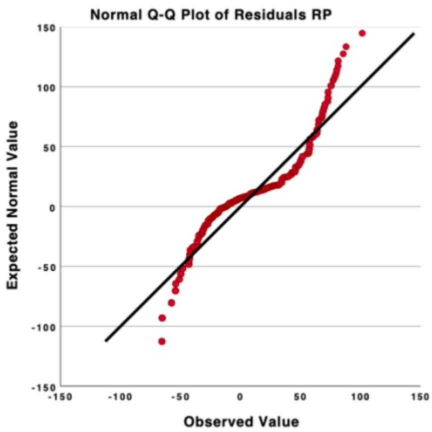

Scatter Plot Number Conditions on RE
Role Emotional
100
80
60
40
20
0
0
1
2
3
4
5
6
7
Number Conditions

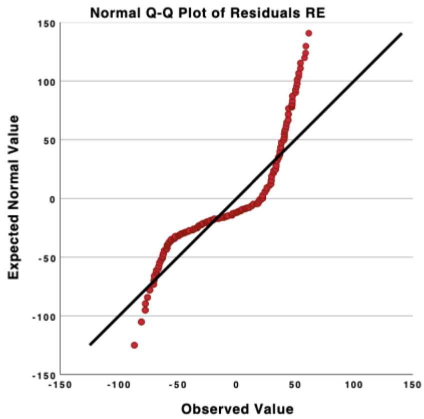
Appendix 3

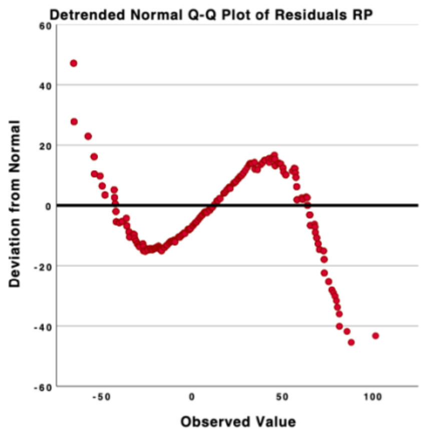
Assumption of Normality Tested for Linear Mixed Models

