

**Supplemental Materials:****Real-world evidence data:**

Table S1: Attrition rate during the study by sex.

Table S2: Overall attrition rate during the study by sex and by time points.

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Figure S2: Individualized sex differences in  $\Delta$ 9-THC and its metabolites pharmacokinetics.

Figure S3: Sex comparison of blood pressure following a single inhalation.

Figure S4: Sex comparison of heart rate following a single inhalation.

**Table S1: Attrition rate during the study by sex**

| Attrition reason                         | Women<br>n=607<br>N (%) | Women<br>proportion<br>(CI 95%) | Men<br>n=513<br>N (%) | Men<br>proportional<br>(CI 95%)   | Overall sample<br>N=1120<br>N (%) | Overall<br>proportion<br>(CI 95%) | Wilson's $X^2$ test<br>(p-value) |
|--|-------------------------|---------------------------------|-----------------------|-----------------------------------|-----------------------------------|-----------------------------------|----------------------------------|
| Total                                    | 433 (71)                | 71.3 (CI<br>95%:67.6-74.8)      | 366 (71)              | 71.3 (CI<br>95%:67.3-75.1)        | 799 (71)                          | 71.3 (CI<br>95%:67.7-74.6)        | 0 (1)                            |
| Ineffectiveness                          | 122 (20)                | 20.1 (CI<br>95%:17.1-23.47)     | 97 (19)               | 18.91 (CI<br>95%:15.76-<br>22.52) | 219 (0)                           | 19.55 (CI<br>95%:17.34-<br>21.98) | 0.18 (0.67)                      |
| Other reason                             | 62 (10)                 | 10.21 (CI<br>95%:8.05-12.88)    | 45 (9)                | 8.77 (CI<br>95%:6.62-11.54)       | 107 (0)                           | 9.55 (CI<br>95%:7.97-11.42)       | 0.51 (0.47)                      |
| Switched to<br>other MC form             | 51 (8)                  | 8.4 CI<br>95%:6.45-10.88)       | 63 (12)               | 12.28 (CI<br>95%:9.72-15.4)       | 114 (0)                           | 10.18 (CI<br>95%:8.54-12.09)      | 4.16 (0.04)                      |
| Financial                                | 35 (6)                  | 5.77 (CI<br>95%:4.17-7.91)      | 31 (6)                | 6.04 (CI<br>95%:4.29-8.45)        | 66 (0)                            | 5.89 (CI<br>95%:4.66-7.43)        | 0 (0.95)                         |
| Adverse Event                            | 35 (6)                  | 5.77 (CI<br>95%:4.17-7.91)      | 26 (5)                | 5.07 (CI<br>95%:3.48-7.32)        | 61 (0)                            | 5.45 (CI<br>95%:4.26-6.93)        | 0.15 (0.7)                       |
| Switched to<br>other non-MC<br>treatment | 27 (4)                  | 4.45 CI<br>95%:3.07-6.39)       | 15 (3)                | 2.92 (CI<br>95%:1.78-4.77)        | 42 (0)                            | 3.75 (CI<br>95%:2.79-5.03)        | 1.39 (0.24)                      |
| Physician<br>decision<br>permanently     | 23 (4)                  | 3.79 (CI<br>95%:2.54-5.62)      | 24 (5)                | 4.68 (CI<br>95%:3.16-6.87)        | 47 (0)                            | 4.2 (CI<br>95%:3.17-5.54)         | 0.35 (0.56)                      |
| License expired                          | 21 (3)                  | 3.46 (CI<br>95%:2.27-5.23)      | 13 (3)                | 2.53 (CI<br>95%:1.49-4.29)        | 34 (0)                            | 3.04 (CI<br>95%:2.18-4.21)        | 0.53 (0.47)                      |
| Improved health                          | 19 (3)                  | 3.13 (CI<br>95%:2.01-4.84)      | 14 (3)                | 2.73 (CI<br>95%:1.63-4.53)        | 33 (0)                            | 2.95 (CI<br>95%:2.11-4.11)        | 0.05 (0.83)                      |

