

Supplementary Material for
“General Psychopathology Links Recent Life Events and Psychosis in a Network Approach”

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PRONIA consortium members.

Supplementary Tables

Supplementary Table 1. Diagnosis ascertained by the Structured Clinical Interview for DSM-IV (SCID) in the Clinical High-Risk (CHR) and Recent Onset Psychosis (ROP) sample.

| Diagnosis | Frequency (%) |
|---|---------------|
| CHR (n = 265) | |
| Major depressive disorder | 51.3 |
| No current axis I disorder | 22.3 |
| Obsessive compulsive disorder | 3.8 |
| Panic disorder | 3.8 |
| Generalized anxiety disorder | 3.0 |
| Adjustment disorder | 1.9 |
| Dysthymic disorder | 1.9 |
| Anxiety disorder NOS | 1.5 |
| Bipolar II disorder | 1.5 |
| Depressive disorder NOS | 1.5 |
| Cannabis dependence | 1.1 |
| Dissociative disorder | 1.1 |
| Social phobia | 1.1 |
| Bipolar I disorder | 0.08 |
| Other axis I disorder | 0.08 |
| Specific phobia | 0.08 |
| Anorexia | 0.08 |
| Bipolar disorder other | 0.08 |
| Body dysmorphic disorder | 0.08 |
| Somatization disorder | 0.08 |
| ROP (n = 282) | |
| Schizophrenia | 36.9 |
| Psychotic disorder NOS | 14.5 |
| Schizophreniform disorder | 12.8 |
| Brief psychotic disorder | 8.2 |
| Schizoaffective disorder | 8.2 |
| Major depressive disorder (with psychotic features) | 7.4 |
| Delusional disorder | 6.7 |
| Bipolar I disorder (with psychotic features) | 5.0 |
| Bipolar II disorder (with psychotic features) | 0.04 |

Abbreviations: CHR: Clinical High-Risk; NOS: Not Otherwise Specified; ROP: Recent Onset Psychosis.

Supplementary Table 2. Comparison of baseline demographic and clinical characteristics of women and men. Means (SD) unless stated otherwise.

| Variable | Women (n = 260) | Men (n = 287) | Comparison |
|--|----------------------------|--------------------------|---------------------------|
| Studygroup (% ROP) | 46.2 | 56.4 | $\chi^2 = 5.79, p = .020$ |
| Age | 24.8 (5.9) | 24.5 (5.4) | $Z = -0.50, p = .617$ |
| PANSS (subscale scores) | | | |
| Positive | 14.3 (5.9) | 15.5 (6.4) | $Z = 2.16, p = .029$ |
| Negative | 14.3 (7.3) | 15.4 (7.2) | $Z = 1.74, p = .081$ |
| General | 31.9 (9.9) | 32.3 (10.0) | $Z = 0.39, p = .701$ |
| Total | 60.6 (19.7) | 63.3 (19.6) | $Z = 1.56, p = .117$ |
| Number of recent life events (median, range) | 4 (0-10) | 3 (0-10) | $Z = -3.90, p < .001$ |
| Burden of recent life events (sum) | 7.5 (7.0) | 5.6 (5.6) | $Z = -3.40, p = .001$ |
| CTQ-SF (subscale scores) | | | |
| Emotional Abuse | 10.8 (4.8) | 9.3 (4.1) | $Z = -3.45, p < .001$ |
| Physical Abuse | 6.6 (3.4) | 6.4 (2.6) | $Z = -1.05, p = .302$ |
| Sexual Abuse | 6.5 (3.4) | 5.7 (2.2) | $Z = -3.04, p = .002$ |
| Emotional Neglect | 11.7 (4.4) | 11.6 (3.8) | $Z = -0.25, p = .804$ |
| Physical Neglect | 7.5 (3.0) | 7.5 (2.6) | $Z = 0.01, p = 1$ |
| GAF-Disability (past month) | 49.6 (14.7) | 47.6 (13.4) | $Z = -1.63, p = .104$ |
| GAF-Symptoms (past month) | 46.9 (13.9) | 45.9 (14.2) | $Z = -0.83, p = .400$ |
| BDI-II (total score) | 25.9 (12.9) | 22.1 (12.6) | $Z = -3.21, p = .002$ |

Abbreviations: BDI: Beck Depression Inventory; CTQ-SF: Childhood Trauma Scale-Short Form; GAF: Global Assessment of Functioning; PANSS = Positive and Negative Syndrome Scale; ROP = Recent-Onset Psychosis

Supplementary Table 3. Comparison of baseline demographic and clinical characteristics of those participants included in longitudinal modeling and those participants excluded due to missing data. Means (SD) unless stated otherwise.

