Supplementary information to: Long-term sequelae of SARS-CoV-2 two years following infection: exploring the interplay of biological, psychological and social factors.

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# Supplementary Table 1. Baseline characteristics of those who did and did not complete the month 24 visit.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Levels | Not included participants | Included participants | p-value |
| Total N (%) |  | N=114 | N=235 |  |
| Sex | Male | 59 (52%) | 137 (58%) | 0.25 |
|  | Female | 55 (48%) | 98 (42%) |  |
| Age, years | Median (IQR) | 48.0 (32.0-64.0) | 52.0 (38.0-62.0) | 0.25 |
| BMI, kg/m2 | Median (IQR) | 27.2 (23.6-31.2) | 25.8 (23.2-29.3) | 0.12 |
| Migration background\* | Dutch | 38 (33%) | 156 (66%) | 0.007 |
|  | Non-Dutch, OECD HIC | 12 (11%) | 28 (12%) |  |
|  | Non-Dutch, OECD LMIC | 30 (26%) | 50 (21%) |  |
|  | (Missing) | 34 (30%) | 1 (0%) |  |
| Education level | No formal education | 12 (11%) | 33 (14%) | 0.28 |
|  | Primary education | 23 (20%) | 54 (23%) |  |
|  | Secondary education | 39 (34%) | 147 (63%) |  |
|  | (Missing) | 40 (35%) | 1 (0%) |  |
| Number of COVID-19 high-risk comorbidities\*\* | 0 | 60 (53%) | 129 (55%) | 0.32 |
|  | 1 | 23 (20%) | 58 (25%) |  |
|  | 2 | 17 (15%) | 32 (14%) |  |
|  | 3 | 14 (12%) | 16 (7%) |  |
| Smoking status | Non-smoker | 64 (56%) | 143 (61%) | 0.70 |
|  | Smoker | 6 (5%) | 16 (7%) |  |
|  | Ex-smoker | 27 (24%) | 75 (32%) |  |
|  | (Missing) | 17 (15%) | 1 (0%) |  |
| Hospitalization for COVID-19 | No | 31 (27%) | 133 (57%) | <0.001 |
|  | Yes | 77 (68%) | 102 (43%) |  |
|  | (Missing) | 6 (5%) | 0 (0%) |  |

Abbreviations: BMI, Body Mass Index; COVID-19, coronavirus disease 2019; HIC, high-income country; LMIC, low- and middle-income country; OECD, Organisation for Economic Co-operation, and Development.

\* Migration background was based on country of birth of participant and that of their parents and included first and second-generation migrants.

