

## **Supplementary Material**

Article Title: Relationship Between Sporadic Behavioral Variant Frontotemporal Dementia and Primary

Psychiatric Disorders: A Study in Families

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## **Appendix 1. Questionnaire QFTD-NL 1.0**

## **Instruction manual QFTD-NL 1.0**

Questionnaire QFTD-NL 1.0 – Drawn up December 2012, supplemented January 2015, translated in English October 2019

- Interviewer should at least have a Bachelor's degree in Medicine or a related field
- Interviewer received a short practical instruction of carrying out questionnaire QFTD-NL
   1.0 by a psychiatrist
- Interviewer has read the general instruction manual of the *M.I.N.I. Plus International Neuropsychiatric Interview Dutch version 5.0.0. (2000)* including questionnaires for the following disorders: depression, bipolar disorder, psychotic disorders, ADHD, alcohol, drug and substance use
- Questionnaire QFTD-NL 1.0 can be carried out real-life or by phone. In case of a cognitive stable participant questions can be asked to the participant directly. In case of a cognitive unhealthy participant questions should be asked to a relative who knows the medical and family history of the participant. Answers to the questions should be write down by the interviewer on a form.
- Part C should not be filled out in the case a participant scores negative on part B; or in the case of a cognitive healthy subject also positive on part A.
- In the case part C is filled out, a family tree should always be drawn or be described for all questioned disorders

# Screening questionnaire healthy control subject PART A

| Code number                 |   |         |
|-----------------------------|---|---------|
| Name participant            | :   |         |
| Date of birth               | _ / / Date of interview / /   |         |
| Name researcher             | :   |         |
| 1. Have you eve             | r been treated by a psychologist or psychiatrist, and if so, why?   |         |
| 2. Have you eve if so, why? | r visited your general practitioner with complaints of mental illne   | ss, and |
|                             |   |         |
| =                           | e you addicted to a substance use or action. And if so, did you or erience a negative influence of this use/action? Please explain. | your    |
|                             |   |         |
|                             |   |         |
| 4. Have you eve             | r been treated by a neurologist, and if so, why?  |         |
|                             |   |         |
|                             |   |         |

| 5. | Does your environment notice that your behavior changed recen explain                                       | itly? If so, please     |
|----|---|-------------------------|
|    |   |                         |
| 6. | Mapping subjective complaints   |                         |
|    | Do you experience memory complaints?  | yes/no                  |
|    | If so, which complaints do you experience?  |                         |
|    | <ul> <li>Is your memory deteriorated compared to the past?</li> <li>If so, how do you notice it?</li> </ul> | yes/no                  |
|    | Is your memory worse than your peers?   | yes/no                  |
|    | Do you worry about your memory?   | yes/no                  |
| 7. | Do you know all your (biological) first-degree family members? If   | f not, please specify.  |
|    |   |                         |
| 8. | Is a close family member possibly diagnosed with frontotempora are you related to him/her?                  | al dementia? If so, how |
|    |   |                         |

# QUESTIONNAIRE bvFTD (QFTD-NL 1.0) PART B

(to be filled out by researcher)

| Code number   |   |
|---|---|
| Name participant: 0 Male 0 Female   | - |
| Date of birth/ Date of interview//  |   |
| Name researcher:  |   |
|   | _ |
| 1. Participant agreed to use encoded data, obtained by this questionnaire, for scientific research  |   |
| O Yes O No  |   |
| 2. To which patient group does the participant belong?  |   |
| 0 1. Behavioral variant Frontotemporal Dementia   |   |
| 0 2. Alzheimer's disease  |   |
| 0 3. Healthy control subjects   |   |
| 0 4. Bipolar disorder   |   |
| 3. Participant meets inclusion criteria for respective patient group as can be read in the article of Icho et al. (2019)  |   |
| O Yes O No  |   |
| 4. Participant does not meet one or more of the exclusion criteria for respective patient group as can be read in the article of Icho et al. (2019)  O Yes O No | Ċ |
| 5. Questionnaire was answered by (a well-known of ) the participant, depending on th patient group 0 Yes 0 No   | е |