| Variable | Included (n = 337) | Excluded (n = 210) | Comparison |
|--|-------------------------------|-------------------------------|---------------------------|
| Studygroup (% ROP) | 50.1 | 53.8 | $\chi^2 = 0.69, p = .412$ |
| Sex (% female) | 46.0 | 50.0 | $\chi^2 = 0.83, p = .386$ |
| Age | 24.6 (5.6) | 24.8 (5.6) | $Z = 0.50, p = .620$ |
| PANSS (subscale scores) | | | |
| Positive | 15.2 (6.4) | 14.6 (6.0) | $Z = -1.10, p = .271$ |
| Negative | 15.2 (7.0) | 14.4 (7.7) | $Z = -1.24, p = .218$ |
| General | 32.8 (9.6) | 31.0 (10.4) | $Z = -2.09, p = .038$ |
| Total | 63.2 (19.0) | 60.0 (20.6) | $Z = -1.86, p = .059$ |
| Number of recent life events (median, range) | 3 (0-10) | 3 (0-10) | $Z = -1.91, p = .060$ |
| Burden of recent life events (sum) | 6.8 (6.4) | 5.9 (6.3) | $Z = -1.66, p = .101$ |
| CTQ (subscale scores) | | | |
| Emotional Abuse | 9.8 (4.3) | 10.4 (4.8) | $Z = 1.28, p = .202$ |
| Physical Abuse | 6.3 (2.8) | 6.8 (2.4) | $Z = 1.51, p = .135$ |
| Sexual Abuse | 6.1 (2.8) | 6.0 (3.1) | $Z = -0.11, p = .920$ |
| Emotional Neglect | 11.4 (4.0) | 12.1 (4.3) | $Z = 1.58, p = .115$ |
| Physical Neglect | 7.3 (2.7) | 8.0 (3.0) | $Z = 2.50, p = .011$ |
| GAF-Disability (past month) | 48.7 (14.3) | 48.4 (13.7) | $Z = -0.25, p = .804$ |
| GAF-Symptoms (past month) | 46.0 (14.0) | 47.0 (14.1) | $Z = 0.76, p = .437$ |
| BDI (total score) | 23.8 (12.2) | 24.3 (14.0) | $Z = 0.42, p = .682$ |

Abbreviations: BDI: Beck Depression Inventory; CTQ-SF: Childhood Trauma Scale-Short Form; GAF: Global Assessment of Functioning; PANSS = Positive and Negative Syndrome Scale; ROP = Recent-Onset Psychosis

Supplementary Results

Supplementary Results 1. Robustness analyses.

The CS-coefficient indicated high stability for the edge weights of the network in figure 1a (original network without controlling for covariates), as 75% of the sample could be dropped while maintaining a correlation of at least $r = .7$ with the edge weights of the original network model. The corresponding plot is available in supplementary figure 3. Regarding estimates of individual edges, the bootstrapping analysis suggested that all edges present in the original network were also included in the majority of network models built on bootstrapped samples, and that the edge weights were overall estimated with good accuracy (supplementary figure 2). Overall, we found a similar pattern for the network model when additionally including different types of childhood trauma as covariates (figure 1b). CS-coefficient suggested high stability ($CS = 0.75$, supplementary figure 5). Edges retained in the original covariate network model were present in the majority of bootstrapped networks, and edge weights were overall estimated with good accuracy (supplementary figure 4).

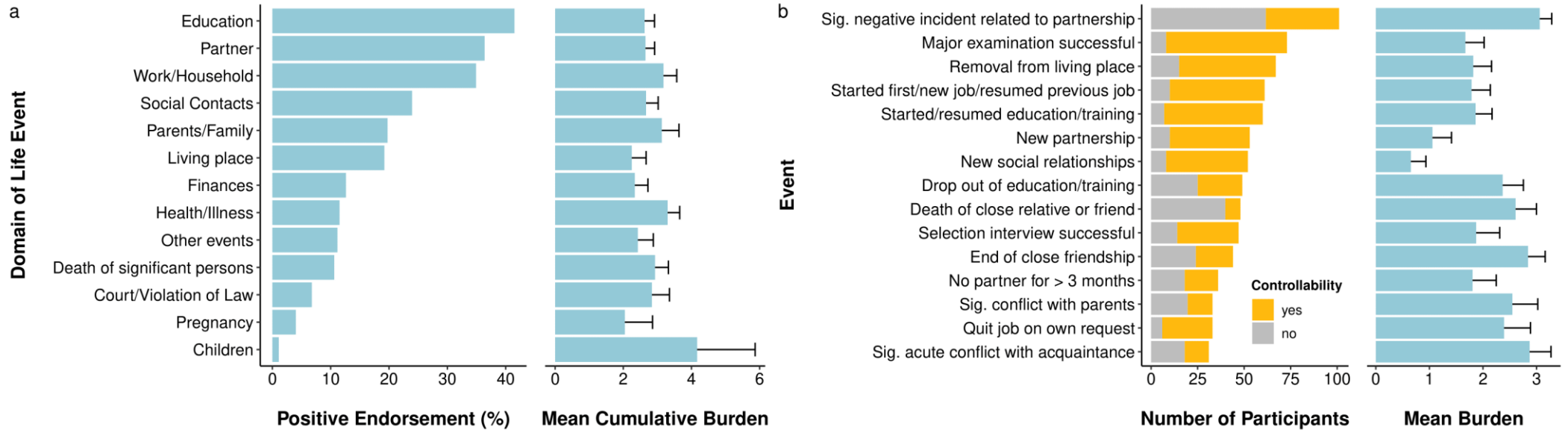
Supplementary Results 2. Comparison of networks estimated in CHR and ROP.

Statistical network comparison based on permutation tests indicated no significant differences in network structure (Test statistic $M = 0.25$, $p = .075$), global strength (Test statistic $S = 1.31$, $p = .157$) nor any individual edge weights (all p 's $> .210$ after controlling the false discovery rate) between networks estimated in CHR and ROP (for a visualization of the networks, supplementary figure 6).