|                              |        |                         |        |                         |        |                         |             |
|------------------------------|--------|-------------------------|--------|-------------------------|--------|-------------------------|-------------|
| Health Worsening             | 16 (3) | 2.64 (CI 95%:1.63-4.24) | 12 (2) | 2.34 (CI 95%:1.34-4.04) | 28 (0) | 2.5 (CI 95%:1.74-3.59)  | 0.02 (0.9)  |
| Deceased                     | 11 (2) | 1.81 (CI 95%:1.01-3.22) | 17 (3) | 3.31 (CI 95%:2.08-5.24) | 28 (0) | 2.5 (CI 95%:1.74-3.59)  | 1.99 (0.16) |
| Physician decision temporary | 6 (1)  | 0.99 CI 95%:0.45-2.14)  | 5 (1)  | 0.97 (CI 95%:0.42-2.26) | 11 (0) | 0.98 (CI 95%:0.55-1.75) | 0 (1)       |
| Immigration                  | 3 (0)  | 0.49 (CI 95%:0.17-1.44) | 1 (0)  | 0.19 (CI 95%:0.03-1.1)  | 4 (0)  | 0.36 (CI 95%:0.14-0.91) | 0.11 (0.74) |
| Intermittently continued     | 1 (0)  | 0.16 (CI 95%:0.03-0.93) | 2 (0)  | 0.39 (CI 95%:0.11-1.41) | 3 (0)  | 0.27 (CI 95%:0.09-0.78) | 0.02 (0.88) |
| Sudden illness temp          | 1 (0)  | 0.16 CI 95%:0.03-0.93)  | 1 (0)  | 0.19 CI 95%:0.03-1.1)   | 2 (0)  | 0.18 (CI 95%:0.05-0.65) | 0 (1)       |

MC, Medical cannabis; Numbers do not add up to 100% due to concomitant reasons.