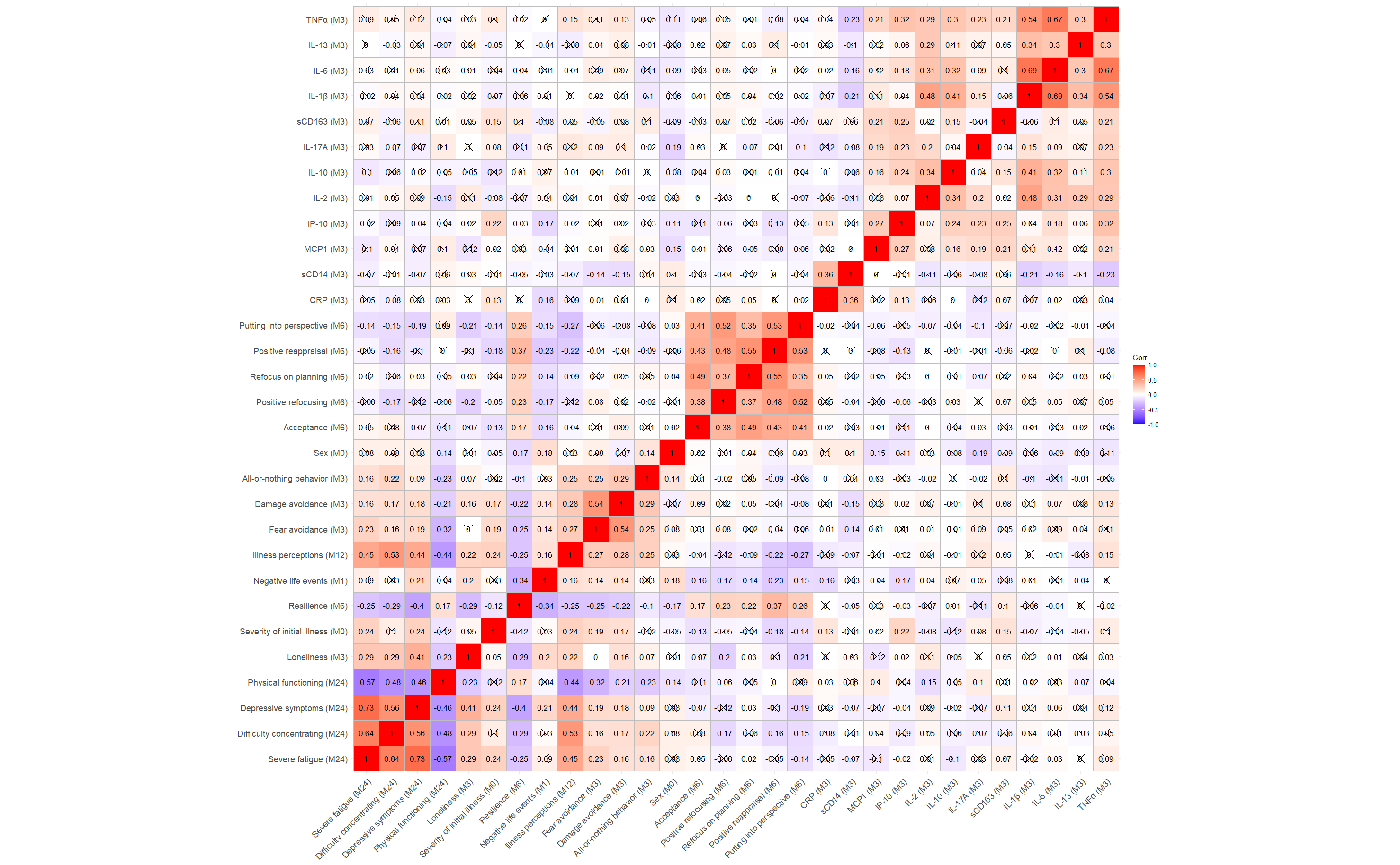
\*\* COVID-related comorbidities are based on World Health Organisation Clinical Management Guidelines (World Health Organization, 2021) and include: cardiovascular disease (including hypertension), chronic pulmonary disease (excluding asthma), renal disease, liver disease, cancer, immunosuppression (excluding HIV, including previous organ transplantation), previous psychiatric illness and dementia.

# Supplementary Table 2. Stability of edges in Figure 2.

|  |  |
| --- | --- |
| Edge | Stability score (%) |
| Fear avoidance and damage avoidance | 100 |
| IL-1β and IL-6 | 100 |
| IL-6 and TNF-α | 100 |
| Fatigue and depressive symptoms | 99 |
| CRP and sCD14 | 98 |
| Resilience and CERQ | 97 |
| Fatigue and physical functioning | 88 |
| IL-2 and IL-1β | 87 |
| Fatigue and concentration | 83 |
| IP-10 and TNF-α | 78 |
| Severity of the initial illness and IP-10 | 74 |
| Concentration and depressive symptoms | 73 |
| Concentration and illness perceptions | 63 |
| Loneliness and depressive symptoms | 62 |
| IL-1β and IL-13 | 61 |
| IL-2 and IL-10 | 60 |
| All-or-nothing behavior and illness perceptions | 59 |
| MCP1 and IP-10 | 58 |
| Loneliness and resilience | 57 |
| All-or-nothing behavior and damage avoidance | 57 |
| IP-10 and IL-10 | 57 |
| Negative life events and IP-10 | 56 |
| Negative life events and resilience | 54 |
| Physical functioning and fear avoidance | 51 |
| MCP1 and sCD163 | 51 |