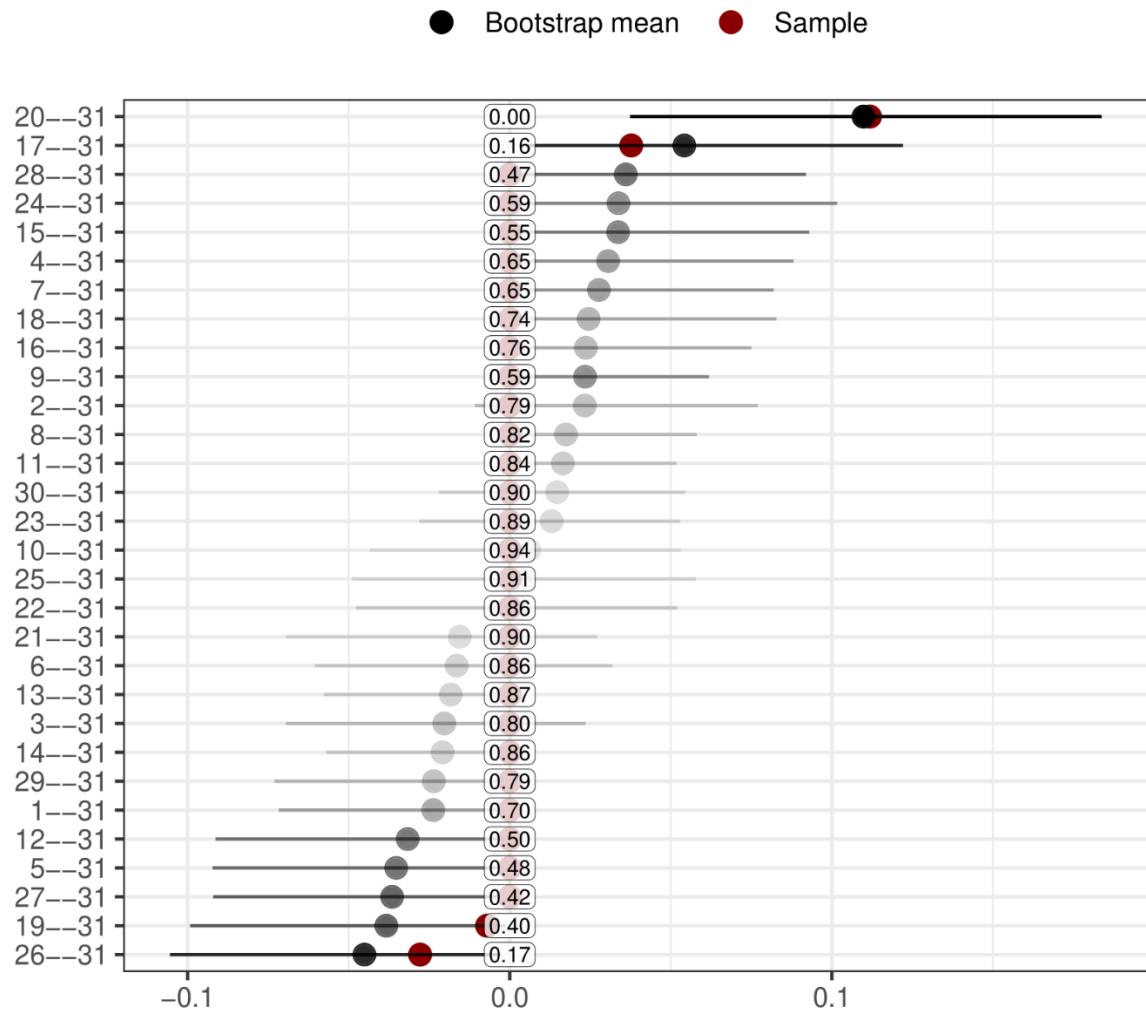
Supplementary Results 3. Comparison of networks estimated in women and men.

Statistical network comparison based on permutation tests indicated no significant differences in network structure (Test statistic $M = 0.20$, $p = .391$), global strength (Test statistic $S = 1.44$, $p = .110$) nor any individual edge weights (all p 's $> .240$ after controlling the false discovery rate) between networks estimated in women and men (for a visualization of the networks, supplementary figure 7).