**Table S2: Overall attrition rate during the study by sex and by time points**

| <b>Time point range (days)</b>         | <b>Women<br/>n=607<br/>N (%)</b> | <b>Women proportion<br/>(CI 95%)</b> | <b>Men<br/>n=513<br/>N (%)</b> | <b>Men proportional<br/>(CI 95%)</b> | <b>Overall sample<br/>N=1120<br/>N (%)</b> | <b>Overall proportion<br/>(CI 95%)</b> | <b>Wilson's <math>X^2</math> test<br/>(p-value)</b> |
|--|----------------------------------|--------------------------------------|--------------------------------|--------------------------------------|--|--|---|
| <b>D<sub>0</sub>-D<sub>1</sub></b>     | 3 (0)                            | 0.5 (CI 95%:0.17-1.45)               | 4 (1)                          | 0.79 (CI 95%:0.31-2                  | 7 (1)                                      | 0.63 (CI 95%:0.16-0.05)                | 0.05 (0.82)   |
| <b>D<sub>1</sub>-D<sub>7</sub></b>     | 5 (1)                            | 0.83 ((CI 95%:0.36-1.94)             | 6 (1)                          | 1.19 (CI 95%:0.55-2.58               | 11 (1)                                     | 1 (CI 95%:0.41-0.07)                   | 0.09 (0.77)   |
| <b>D<sub>7</sub>-D<sub>14</sub></b>    | 10 (2)                           | 1.7 (CI 95%:0.92-3.1                 | 8 (2)                          | 1.62 (CI 95%:0.82-3.16               | 18 (2)                                     | 1.66 (CI 95%:0.9-0.09)                 | 0 (1)   |
| <b>D<sub>14</sub>-D<sub>21</sub></b>   | 18 (3)                           | 3.15 (CI 95%:2-4.93                  | 15 (3)                         | 3.13 (CI 95%:1.9-5.09                | 33 (3)                                     | 3.14 (CI 95%:2.09-0.14)                | 0 (1)   |
| <b>D<sub>21</sub>-D<sub>30</sub></b>   | 30 (6)                           | 5.55 (CI 95%:3.91-7.81               | 20 (4)                         | 4.35 (CI 95%:2.83-6.62               | 50 (4)                                     | 5 (CI 95%:3.65-0.18)                   | 0.52 (0.47)   |
| <b>D<sub>30</sub>-D<sub>60</sub></b>   | 61 (13)                          | 12.71 (CI 95%:10.02-15.99            | 45 (11)                        | 10.84 (CI 95%:8.2-14.2               | 106 (9)                                    | 11.84 (CI 95%:9.73-0.33)               | 0.57 (0.45)   |
| <b>D<sub>60</sub>-D<sub>90</sub></b>   | 35 (8)                           | 7.87 (CI 95%:5.71-10.74              | 42 (11)                        | 11.26 (CI 95%:8.44-14.87             | 77 (7)                                     | 9.41 (CI 95%:7.41-0.29)                | 2.36 (0.13)   |