# QUESTIONNAIRE bvFTD (QFTD-NL 1.0) PART C

(to be filled out by researcher)

| Code number  |
|--|
| Name participant: 0 Male 0 Female  |
| Date of birth / / Date of interview / / /                                      |
| Name researcher:   |
|  |
| 5. What is your cultural origin?   |
| 0 1. The Netherlands   |
| 0 2. Surinam or the Nederland's Antilles                                       |
| 0 3. Turkey  |
| 0 4. Morocco   |
| 0 5. Asia  |
| 0 6. Other:  |
| 6. What is your current marital status?  |
| 0 1. Married or cohabitants  |
| 0 2. Living apart together   |
| 0 3. Single  |
| 0 4. Divorced  |
| 0 5. Widow(er)   |
| 7. What is your highest completed education?                                   |
| 0 1. Less than primary school  |
| 0 2. Primary school completed  |
| 0 3. Primary school and further education less than 2 years                    |
| 0 4. Less than general secondary education (MAVO), for example LTS, LEAO, LHNO |
| 0 5. General secondary education, for example MULO/MAVO/MEAO                   |
| 0 6. Higher secondary education, for example HAVO/VWO/HEAO/HBS/HBO             |
| 0 7. University degree   |
| 8. Do you smoke?   |
| 0 Yes 0 No 0 Ceased  |
| 0 Cigarettes 0 Cigars 0 Pipe   |
| If yes/ceased: amount/day, during years =packyears                             |
| 9. Do you drink alcohol?   |

| O Yes O No<br>If yes/ceased            | O Ceased amount                                     | _ units/week, dur | ing     |        | years         |       |
|--|---|-------------------|---------|--------|---------------|-------|
| •                                      | ever used sleeping<br>benzodiazepines of            | •                 | cs?     |        |               |       |
| <b>11</b> . <b>Have you</b> 0 Yes 0 No | ever used cannabis                                  | (marihuana or h   | asj)?   |        |               |       |
| -                                      | <b>ever used other red</b><br>e answer possibilitie | _                 | •       |        |               |       |
| 0 1. Stimulan                          | ts (for example Amp                                 | hetamines, Rital  | in®)    |        |               |       |
|  | for example Heroine                                 |                   | -       |        |               |       |
| 0 3. Cocaine                           |   |                   |         |        |               |       |
|  | gens (for example L<br>e.)                          |                   |         | oms)   |               |       |
| -                                      | <b>ever been exposed</b><br>pestos, ammoniac, p     |                   |         | -      | -             | -     |
|  | name  |                   | am      | ount   |               | vears |
| , , , , , ,                            | name  |                   |         |        |               |       |
|  | name  |                   |         |        |               |       |
| O Yes O No                             | <b>xperience thyroid pr</b><br>yroidism / hyperthy  |                   | ıt what | does n | ot apply)     |       |
| Medication u                           |   | )                 |         |        | 11 //         |       |
| 15. Are you fa                         | amiliar with cardiov<br>e answers possible          |                   |         |        |               |       |
| 1. Hypertensi                          | on  |                   | 0 Yes   | 0 No   |               |       |
| 2. Diabetes m                          | ellitus   |                   | 0 Yes   | 0 No   | If yes: Type: |       |
| 3. Hyperchole                          | esterolemia   |                   | 0 Yes   | 0 No   |               |       |
| 4. Myocardia                           | infarction  |                   | 0 Yes   | 0 No   |               |       |
| <b>16. Have you</b> O Yes O No         | ever had a head tra                                 | numa in the past  | ?       |        |               |       |
| If yes:                                | Amnesia   |                   | 0 Yes   | 0 No   | 0 Don't know  |       |
|  | Loss of consciousne                                 | ess               | 0 Yes   | 0 No   | 0 Don't know  |       |

| <b>17.</b> Have you ever per Note: More possible as | formed a sport associated nswers               | d with head trauma?  |   |
|---|--|--|---|
| O Yes O No  |  |  |   |
| 0 1. Boxing   |  |  |   |
| 0 2. Football                                       |  |  |   |
| 0 3. Else (namely)                                  |  | -  |   |
| Couple of years                                     | , frequency                                    | /week  |   |
| of no/don't know or no                              | ot applicable<br>/ certainly, please explain i | red for <u>each</u> family member, also in the caso<br>in the family tree, please also report age of |   |
| 18. How many siblings Brothers: Sisters:            |  | deceased ones)?  | _ |
| <b>19. How many childre</b> Children:               | n do you have (including o                     | deceased ones)?  |   |
| 20. Do you have a clos                              | se family member (grandp                       | parents, parents, siblings or children) with   | а |

medical history of <u>FRONTOTEMPORAL DEMENTIA</u>?