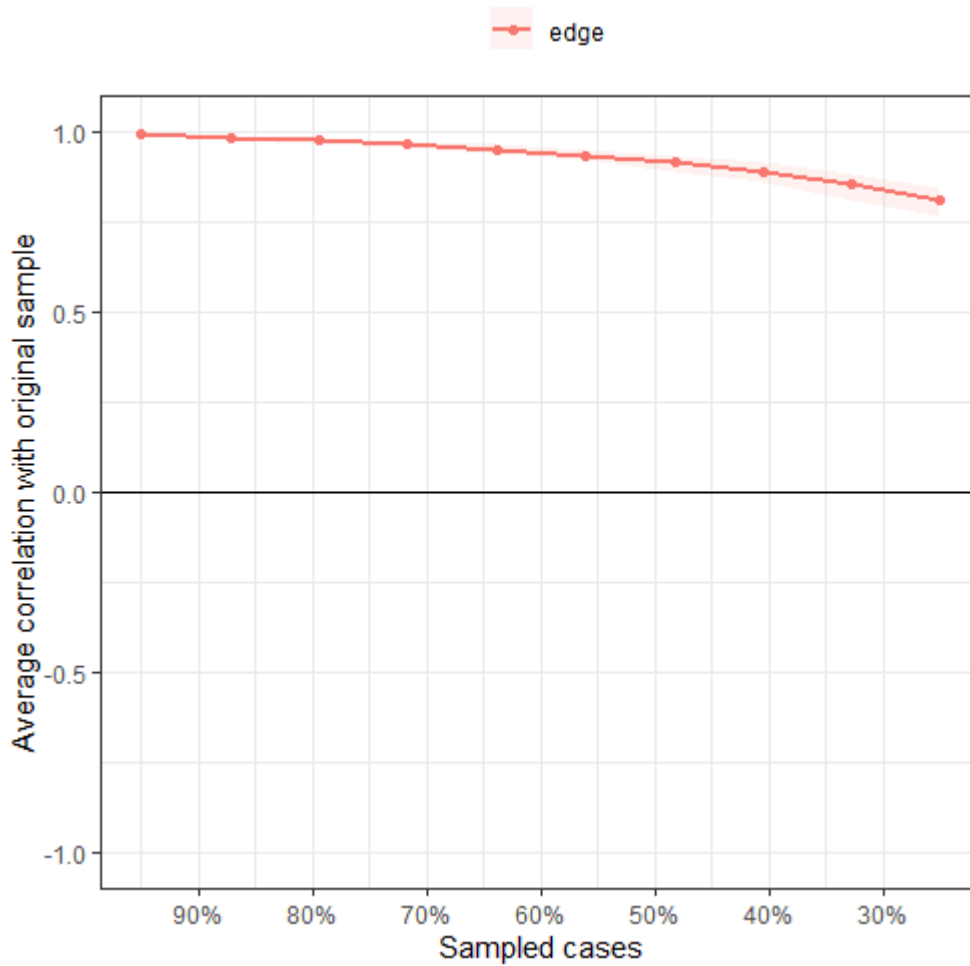
Supplementary Figures



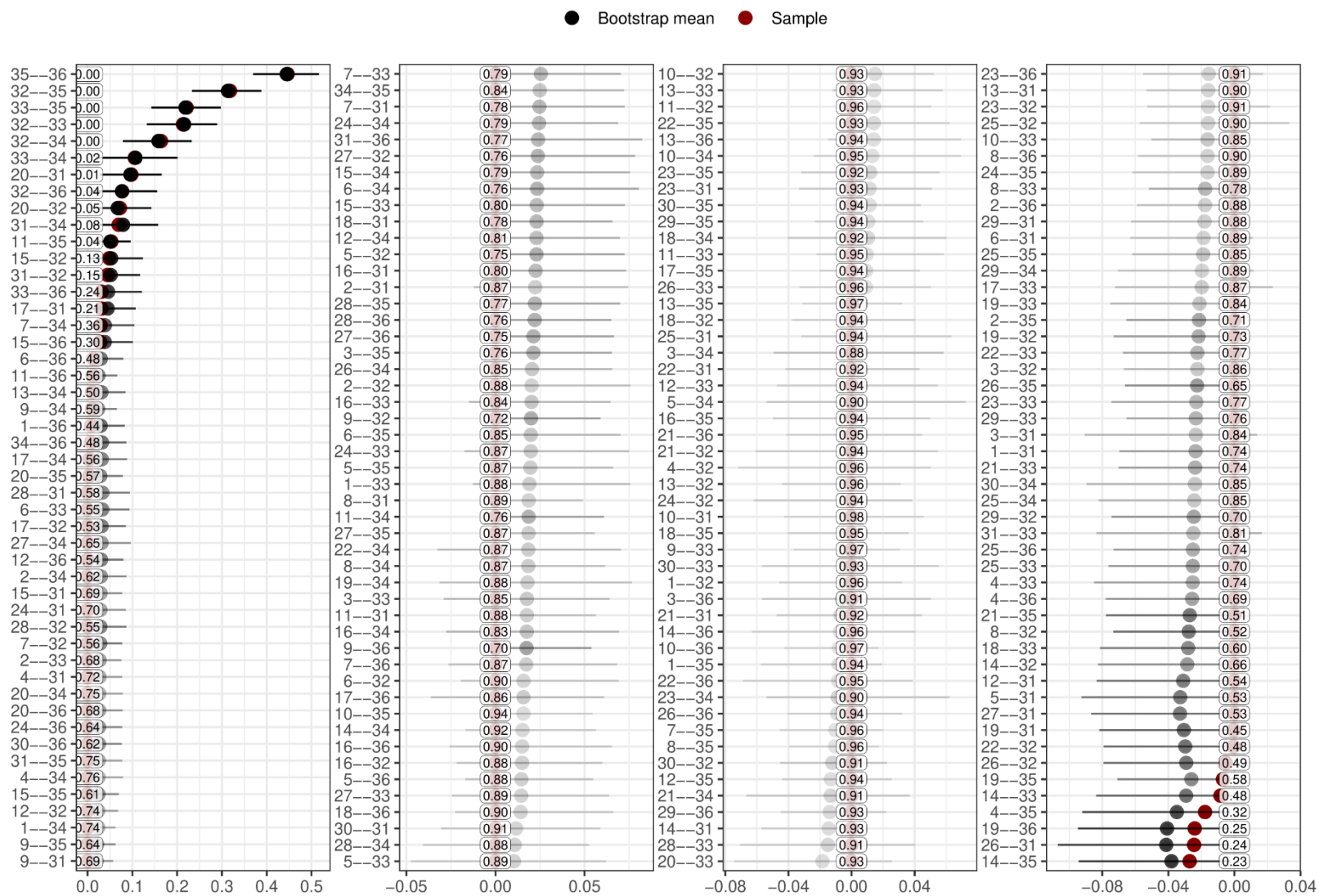
Supplementary Figure 1. Life events in the early psychosis spectrum reported at baseline ($N = 547$). a) Domains of the Cologne Chart of Life Events (CoLE³) with rates of positive endorsement and mean cumulative burden. Positive endorsement indicates if a participant reported at least one life event of the respective domain. Mean burden is cumulative as participants could name multiple life events per domain. Life events directly linked to the mental health status of the participants (e.g. hospitalization, start of treatment) were excluded. b) The fifteen most reported individual life events, along with their reported mean burden. Controllability depicts the number of participants that experienced the life event as controllable. Error bars represent the 95% confidence interval.