| <b>D<sub>90</sub>-D<sub>120</sub></b>  | 25 (6)                           | 5.95 (CI 95%:4.06-8.64               | 26 (7)                         | 7.49 (CI 95%:5.16-10.75              | 51 (5)                                     | 6.65 (CI 95%:4.89-0.24)                | 0.5 (0.48)  |
| <b>D<sub>120</sub>-D<sub>180</sub></b> | 43 (11)                          | 11.41 (CI 95%:8.58-15.01             | 33 (11)                        | 10.51 (CI 95%:7.58-14.39             | 76 (7)                                     | 11 (CI 95%:8.67-0.34)                  | 0.06 (0.8)  |
| <b>D<sub>180</sub>-D<sub>240</sub></b> | 18 (5)                           | 5.01 (CI 95%:3.19-7.79               | 14 (5)                         | 4.67 (CI 95%:2.8-7.68                | 32 (3)                                     | 4.86 (CI 95%:3.21-0.21)                | 0 (0.98)  |
| <b>D<sub>240</sub>-D<sub>360</sub></b> | 13 (4)                           | 3.76 (CI 95%:2.21-6.32               | 11 (4)                         | 3.81 (CI 95%:2.14-6.69               | 24 (2)                                     | 3.78 (CI 95%:2.3-0.19)                 | 0 (1)   |

|  |        |                         |       |                         |        |                         |            |
|--|--------|-------------------------|-------|-------------------------|--------|-------------------------|------------|
| <b>D<sub>360</sub>-D<sub>540</sub></b>   | 11 (3) | 3.28 (CI 95%:1.84-5.78) | 6 (2) | 2.12 (CI 95%:0.98-4.55) | 17 (2) | 2.75 (CI 95%:1.46-0.16) | 0.4 (0.53) |
| <b>D<sub>540</sub>-D<sub>720</sub></b>   | 3 (1)  | 0.9 (CI 95%:0.31-2.62)  | 6 (2) | 2.17 (CI 95%:1-4.64)    | 9 (1)  | 1.48 (CI 95%:0.52-0.11) | NA         |
| <b>D<sub>720</sub>-D<sub>900</sub></b>   | 1 (0)  | 0.3 (CI 95%:0.05-1.69)  | 2 (1) | 0.73 (CI 95%:0.2-2.61)  | 3 (0)  | 0.5 (CI 95%:0-0.06)     | NA         |
| <b>D<sub>900</sub>-D<sub>1080</sub></b>  | 2 (1)  | 0.61 (CI 95%:0.17-2.19) | 3 (1) | 1.1 (CI 95%:0.38-3.19)  | 5 (0)  | 0.83 (CI 95%:0.11-0.08) | NA         |
| <b>D<sub>1080</sub>-D<sub>1260</sub></b> | 2 (1)  | 0.61 (CI 95%:0.17-2.2)  | 3 (1) | 1.12 (CI 95%:0.38-3.23) | 5 (0)  | 0.84 (CI 95%:0.11-0.08) | NA         |

MC, Medical cannabis; Numbers do not add to 100% due to concomitant reasons; only time points with dropout reports are indicated.