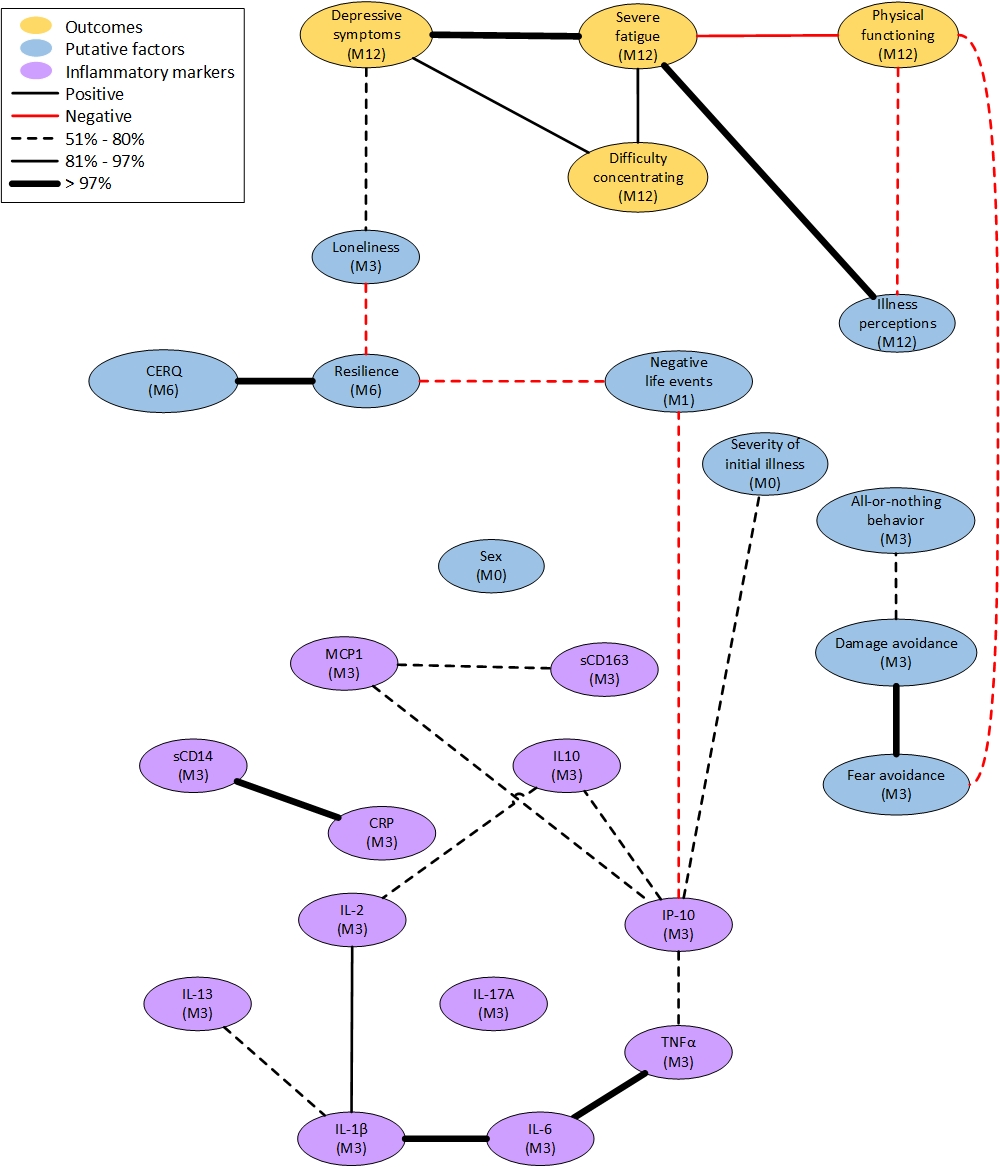
Abbreviations: CERQ, Cognitive Emotion Regulation Questionnaire; CRP, C-reactive protein; IL, Interleukin; IP-10, Interferon-γ-inducible Protein; MCP-1, Monocyte Chemoattractant Protein; TNF, Tumor Necrosis Factor.

# Supplementary Figure 1. Correlation plot of all variables in the structural network model



This correlation plot is computed on variables after baseline covariate adjustment (see Table 1 for baseline covariates). Cross signs mean the corresponding correlation coefficient is not significant (p-value > 0.05).