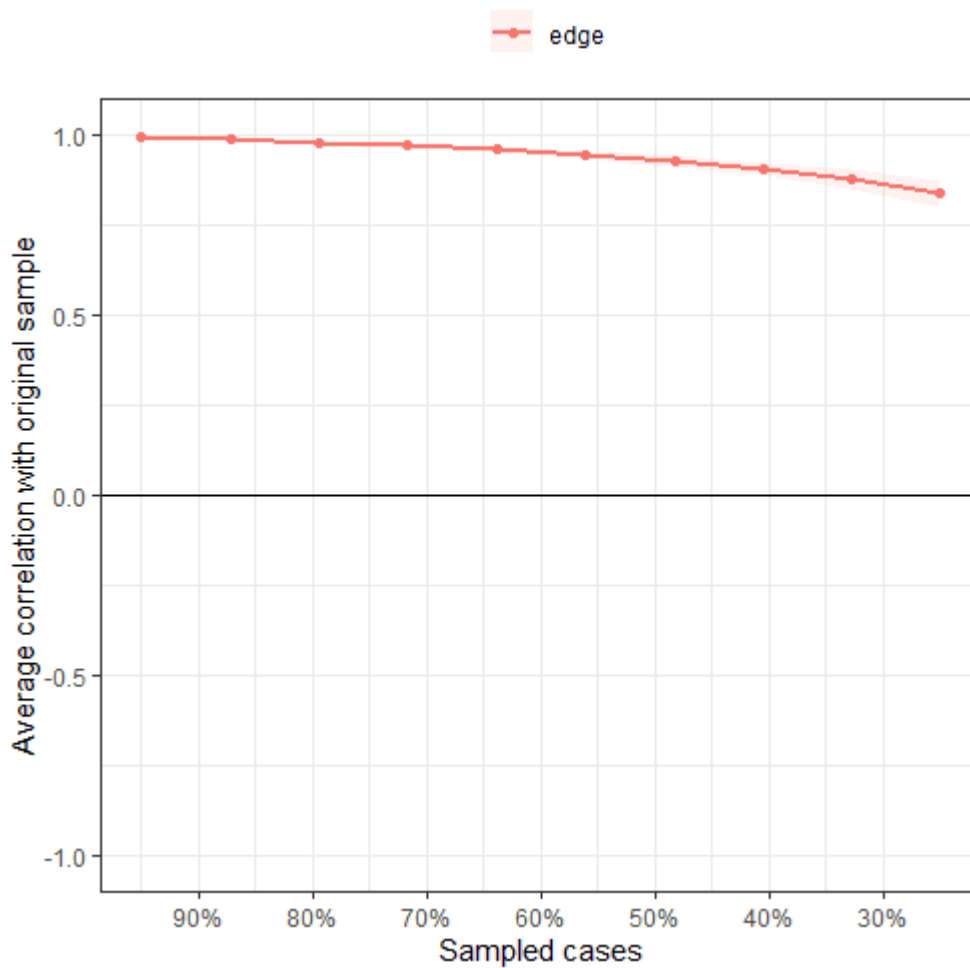
Supplementary Figure 2. Edge values with 95% confidence intervals obtained from bootstrapping in the original sample for the main network model. For readability, we only plot edges related to burden of life events. Confidence intervals are calculated based on those networks in which the edge was included (rather than set to zero). The transparency of the confidence interval reflects how often the edge was included in the networks generated in the bootstrapping procedure. The number in the box gives the proportion of sampled networks in which each edge was set to zero. For the node labels, see figure 1 in the main text.



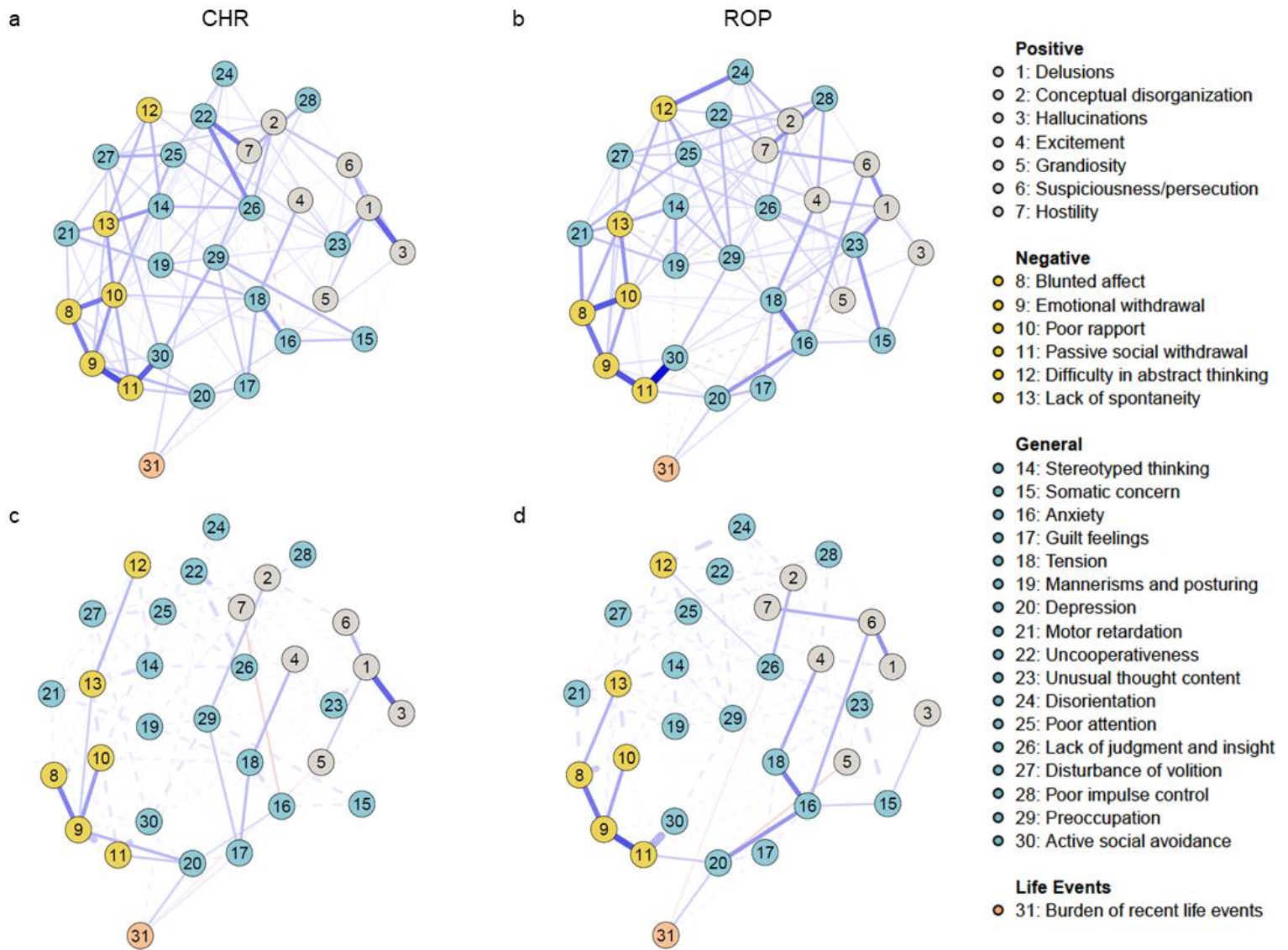
Supplementary Figure 3. Case-dropping bootstrap for the main network model. The x-axis depicts the percentage of cases of the sample used at each step. The y-axis depicts the average of correlations between the edge weights from the original network and the edge weights from networks that were re-estimated after dropping increasing percentages of cases. Lines indicate the means and areas indicate the range from the 2.5th quantile to the 97.5th quantile. The maximum proportion of observations that could be dropped while confidently (95%) retaining results that correlate highly ($r > .7$) with the edge weights in the original sample was 75%, indicating high stability¹.