**Table S3: Specific reasons for attrition rates during the study by sex and by time points**

| <b>Time period</b>                  | <b>Attrition Reason</b>        | <b>Women<br/>n=607<br/>N (%)</b> | <b>Women<br/>proportion<br/>(CI 95%)</b> | <b>Men<br/>n=513<br/>N (%)</b> | <b>Men<br/>proportional<br/>(CI 95%)</b> | <b>Overall<br/>sample<br/>N=1120<br/>N (%)</b> | <b>Overall<br/>proportion<br/>(CI 95%)</b> | <b>Wilson's <math>X^2</math><br/>test<br/>(p-value)</b> |
|-------------------------------------|--------------------------------|----------------------------------|--|--------------------------------|--|--|--|---|
| <b>D<sub>0</sub>-D<sub>1</sub></b>  | Adverse Event                  | 2 (0)                            | 0.33 CI 95%:0.09-1.2                     | 1 (0)                          | 0.2 CI 95%:0.03-1.1                      | 3 (0)  | 0.27 (CI 95%:0-0.03)                       | NA  |
| <b>D<sub>0</sub>-D<sub>1</sub></b>  | Other reason                   | 1 (0)                            | 0.17 CI 95%:0.03-0.93                    | 1 (0)                          | 0.2 CI 95%:0.03-1.1                      | 2 (0)  | 0.18 (CI 95%:0-0.03)                       | NA  |
| <b>D<sub>0</sub>-D<sub>1</sub></b>  | Ineffectiveness                | 0 (0)                            | 0 CI 95%:0-0.63                          | 1 (0)                          | 0.2 CI 95%:0.03-1.1                      | 1 (0)  | 0.09 (CI 95%:0-0.02)                       | NA  |
| <b>D<sub>0</sub>-D<sub>1</sub></b>  | Physician decision temporarily | 0 (0)                            | 0 CI 95%:0-0.63                          | 1 (0)                          | 0.2 CI 95%:0.03-1.1                      | 1 (0)  | 0.09 (CI 95%:0-0.02)                       | NA  |
| <b>D<sub>0</sub>-D<sub>1</sub></b>  | Switched to other MC form      | 0 (0)                            | 0 CI 95%:0-0.63                          | 1 (0)                          | 0.2 CI 95%:0.03-1.11                     | 1 (0)  | 0.09 (CI 95%:0-0.02)                       | NA  |
| <b>D<sub>1</sub>-D<sub>7</sub></b>  | Adverse Event                  | 3 (0)                            | 0.5 CI 95%:0.17-1.46                     | 2 (0)                          | 0.4 CI 95%:0.11-1.43                     | 5 (0)  | 0.45 (CI 95%:0.03-0.04)                    | NA  |
| <b>D<sub>1</sub>-D<sub>7</sub></b>  | Other reason                   | 2 (0)                            | 0.33 CI 95%:0.09-1.21                    | 2 (0)                          | 0.4 CI 95%:0.11-1.44                     | 4 (0)  | 0.36 (CI 95%:0-0.04)                       | NA  |
| <b>D<sub>1</sub>-D<sub>7</sub></b>  | Switched to other MC form      | 0 (0)                            | 0 CI 95%:0-0.64                          | 2 (0)                          | 0.4 CI 95%:0.11-1.45                     | 2 (0)  | 0.18 (CI 95%:0-0.03)                       | NA  |
| <b>D<sub>1</sub>-D<sub>7</sub></b>  | Deceased                       | 0 (0)                            | 0 CI 95%:0-0.64                          | 1 (0)                          | 0.2 CI 95%:0.03-1.11                     | 1 (0)  | 0.09 (CI 95%:0-0.02)                       | NA  |
| <b>D<sub>1</sub>-D<sub>7</sub></b>  | Health Worsening               | 0 (0)                            | 0 CI 95%:0-0.64                          | 1 (0)                          | 0.2 CI 95%:0.04-1.12                     | 1 (0)  | 0.09 (CI 95%:0-0.02)                       | NA  |
| <b>D<sub>1</sub>-D<sub>7</sub></b>  | Ineffectiveness                | 0 (0)                            | 0 CI 95%:0-0.64                          | 1 (0)                          | 0.2 CI 95%:0.04-1.12                     | 1 (0)  | 0.09 (CI 95%:0-0.02)                       | NA  |
| <b>D<sub>7</sub>-D<sub>14</sub></b> | Other reason                   | 3 (1)                            | 0.51 CI 95%:0.17-1.48                    | 4 (1)                          | 0.82 CI 95%:0.32-2.09                    | 7 (1)  | 0.65 (CI 95%:0.03-0.05)                    | NA  |