|  |                              | ш        | 9         | Z       | ABIF         |
|--|------------------------------|----------|-----------|---------|--------------|
|  | 9                            | POSSIBLE | DIAGNOSED | UNKNOWN | INAPPLICABLE |
| a. Mother  |                              |          |           |         |              |
| b. Grandmother maternal side<br>c. Grandfather maternal side   |                              |          |           |         |              |
| d. Father  |                              |          |           |         |              |
| e. Grandmother paternal side<br>f. Grandfather paternal side   |                              |          |           |         |              |
| g. Siblings  |                              |          |           |         |              |
| h. Children  21. Do you have a close family me   | -                            | -        |           | -       |              |
| 21. Do you have a close family mo<br>medical history of a <u>DEPRESSION</u>  | -                            | -        |           | -       |              |
| 21. Do you have a close family me<br>nedical history of a <u>DEPRESSION</u><br>M.I.N.I. Plus p. 9-15)  | <b>?</b> (no bi <sub>l</sub> | polar di | isorder,  | , so no | pas          |
| 21. Do you have a close family memedical history of a <u>DEPRESSION</u> M.I.N.I. Plus p. 9-15)  a. Mother b. Grandmother maternal side                                 | <b>?</b> (no bi <sub>l</sub> | polar di | isorder,  | , so no | pas          |
| 21. Do you have a close family memedical history of a DEPRESSION M.I.N.I. Plus p. 9-15)  a. Mother b. Grandmother maternal side c. Grandfather maternal side d. Father | <b>?</b> (no bi <sub>l</sub> | polar di | isorder,  | , so no | pas          |
|  | <b>?</b> (no bi <sub>l</sub> | polar di | isorder,  | , so no | pas          |

**22.** Do you have a close family member (grandparents, parents, siblings or children) with a medical history of a <u>BIPOLAR DISORDER?</u> (so with a past history of a (hypo)mania combined with a depression; M.I.N.I. Plus p. 17-20)

|   | ON. | POSSIBLE | DIAGNOSED | UNKNOWN | INAPPLICABLE |
|---|-----|----------|-----------|---------|--------------|
| a. Mother     b. Grandmother maternal side     c. Grandfather maternal side |     |          |           |         |              |
| d. Father e. Grandmother paternal side f. Grandfather paternal side         |     |          |           |         |              |
| g. Siblings<br>h. Children  |     |          |           |         |              |

| nallucinations; M.I.N.I. Plus p. 41   | 47)             |               |              |         | щ            |
|---|-----------------|---------------|--------------|---------|--------------|
|   | O<br>N          | POSSIBLE      | DIAGNOSED    | UNKNOWN | INAPPLICABLE |
| a. Mother   |                 |               |              |         |              |
| . Grandmother maternal side   |                 |               |              |         |              |
| Grandfather maternal side   |                 |               |              |         |              |
| . Father  |                 |               |              |         |              |
| . Grandmother paternal side   |                 |               |              |         |              |
| Grandfather paternal side   |                 |               |              |         |              |
| . Siblings  |                 |               |              |         |              |
| n. Children   |                 |               |              |         |              |
|   | ⊔<br>nember (   | <br>∕grandn   | ⊔<br>arents  | . pare  | uts. s       |
| 24. Do you have a close family n<br>nedical history of <u>SUICIDE</u> and/  | or a <u>SEV</u> | SSIBLE SSIBLE | AGNOSED AGIO | NMONX   | APPLICABLE : |
| 4. Do you have a close family n<br>nedical history of <u>SUICIDE</u> and/   |                 | ERE SU        | DIDE A       | ATTEM   | IPT?         |
| 4. Do you have a close family nedical history of SUICIDE and/he last case)  | or a <u>SEV</u> | SSIBLE SUBLE  | AGNOSED AGIO | NMONX   | APPLICABLE : |
| 4. Do you have a close family needical history of SUICIDE and/ne last case)  a. Mother b. Grandmother maternal side   | or a <u>SEV</u> | SSIBLE SUBLE  | AGNOSED AGIO | NMONX   | APPLICABLE : |
| 4. Do you have a close family nedical history of SUICIDE and/he last case)  a. Mother b. Grandmother maternal side  | or a <u>SEV</u> | SSIBLE SUBLE  | AGNOSED AGIO | NMONX   | APPLICABLE : |
| A. Do you have a close family nedical history of SUICIDE and/he last case)  a. Mother b. Grandmother maternal side c. Grandfather maternal side   | or a <u>SEV</u> | SSIBLE SUBLE  | AGNOSED AGIO | NMONX   | APPLICABLE : |
| 4. Do you have a close family needical history of SUICIDE and/he last case)  a. Mother b. Grandmother maternal side c. Grandfather maternal side d. Father e. Grandmother paternal side   | or a <u>SEV</u> | SSIBLE SUBLE  | AGNOSED AGIO | NMONX   | APPLICABLE : |
| 24. Do you have a close family nedical history of SUICIDE and/the last case)  a. Mother b. Grandmother maternal side c. Grandfather maternal side d. Father e. Grandmother paternal side  | or a <u>SEV</u> | SSIBLE SUBLE  | AGNOSED AGIO | NMONX   | APPLICABLE : |
| 24. Do you have a close family nedical history of SUICIDE and/the last case)  a. Mother b. Grandmother maternal side c. Grandfather maternal side d. Father e. Grandmother paternal side f. Grandfather paternal side g. Siblings h. Children | or a <u>SEV</u> | SSIBLE SUBLE  | AGNOSED AGIO | NMONX   | APPLICABLE : |