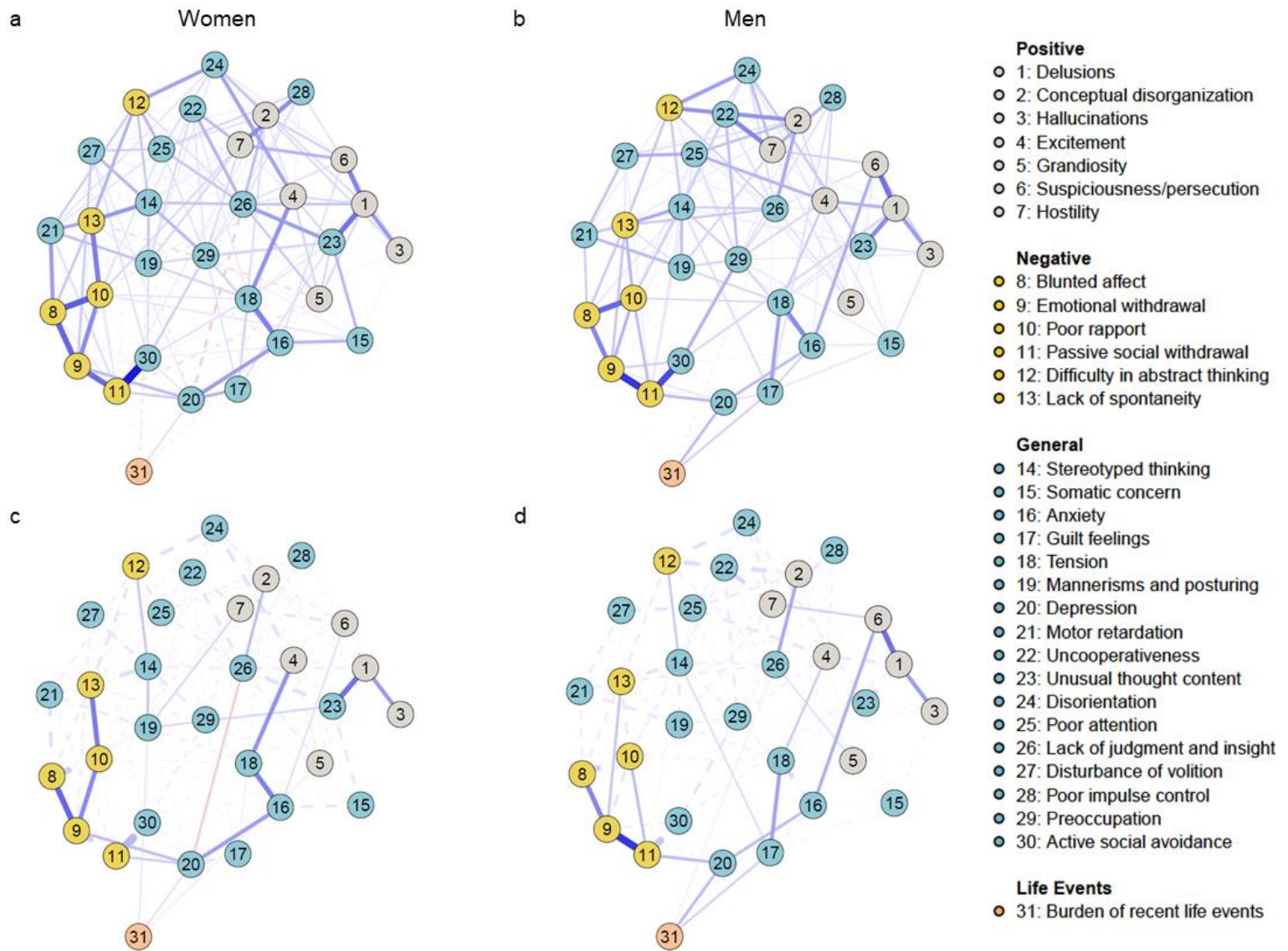
Supplementary Figure 4. Edge values with 95% confidence intervals obtained from bootstrapping for the main network model after inclusion of different childhood trauma types as covariates. For readability, we only plot edges related to life events and the types of childhood trauma. Confidence intervals are calculated based on those networks in which the edge was included (rather than set to zero). The transparency of the confidence interval reflects how often the edge was included in the networks generated in the bootstrapping procedure. The number in the box gives the proportion of sampled networks in which each edge was set to zero. For the node labels, see figure 1 in the main text.