|                                      |                                    |        |                       |        |                       |        |                         |             |
|--------------------------------------|------------------------------------|--------|-----------------------|--------|-----------------------|--------|-------------------------|-------------|
| <b>D<sub>7</sub>-D<sub>14</sub></b>  | Physician decision permanently     | 4 (1)  | 0.68 CI 95%:0.27-1.74 | 0 (0)  | 0 CI 95%:0-0.78       | 4 (0)  | 0.37 (CI 95%:0.1-0.04)  | NA          |
| <b>D<sub>7</sub>-D<sub>14</sub></b>  | Ineffectiveness                    | 1 (0)  | 0.17 CI 95%:0.03-0.95 | 4 (1)  | 0.81 CI 95%:0.32-2.07 | 5 (0)  | 0.46 (CI 95%:0-0.04)    | NA          |
| <b>D<sub>7</sub>-D<sub>14</sub></b>  | Switched to other MC form          | 2 (0)  | 0.34 CI 95%:0.09-1.24 | 3 (1)  | 0.62 CI 95%:0.21-1.8  | 5 (0)  | 0.47 (CI 95%:0-0.05)    | NA          |
| <b>D<sub>7</sub>-D<sub>14</sub></b>  | Adverse Event                      | 3 (1)  | 0.5 CI 95%:0.17-1.47  | 1 (0)  | 0.2 CI 95%:0.04-1.13  | 4 (0)  | 0.37 (CI 95%:0.03-0.04) | NA          |
| <b>D<sub>7</sub>-D<sub>14</sub></b>  | Deceased                           | 1 (0)  | 0.17 CI 95%:0.03-0.95 | 1 (0)  | 0.2 CI 95%:0.04-1.13  | 2 (0)  | 0.18 (CI 95%:0-0.03)    | NA          |
| <b>D<sub>7</sub>-D<sub>14</sub></b>  | Improved health                    | 1 (0)  | 0.17 CI 95%:0.03-0.95 | 1 (0)  | 0.2 CI 95%:0.04-1.13  | 2 (0)  | 0.18 (CI 95%:0-0.03)    | NA          |
| <b>D<sub>14</sub>-D<sub>21</sub></b> | Ineffectiveness                    | 10 (2) | 1.77 CI 95%:0.96-3.22 | 6 (1)  | 1.28 CI 95%:0.59-2.76 | 16 (2) | 1.54 (CI 95%:0.59-0.09) | 0.15 (0.7)  |
| <b>D<sub>14</sub>-D<sub>21</sub></b> | Adverse Event                      | 6 (1)  | 1.04 CI 95%:0.48-2.25 | 7 (1)  | 1.46 CI 95%:0.71-2.99 | 13 (1) | 1.23 (CI 95%:0.25-0.08) | 0.12 (0.73) |
| <b>D<sub>14</sub>-D<sub>21</sub></b> | Switched to other MC form          | 6 (1)  | 1.08 CI 95%:0.5-2.34  | 5 (1)  | 1.09 CI 95%:0.47-2.54 | 11 (1) | 1.09 (CI 95%:0.27-0.07) | 0 (1)       |
| <b>D<sub>14</sub>-D<sub>21</sub></b> | Other reason                       | 5 (1)  | 0.89 CI 95%:0.38-2.07 | 5 (1)  | 1.08 CI 95%:0.46-2.49 | 10 (1) | 0.97 (CI 95%:0.18-0.07) | 0 (1)       |
| <b>D<sub>14</sub>-D<sub>21</sub></b> | Switched to other non-MC treatment | 4 (1)  | 0.73 CI 95%:0.28-1.85 | 0 (0)  | 0 CI 95%:0-0.83       | 4 (0)  | 0.4 (CI 95%:0.11-0.04)  | NA          |
| <b>D<sub>14</sub>-D<sub>21</sub></b> | Financial                          | 2 (0)  | 0.35 CI 95%:0.1-1.26  | 1 (0)  | 0.21 CI 95%:0.04-1.18 | 3 (0)  | 0.29 (CI 95%:0-0.04)    | NA          |
| <b>D<sub>14</sub>-D<sub>21</sub></b> | Physician decision permanently     | 1 (0)  | 0.18 CI 95%:0.03-1    | 2 (0)  | 0.43 CI 95%:0.12-1.56 | 3 (0)  | 0.29 (CI 95%:0-0.04)    | NA          |
| <b>D<sub>14</sub>-D<sub>21</sub></b> | Physician decision temporarily     | 0 (0)  | 0 CI 95%:0-0.68       | 1 (0)  | 0.22 CI 95%:0.04-1.22 | 1 (0)  | 0.1 (CI 95%:0-0.02)     | NA          |
| <b>D<sub>14</sub>-D<sub>21</sub></b> | Deceased                           | 0 (0)  | 0 CI 95%:0-0.66       | 1 (0)  | 0.21 CI 95%:0.04-1.18 | 1 (0)  | 0.09 (CI 95%:0-0.02)    | NA          |
| <b>D<sub>21</sub>-D<sub>30</sub></b> | Ineffectiveness                    | 14 (3) | 2.67 CI 95%:1.6-4.43  | 10 (2) | 2.28 CI 95%:1.24-4.14 | 24 (2) | 2.49 (CI 95%:1.05-0.12) | 0.03 (0.86) |