| 25. Do you have a close family me medical history of a <u>AUTISM SPEC</u>  |           | -        |           | -       | , Asp            |       | _   |      |        | PDD-N  | IOS) |
|--|-----------|----------|-----------|---------|------------------|-------|-----|------|--------|--------|------|
|  | Q         | POSSIBLE | DIAGNOSED | UNKNOWN | INAPPLICABLE     |       |     |      |        |        |      |
| a. Mother  |           |          |           |         |                  |       |     |      |        |        |      |
| b. Grandmother maternal side c. Grandfather maternal side  |           |          |           |         |                  |       |     |      |        |        |      |
| d. Father e. Grandmother paternal side f. Grandfather paternal side  |           |          |           |         |                  |       |     |      |        |        |      |
| g. Siblings  |           |          |           |         |                  |       |     |      |        |        |      |
| h. Children  |           |          |           |         |                  |       |     |      |        |        |      |
| •  |           |          |           | , pare  |                  | ibli  | ngs | or c | hildre | n) wit | h a  |
| h. Children  26. Do you have a close family me   |           |          |           | , pared | INAPPLICABLE stu | iblii | ngs | or c | hildre | n) wit | h a  |
| h. Children  26. Do you have a close family me   | I. Plus p | . 63-66  | )         |         |                  | ibli  | ngs | or c | hildre | n) wit | h a  |
| h. Children  26. Do you have a close family me medical history of ADHD? (M.I.N.I.  | I. Plus p | . 63-66  | )         |         |                  | iblii | ngs | or c | hildre | n) wit | h a  |
| h. Children  26. Do you have a close family me medical history of ADHD? (M.I.N.I.)  a. Mother b. Grandmother maternal side | I. Plus p | . 63-66  | )         |         |                  | ibli  | ngs | or c | hildre | n) wit | h a  |

| nedical history of <u>ALCOHOLISM</u> ?  |                | ·        |                 |         | BLE          |
|---|----------------|----------|-----------------|---------|--------------|
|   | ON<br>O        | POSSIBLE | DIAGNOSED       | UNKNOWN | INAPPLICABLE |
| a. Mother   |                |          |                 |         |              |
| Grandmother maternal side Grandfather maternal side   |                |          |                 |         |              |
| R. Father   |                |          |                 |         |              |
| g. Siblings   | П              |          |                 |         |              |
| -   |                |          |                 |         |              |
| n. Children<br>8. Do you have a close family m  |                |          |                 | -       | us p.        |
| h. Children<br>28. Do you have a close family m   |                |          |                 | -       |              |
| n. Children  8. Do you have a close family medical history of <u>DRUG OR SUB</u>  | <u>SSTANCE</u> | ABUSE    | <u>:?</u> (M.I. | N.I. Pl | us p.        |
| h. Children  28. Do you have a close family medical history of DRUG OR SUB  a. Mother b. Grandmother maternal side c. Grandfather maternal side           | <u>SSTANCE</u> | ABUSE    | <u>:?</u> (M.I. | N.I. Pl | us p.        |
| h. Children  28. Do you have a close family m  medical history of <u>DRUG OR SUB</u> a. Mother  b. Grandmother maternal side                              | <u>SSTANCE</u> | ABUSE    | <u>:?</u> (M.I. | N.I. Pl | us p.        |
| h. Children  28. Do you have a close family medical history of DRUG OR SUB  a. Mother b. Grandmother maternal side c. Grandfather maternal side d. Father | <u>SSTANCE</u> | ABUSE    | <u>:?</u> (M.I. | N.I. Pl | us p.        |