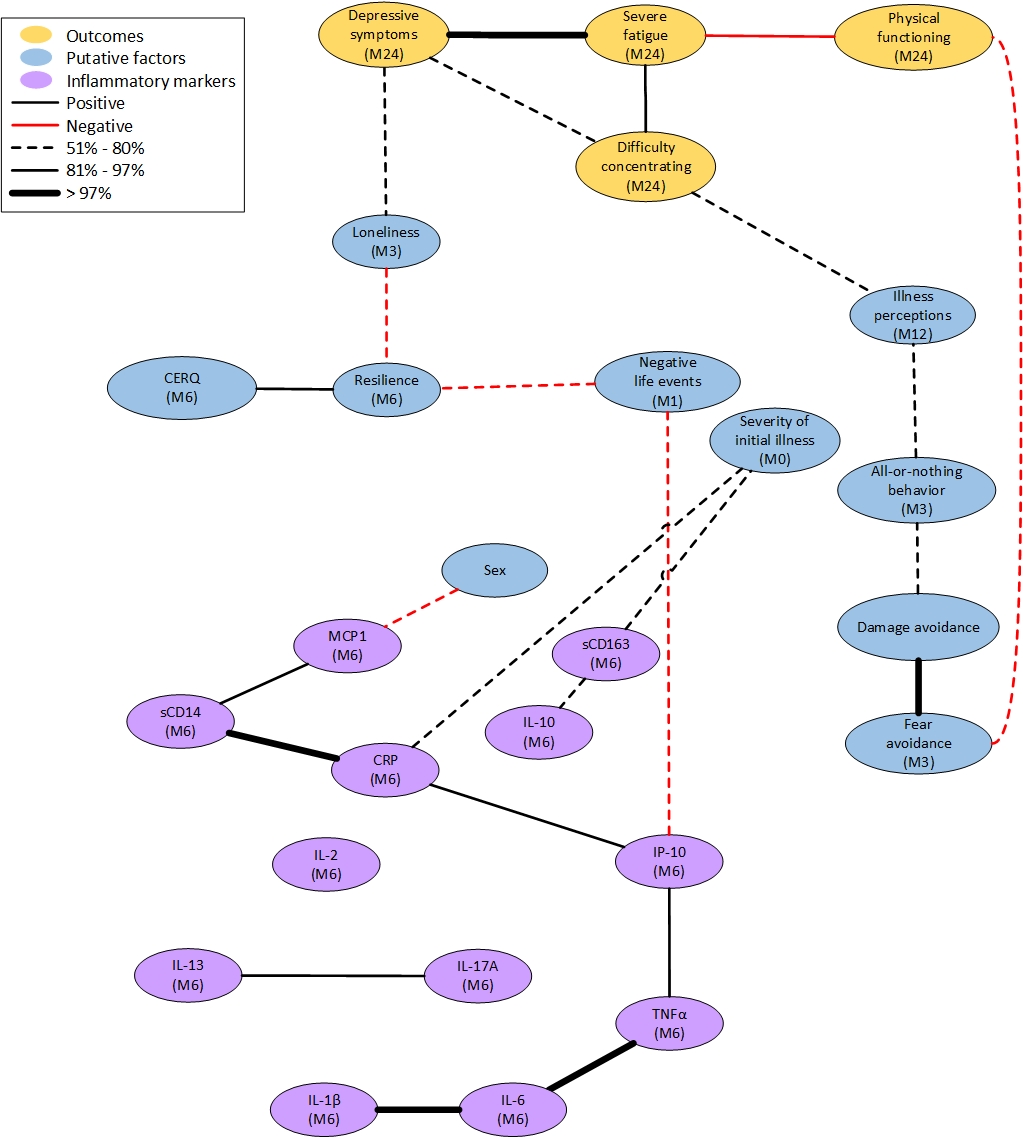
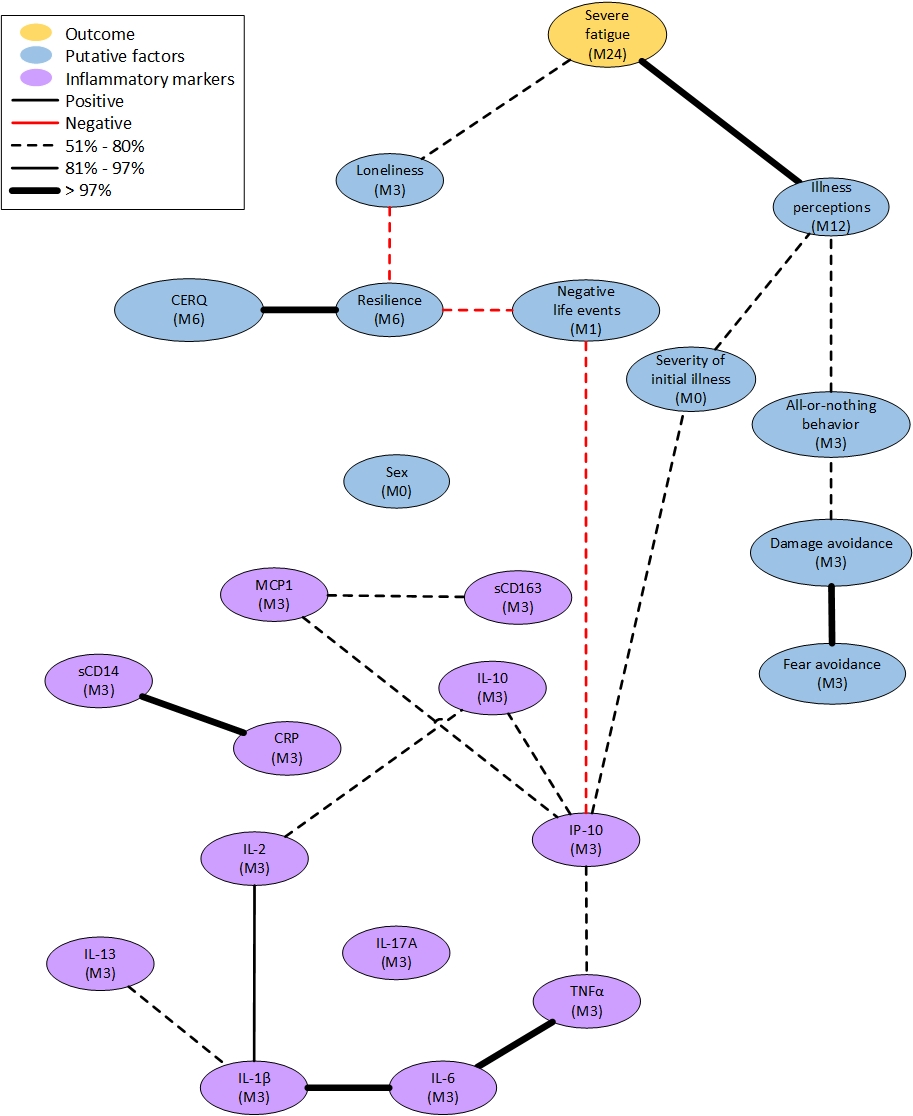
# Supplementary Figure 2. Structural network model with outcomes assessed at month 12 and inflammatory markers at month 3.