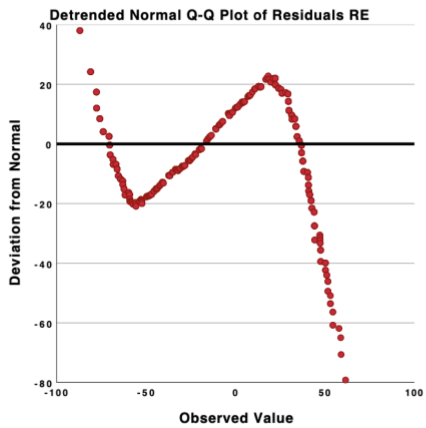





Normal Q-Q Plot of Residuals RP
Expected Normal Value
Observed Value

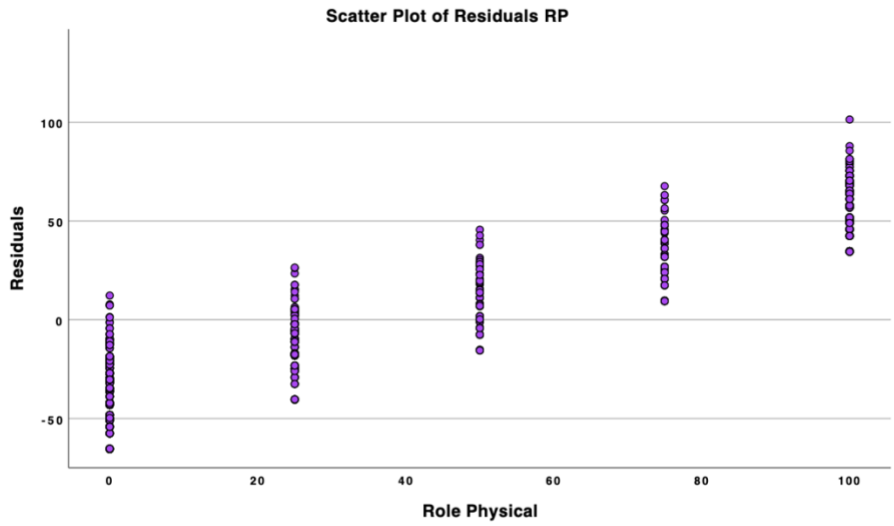

Normal Q-Q Plot of Residuals RE
Expected Normal Value
Observed Value

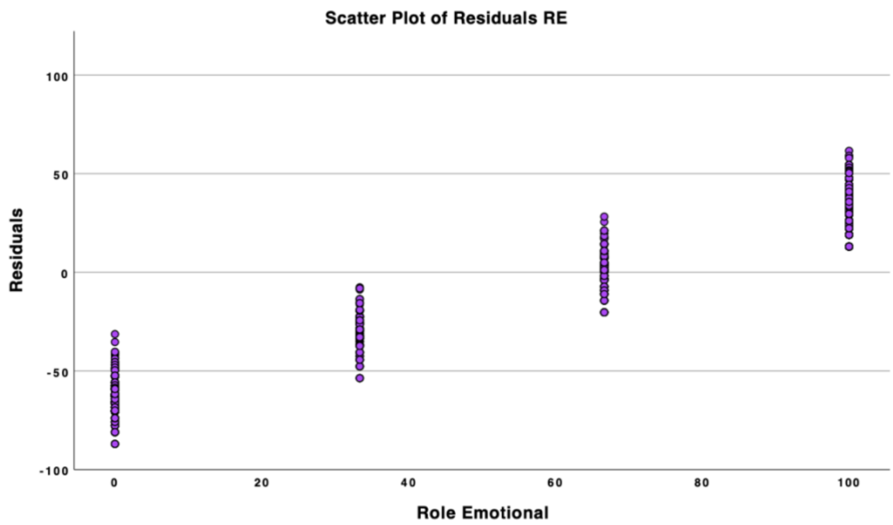

Detrended Normal Q-Q Plot of Residuals RP
Deviation from Normal
Observed Value


Detrended Normal Q-Q Plot of Residuals RE
Deviation from Normal
Observed Value

Appendix 4

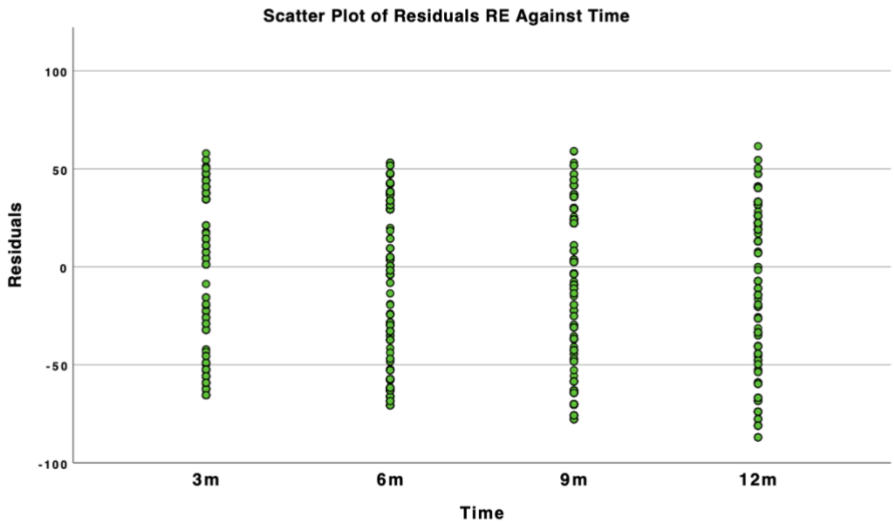
Assumption of Homoscedasticity Tested for Linear Mixed Models

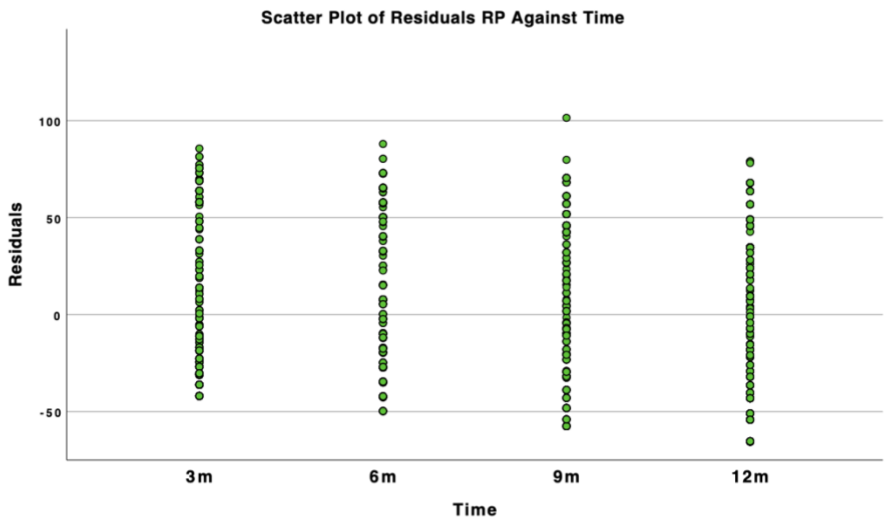




Appendix 5

Assumption of Independence Tested for Linear Mixed Models





Appendix 6

The course of HRQOL Subscales Over Time in Previously Hospitalized COVID-19 Patients