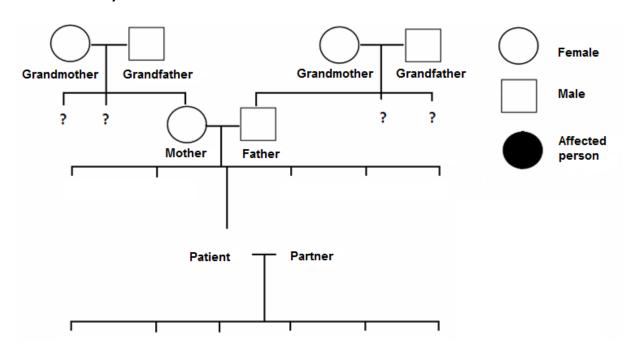
| medical history of MOVEMENT D<br>degeneration (CBD), progressive s   |         |          |           |              |              | ALS, | Cortio | cobas | aal   |
|--|---------|----------|-----------|--------------|--------------|------|--------|-------|-------|
|  | ON      | POSSIBLE | DIAGNOSED | UNKNOWN      | INAPPLICABLE |      |        |       |       |
| a. Mother b. Grandmother maternal side c. Grandfather maternal side  |         |          |           |              |              |      |        |       |       |
| d. Father e. Grandmother paternal side f. Grandfather paternal side  |         |          |           |              |              |      |        |       |       |
| g. Siblings  |         |          |           |              |              |      |        |       |       |
| h. Children  |         | Ш        | Ш         |              | Ш            |      |        |       |       |
|  |         |          |           |              | imer'        |      |        | -     | ents, |
| h. Children  30. (Only for patients with bvFTD   |         |          |           |              | -            |      |        | -     | ents, |
| h. Children  30. (Only for patients with bvFTD   | n a med | ical his | tory of   | <u>Alzhe</u> | imer'        |      |        | -     | ents, |
| h. Children  30. (Only for patients with bvFTD parents, siblings or children) with  a. Mother b. Grandmother maternal side | n a med | ical his | tory of   | <u>Alzhe</u> | imer'        |      |        | -     | ents, |

29. Do you have a close family member (grandparents, parents, siblings or children) with a

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Thank you for taking part

### PART D: Family tree \*



<sup>\*(</sup>Please register siblings and/or children if present)

#### **NOTES:**

| FRONTOTEMPORAL DEMENTIA |      |      |
|-------------------------|------|------|
|                         |      |      |
|                         | <br> | <br> |
|                         |      |      |
|                         | <br> | <br> |
| DEDDESSION              |      |      |
| DEPRESSION              | <br> | <br> |
|                         |      |      |
|                         |      |      |
|                         | <br> |      |
|                         |      |      |
| BIPOLAR DISORDER        | <br> |      |
|                         |      |      |
|                         | <br> | <br> |
|                         |      |      |
|                         | <br> | <br> |
| PSYCHOSES               |      |      |
|                         |      |      |
|                         |      |      |
|                         | <br> |      |
|                         |      | <br> |

| SUICIDE OR SEVERE SUICIDE ATTEMPT |
|-----------------------------------|
|                                   |
|                                   |
|                                   |
|                                   |
| ALITISM SDECTRUM DISORDER         |
| AUTISM SPECTRUM DISORDER          |
|                                   |
|                                   |
|                                   |
|                                   |
| ADHD                              |
|                                   |
|                                   |
|                                   |
|                                   |
| ALCOHOLISM                        |
|                                   |
|                                   |
|                                   |
|                                   |
| DRUG OR CURSTANCE ARUSE           |
| DRUG OR SUBSTANCE ABUSE           |
|                                   |
|                                   |
|                                   |
|                                   |
| MOVEMENT DISORDERS                |
|                                   |
| ·                                 |
|                                   |
|                                   |
| OTHER REMARKS                     |
| OTHER REMARKS                     |
|                                   |
|                                   |
|                                   |