Each line stands for a stable interaction between the two variables it connects, which is not mediated by any other variable in the model. The thickness of a line shows the stability of the interaction: a dashed line has low stability (51%-80%), a solid line is moderately stable (81%-97%), and a bold line very stable (>97%). Red lines refer to a negative correlation between the two connected variables and black lines to a positive correlation. M# gives the month of measurements.

Abbreviations: CRP, C-reactive protein; IL, Interleukin; IP-10, Interferon-γ-inducible Protein; MCP-1, Monocyte Chemoattractant Protein; TNF, Tumor Necrosis Factor.

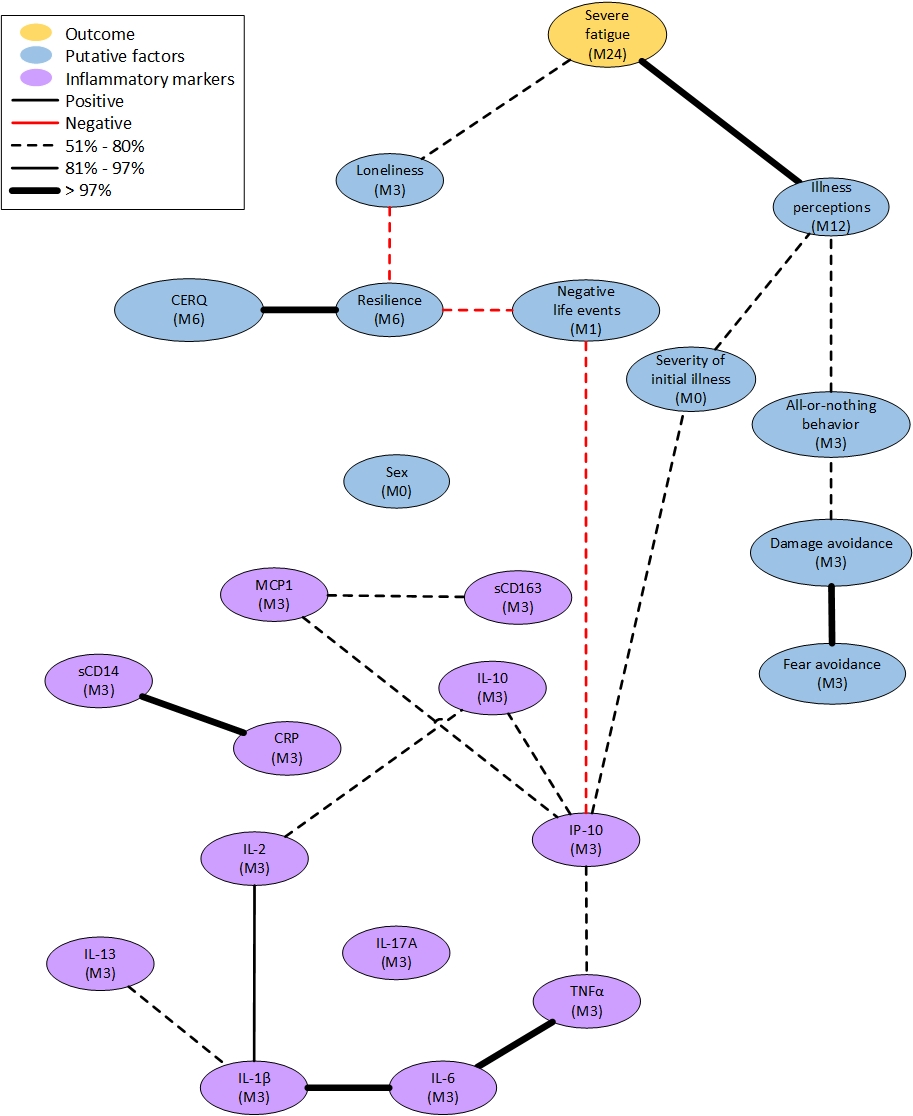
# Supplementary Figure 3. Structural network model with outcomes assessed at month 24 and inflammatory markers at month 6.



Each line stands for a stable interaction between the two variables it connects, which is not mediated by any other variable in the model. The thickness of a line shows the stability of the interaction: a dashed line has low stability (51%-80%), a solid line is moderately stable (81%-97%), and a bold line very stable (>97%). Red lines refer to a negative correlation between the two connected variables and black lines to a positive correlation. M# gives the month of measurements.

Abbreviations: CRP, C-reactive protein; IL, Interleukin; IP-10, Interferon-γ-inducible Protein; MCP-1, Monocyte Chemoattractant Protein; TNF, Tumor Necrosis Factor.

# Supplementary Figure 4. Structural network model with fatigue assessed at month 24 as sole outcome and inflammatory markers at month 3.



Each line stands for a stable interaction between the two variables it connects, which is not mediated by any other variable in the model. The thickness of a line shows the stability of the interaction: a dashed line has low stability (51%-80%), a solid line is moderately stable (81%-97%), and a bold line very stable (>97%). Red lines refer to a negative correlation between the two connected variables and black lines to a positive correlation. M# gives the month of measurements.

Abbreviations: CRP, C-reactive protein; IL, Interleukin; IP-10, Interferon-γ-inducible Protein; MCP-1, Monocyte Chemoattractant Protein; TNF, Tumor Necrosis Factor.