Supplementary Figure 5. Case-dropping bootstrap for the main network model after inclusion of different childhood trauma types as covariates. The x-axis depicts the percentage of cases of the sample used at each step. The y-axis depicts the average of correlations between the edge weights from the original network and the edge weights from networks that were re-estimated after dropping increasing percentages of cases. Lines indicate the means and areas indicate the range from the 2.5th quantile to the 97.5th quantile. The maximum proportion of observations that could be dropped while confidently (95%) retaining results that correlate highly ($r > .7$) with the edge weights in the original sample was 75%, indicating high stability¹.



Supplementary Figure 6. Cross-sectional networks of relationships between burden of recent life events and symptomatology assessed with the Positive and Negative Syndrome Scale (PANSS) estimated separately in Clinical High-Risk (CHR) and Recent Onset Psychosis (ROP) participants. Upper panel: Network depicting unique associations between burden of recent life events and individual symptoms a) in CHR and b) in ROP participants. The wider the edge, the stronger the association. Blue (red) edges reflect positive (negative) connections. Lower panel: Networks highlighting shortest paths² between burden of recent life events and the positive and negative symptom domain of the PANSS c) in CHR and d) in ROP participants. Solid lines represent shortest paths, dashed lines represent connections that do not lie on the shortest paths. The wider the edge, the stronger the association. Blue (red) edges reflect positive (negative) connections.



Supplementary Figure 7. Cross-sectional networks of relationships between burden of recent life events and symptomatology assessed with the Positive and Negative Syndrome Scale (PANSS) estimated separately in women and men. Upper panel: Network depicting unique associations between burden of recent life events and individual symptoms a) in women and b) in men. The wider the edge, the stronger the association. Blue (red) edges reflect positive (negative) connections. Lower panel: Networks highlighting shortest paths² between burden of recent life events and the positive and negative symptom domain of the PANSS c) in women and d) in men. Solid lines represent shortest paths, dashed lines represent connections that do not lie on the shortest paths. The wider the edge, the stronger the association. Blue (red) edges reflect positive (negative) connections.

Supplementary Figure 8. The Cologne Chart of Life Events. The Cologne Chart of Life Events (CoLE³) was adapted from the Munich Life Event List⁴ and comprises a list with 117 events from 12 domains:

PRONIA Assessments

FETZ Chart of Life Events

| 1. In the last ... ¹ , did you experience any special event concerning... | | | 2. After collecting life events and their domains, ask following questions: | | | | 3. Final question! | | | |
|--|---|---|---|--|---------------------------------|--|-----------------------|---|--|--|
| A. Education | Y | N | Event (number according to list on next page) | How many days ago did it start? | Course | Experienced as controllable? | Subjective evaluation | Subjective burden | Rank order | |
| B. Work / Household | Y | N | | Event (number according to list on next page) | How many days ago did it start? | 1,2,3,... = frequency 8 = continuously 9 = not known | Yes / No | 1 = very positive 2 = positive 3 = neutral 4 = negative 5 = very negative | 0 = no burden 1 = slight 2 = moderate 3 = severe 4 = very severe | 1 = most important 2= second most important, 3, 4... |
| C. Partner | Y | N | | | | | | | | |
| D. Pregnancy | Y | N | | | | | | | | |
| E. Children | Y | N | | | | | | | | |
| F. Parents / Family | Y | N | | | | | | | | |
| G. Social Contacts | Y | N | | | | | | | | |
| H. Death | Y | N | | | | | | | | |
| I. Home | Y | N | | | | | | | | |
| J. Finances | Y | N | | | | | | | | |
| K. Court | Y | N | | | | | | | | |
| L. Health/Illness | Y | N | | | | | | | | |
| M. Other events | Y | N | | | | | | | | |
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¹ Healthy Controls and Patients: At T0 ask for the last 12 months
 Healthy Controls: At T1 and T2 ask for period since the last examination (If T1 examination was skipped ask for the whole period since T0)
 Patients: At Follow-up (IV3,6,12,15 and T1/T2) ask for the last 3 months (If the patient did not appear regularly ask for the whole period since the last examination)

PRONIA LIFE EVENTS INSTRUMENT – Coding

A. Education

1. Selection interview successful
2. Selection interview unsuccessful
3. Started/ resumed an education or vocational training
4. Major² examination successful
5. Major examination unsuccessful
6. Drop out of education / training
7. Acute significant conflicts with other students
8. Long-standing conflicts with students/teachers (> 3 months)
9. Significant positive change of conditions at place of education / training ³
10. Significant negative change of conditions at place of education / training (see footnote 2)
11. (1) to (6) happened to a close relative / close friend (if yes, please specify relationship)