### Supplementary table 1 Prevalence of occurrence of PPD in first-degree family members of bvFTD, HC, AD and BD.

|                          | bvFTD | HC     | AD     | BD     |
|--------------------------|-------|--------|--------|--------|
| Depression               | 14/72 | 10/101 | 26/108 | 38/124 |
| Psychosis                | 6/73  | 4/101  | 6/107  | 16/122 |
| Bipolar disorder         | 2/72  | 3/101  | 4/107  | 33/124 |
| Autism spectrum disorder | 5/73  | 4/101  | 1/107  | 2/44   |

Supplementary table 2 Odds ratios (OR), 95% confidence interval (95%CI), Nagelkerke pseudo R square and p-values for the association between study groups compared to healthy control subjects and PPD in first-degree family members. Unadjusted models without correction for confounders and adjusted models corrected for age and education level are displayed. Significant effects are bold displayed.

|                                 | Unadjusted model |              |                | Adjusted model |            |              |                |         |
|---------------------------------|------------------|--------------|----------------|----------------|------------|--------------|----------------|---------|
|                                 | Odds<br>Ratio    | 95%CI        | $\mathbb{R}^2$ | p-<br>value    | Odds Ratio | 95%CI        | $\mathbb{R}^2$ | p-value |
| Depression                      |                  |              |                |                |            |              |                |         |
| bvFTD                           | 2.20             | [0.92-5.27]  | 0.033          | 0.08           | 2.58       | [1.03-6.46]  | 0.045          | 0.04    |
| AD                              | 2.89             | [1.31-6.35]  | 0.059          | <0.01          | 2.95       | [1.26-6.88]  | 0.060          | 0.01    |
| BD Psychosis                    | 4.02             | [1.89-8.57]  | 0.101          | <0.01          | 4.07       | [1.83-9.02]  | 0.113          | <0.01   |
| bvFTD                           |                  |              |                |                |            |              |                |         |
| AD                              | <u>2.17</u>      | [0.59-7.99]  | 0.022          | 0.24           | 3.26       | [0.84-12.56] | 0.086          | 0.09    |
|                                 | <u>1.44</u>      | [0.39-5.26]  | 0.005          | 0.58           | 1.54       | [0.37-6.38]  | 0.010          | 0.55    |
| BD                              | 3.66             | [1.18-11.33] | 0.060          | 0.02           | 5.33       | [1.58-17.34] | 0.120          | <0.01   |
| Bipolar<br>disorders            |                  |              |                |                |            |              |                |         |
| bvFTD                           |                  |              |                |                |            |              |                |         |
| AD                              | 0.93             | [0.15-5.73]  | < 0.001        | 0.94           | 1.62       | [0.26-10.20] | 0.124          | 0.60    |
|                                 | 1.27             | [0.28-5.81]  | 0.002          | 0.76           | 1.10       | [0.20-5.89]  | 0.013          | 0.92    |
| BD                              | 11.85            | [3.51-39.96] | 0.194          | <0.01          | 13.58      | [3.85-47.84] | 0.200          | <0.01   |
| Autism<br>Spectrum<br>Disorders | 11.83            | [3.31-39.90] | 0.194          | <0.01          | 13.36      | [5.63-47.64] | 0.200          | <0.01   |
| bvFTD                           | 1 70             | [0.46.6.99]  | 0.012          | 0.40           | 1 //1      | [0.24.5.00]  | 0.000          | 0.64    |
| AD                              | 1.78             | [0.46-6.88]  | 0.012          | 0.40           | 1.41       | [0.34-5.90]  | 0.080          | 0.64    |
|                                 | 0.23             | [0.03-2.08]  | 0.051          | 0.19           | 0.21       | [0.18-2.28]  | 0.084          | 0.20    |
| BD                              | 1.16             | [0.20-6.55]  | 0.001          | 0.87           | 1.46       | [0.24-9.10]  | 0.024          | 0.68    |