Month	3		6		9		12	
	M	*SE*	*M*	*SE*	*M*	*SE*	*M*	*SE*
PF [a]	59.03	1.14	63.84	1.11	64.98	1.12	66.49	1.15
RP [c]	29.05	1.87	41.22	1.78	45.31	1.82	48.33	1.86
BP [c]	48.20	0.30	48.13	0.28	48.69	0.29	48.44	0.29
GH [b]	55.95	0.70	55.71	0.67	54.86	0.68	54.66	0.70
VT [b]	52.6	0.88	56.0	0.84	57.1	0.86	58.6	0.88
SF [b]	64.13	1.04	70.87	0.99	71.98	1.02	73.00	1.04
RE [c]	58.25	1.86	64.76	1.76	69.34	1.80	72.20	1.83
MH [b]	73.15	0.75	74.85	0.72	74.87	0.73	75.82	0.75

Note. The score ranges from 0 (high perceived restrictions) to 100 (no perceived restrictions).
[a] N = 680, [b] N = 686, [c] N = 687

Appendix 7

Overview of the Results of the Interaction Between Time and Gender on RP

	B	*SE*	*t*	*p*	*95% CI*	
					LB	UB
Intercept	11.011	5.03	2.191	.029	1.157	20.866
Time	7.244	1.30	5.562	< .001	4.690	9.798
Gender	12.515	6.31	1.978	.048	.109	24.920
Time * Gender	-1.719	1.64	-1.047	.295	-4.938	1.500

Note. LB = lower bound; *UB* = upper bound.

Appendix 8

Overview of the Results of the Interaction Between Time and Gender on RE

	B	*SE*	*t*	*p*	*95% CI*	
					LB	UB
Intercept	41.532	5.11	8.125	< .001	31.507	51.556
Time	6.655	1.34	4.957	< .001	4.022	9.288
Gender	13.190	6.43	2.053	.040	.588	25.793
Time * Gender	-3.262	1.69	-1.928	.054	-6.581	.056

Note. LB = lower bound; *UB* = upper bound.

Appendix 9

Average Scores of Role Limitations Due to Physical Health Problems in Men and Women (N=687)

Month	3		6		9		12	
	M	*SE*	*M*	*SE*	*M*	*SE*	*M*	*SE*
Men	32.21	2.34	44.11	2.24	48.35	2.29	49.45	3.35
Women	23.65	3.07	36.38	2.90	40.23	2.97	46.42	3.04

Note. A slight deviation between the plotted mean scores in Figure 4 and the scores in Appendix 5 can be explained by variations in the type of measurement. For plotting Figure 4 mean scores were used to illustrate the average scores in men and women at each time point while Appendix 5 shows predicted scores based on the conducted LMM analysis.

Appendix 10

Average Scores of Role Limitations Due to Psychological Health Problems in Women and Men (N= 687)

Month	3		6		9		12	
	M	*SE*	*M*	*SE*	*M*	*SE*	*M*	*SE*
Men	61.58	2.32	64.51	2.21	68.86	2.27	71.56	2.32
Women	52.32	3.08	65.18	2.87	70.15	2.94	73.27	2.97

Note. A slight deviation between the plotted mean scores in Figure 5 and the scores in Appendix 6 can be explained by variations in the type of measurement. For plotting Figure 5 mean scores were used to illustrate the average scores in men and women at each time point while Appendix 6 shows predicted scores based on the conducted LMM analysis.

Appendix 11

Overview of the Results of the Three-Way-Interaction Between Time, Gender, and the Number of Pre-Existing Medical Conditions on RP

	B	*SE*	*t*	*p*	*95% CI*	
					LB	UB
Intercept	8.155	7.28	1.115	.265	-6.164	22.394
Time	11.486	1.88	6.119	< .001	7.805	15.167
Gender	18.322	9.07	2.021	.043	.545	36.100
Number of PEMC	2.746	4.12	0.667	.505	-5.327	10.818
Gender * Time	-3.710	2.35	-1.581	.114	-8.312	.891
Number of PEMC * Gender	-5.088	5.10	-.998	.318	-15.086	4.911
Number of PEMC * Time	-3.461	1.08	-3.199	< .001	-5.582	-1.339
Number of PEMC * Gender * Time	1.713	1.33	1.285	.199	-.901	4.327

Note. Pre-existing medical conditions have been shortened to PEMC for better readability.

Appendix 12

Overview of the Results of the Three-Way-Interaction Between Time, Gender, and the Number of Pre-Existing Medical Conditions on RE

	B	*SE*	*t*	*p*	*95% CI*	
					LB	UB
Intercept	40.728	7.45	5.468	< .001	26.120	55.335
Time	9.251	1.95	4.757	< .001	5.437	13.065
Gender	14.396	9.27	1.553	.121	-3.786	32.579
Number of PEMC	.507	4.22	.120	.904	-7.768	8.783
Gender * Time	-4.074	2.43	-1.675	.094	-8.844	.696
Number of PEMC * Gender	-1.047	5.22	-.201	.841	-11.281	9.187
Number of PEMC * Time	-1.967	1.12	-1.751	.080	-4.171	.237
Number of PEMC * Gender * Time	.656	1.38	.475	.635	-2.056	3.369

Note. Pre-existing medical conditions have been shortened to PEMC for better readability.