B. Work / Household

12. Selection interview successful
13. Selection interview unsuccessful
14. Started first/new job / resumed previous job (after > 6 months)
15. Quit job on own request
16. Dismissed
17. Acute significant conflicts with colleagues/boss
18. Long-standing conflicts with colleagues/boss (> 3 months)
19. Significant positive change of conditions at work⁴
20. Significant negative change of conditions at work (see footnote 3)
21. Significant professional success
22. Significant professional failure
23. unable to work (> 3 months)
24. unemployed (> 3 months)
25. Long-standing overwhelming due to job/household related tasks (> 3 months)
26. Military / voluntary service started/resumed/finished
27. Early retirement
28. Any significant events according to the list above happening to a close relative / close friend (if yes, please specify relationship)

If not the principle earner:

² major: examination has special meaning for training, i.e. required to proceed or final exams

³ e.g. change of school or class

⁴ e.g. significant impact change of usual working conditions, i.e. procedures or tasks

29. Significant professional success of principal earner
30. Significant professional failure of principal earner
31. Unemployment / other reasons for diminished income⁵ of principal earner

C. Partner

32. New partnership (> 3 months)
33. First sexual intercourse
34. Significant negative incident related to partnership⁶, including failure to establish new partnership with a person known for > 3 months
35. Significant positive incident (including marriage, decision to cohabit)
36. Significant long-standing conflict with partner (> 3 months)
37. No partner for > 3 months
38. Any significant positive event happening to partner
39. Any significant negative event happening to partner

D. Pregnancy

40. Infertility
41. Pregnancy
42. Pre/postnatal complications
43. Miscarriage
44. Termination of pregnancy
45. Birth
46. Stillbirth
47. Sterilization
48. Any of the events above happened to partner
49. Any of the events above happened to close relative /close friend

E. Children

50. Moving out / in again
51. Any negative acute change in relationship to children
52. Any longstanding conflict with children with impact on relationship (> 3 months)
53. Any significant physical or mental health problems of children⁷
54. Conflict with law / becoming criminal
55. Acute adverse events (e.g. victim of significant violence)

⁵ e.g. unable to work due to illness

⁶ Separation, divorce, adultery of partner/respondent, significant crisis due to other reasons

⁷ [experienced as] life threatening, leading to disability, hospitalization, drug abuse etc.

- 56. Long-standing adverse events (e.g. bullying)
- 57. Marriage Separation/Divorce

F. Parents / Family

- 58. Moving out of parent's home
- 59. Moving back to parents (< 6 months after leaving)
- 60. Significant conflict with parents
- 61. Significant conflict with close relatives living in the same household
- 62. Significant conflict with close relatives living outside household
- 63. Significant long-standing conflict with parents
- 64. Significant long-standing conflict with close relatives living in the same household
- 65. Significant long-standing conflict with close relatives living outside household
- 66. Significant conflict of parents
- 67. Separation / divorce of parents

G. Social Contacts

- 68. New social relationships (> 3 months, not partnership)
- 69. End of close friendship
- 70. Significant acute conflict with acquaintance
- 71. Long-standing conflict with acquaintance
- 72. Loneliness (> 3 months)

H. Death of personally significant persons

- 73. Partner
- 74. Child
- 75. Parent
- 76. Close relative or close friend
- 77. Other personally significant person

I. Living place

- 78. Removal
- 79. Building house
- 80. Major refurbishment / conversion
- 81. Moving to a favorable neighborhood (save, good relationships)
- 82. Moving to an adverse neighborhood (dangerous, violent, criminality)
- 83. Significant acute conflict with neighbors
- 84. Significant long-standing conflict with neighbors (> 3 months)
- 85. Contract was terminated by owner
- 86. Becoming homeless
- 87. Any significant events according to the list above happening to a close relative / close friend (if yes, please specify relationship)

J. Finances

- 88. Significant financial problems

- 89. Significant improvement of financial conditions
- 90. Significant worsening of financial conditions
- 91. Any significant events according to the list above happening to a close relative / close friend (if yes, please specify relationship)

K. Court/Violation of Law

- 92. Criminal offense against person
- 93. Criminal offense against person's properties
- 94. Committed crime
- 95. Prosecuted
- 96. Contact to police (as a suspect)
- 97. Detention
- 98. Imprisoned / brought to corresponding institution (not hospital)
- 99. Fine or corresponding penalty (not prison or corresponding institution)
- 100. Any significant events according to the list above happening to a close relative / close friend (if yes, please specify relationship)

L. Health/Illness

- 101. Accident with personal damage
- 102. Hospitalization (incl. day time clinic)
- 103. Surgery
- 104. Significant somatic illness (requiring continuous treatment or disabling)
- 105. Significant mental illness (requiring continuous treatment or disabling)
- 106. Suicide attempt
- 107. Discharge from hospital / day time clinic
- 108. Starting pharmacological treatment
- 109. Starting psychological consultation / treatment
- 110. Any significant events according to the list above happening to a close relative / close friend (if yes, please specify relationship)

M. Other events

- 111. Accident (no personal damage)
- 112. Disaster victim (fire, hurricane etc.)
- 113. Unwanted reduction / cessation of personally significant leisure time activities (sports, music, travelling etc.)
- 114. Getting reminded of traumatic events
- 115. Getting a pet
- 116. Losing a pet (if significant relationship)
- 117. Any significant events according to the list above happening to a close relative / close friend (if yes, please specify relationship)

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PRONIA consortium members

PRONIA consortium members listed here performed the screening, recruitment, rating, examination, and follow-up of the study participants and were involved in implementing the examination protocols of the study, setting up its information technological infrastructure, and organizing the flow and quality control of the data analyzed in this article between the local study sites and the central study database:

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