|                                      |                                    |        |                        |        |                       |        |                         |             |
|--------------------------------------|------------------------------------|--------|------------------------|--------|-----------------------|--------|-------------------------|-------------|
| <b>D<sub>21</sub>-D<sub>30</sub></b> | Other reason                       | 11 (2) | 2.14 CI 95%:1.2-3.79   | 5 (1)  | 1.16 CI 95%:0.5-2.68  | 16 (2) | 1.69 (CI 95%:0.77-0.1)  | 0.84 (0.36) |
| <b>D<sub>21</sub>-D<sub>30</sub></b> | Financial                          | 6 (1)  | 1.11 CI 95%:0.51-2.4   | 5 (1)  | 1.11 CI 95%:0.47-2.57 | 11 (1) | 1.11 (CI 95%:0.28-0.08) | 0 (1)       |
| <b>D<sub>21</sub>-D<sub>30</sub></b> | Switched to other MC form          | 4 (1)  | 0.79 CI 95%:0.31-2     | 4 (1)  | 0.94 CI 95%:0.36-2.38 | 8 (1)  | 0.85 (CI 95%:0.13-0.07) | NA          |
| <b>D<sub>21</sub>-D<sub>30</sub></b> | Adverse Event                      | 4 (1)  | 0.73 CI 95%:0.29-1.87  | 1 (0)  | 0.22 CI 95%:0.04-1.23 | 5 (0)  | 0.5 (CI 95%:0.11-0.05)  | NA          |
| <b>D<sub>21</sub>-D<sub>30</sub></b> | Switched to other non-MC treatment | 2 (0)  | 0.39 CI 95%:0.11-1.43  | 1 (0)  | 0.23 CI 95%:0.04-1.32 | 3 (0)  | 0.32 (CI 95%:0-0.04)    | NA          |
| <b>D<sub>21</sub>-D<sub>30</sub></b> | Health Worsening                   | 1 (0)  | 0.19 CI 95%:0.03-1.04  | 2 (0)  | 0.45 CI 95%:0.12-1.61 | 3 (0)  | 0.3 (CI 95%:0-0.04)     | NA          |
| <b>D<sub>21</sub>-D<sub>30</sub></b> | Physician decision permanently     | 1 (0)  | 0.19 CI 95%:0.03-1.1   | 1 (0)  | 0.23 CI 95%:0.04-1.3  | 2 (0)  | 0.21 (CI 95%:0-0.03)    | NA          |
| <b>D<sub>21</sub>-D<sub>30</sub></b> | License expired                    | 0 (0)  | 0 CI 95%:0-0.73        | 2 (0)  | 0.46 CI 95%:0.13-1.65 | 2 (0)  | 0.21 (CI 95%:0-0.03)    | NA          |
| <b>D<sub>30</sub>-D<sub>60</sub></b> | Ineffectiveness                    | 35 (8) | 8.05 CI 95%:5.84-10.98 | 21 (5) | 5.48 CI 95%:3.61-8.24 | 56 (7) | 6.85 (CI 95%:4.04-0.24) | 1.72 (0.19) |
| <b>D<sub>30</sub>-D<sub>60</sub></b> | Switched to other MC form          | 12 (3) | 2.93 CI 95%:1.68-5.05  | 12 (3) | 3.35 CI 95%:1.93-5.77 | 24 (3) | 3.12 (CI 95%:1.18-0.15) | 0.02 (0.9)  |
| <b>D<sub>30</sub>-D<sub>60</sub></b> | Financial                          | 13 (3) | 2.71 CI 95%:1.59-4.59  | 11 (3) | 2.71 CI 95%:1.52-4.79 | 24 (3) | 2.71 (CI 95%:1.07-0.13) | 0 (1)       |
| <b>D<sub>30</sub>-D<sub>60</sub></b> | Other reason                       | 10 (2) | 2.35 CI 95%:1.28-4.28  | 7 (2)  | 1.86 CI 95%:0.9-3.79  | 17 (2) | 2.12 (CI 95%:0.87-0.12) | 0.06 (0.81) |
| <b>D<sub>30</sub>-D<sub>60</sub></b> | Adverse Event                      | 11 (2) | 2.22 CI 95%:1.24-3.93  | 6 (1)  | 1.43 CI 95%:0.66-3.08 | 17 (2) | 1.86 (CI 95%:0.81-0.11) | 0.41 (0.53) |
| <b>D<sub>30</sub>-D<sub>60</sub></b> | Health Worsening                   | 6 (1)  | 1.27 CI 95%:0.58-2.74  | 2 (0)  | 0.5 CI 95%:0.14-1.79  | 8 (1)  | 0.91 (CI 95%:0.34-0.07) | NA          |
| <b>D<sub>30</sub>-D<sub>60</sub></b> | Physician decision permanently     | 3 (1)  | 0.71 CI 95%:0.24-2.07  | 5 (1)  | 1.35 CI 95%:0.58-3.12 | 8 (1)  | 1.01 (CI 95%:0.08-0.08) | NA          |
| <b>D<sub>30</sub>-D<sub>60</sub></b> | Deceased                           | 4 (1)  | 0.81 CI 95%:0.32-2.07  | 3 (1)  | 0.72 CI 95%:0.24-2.09 | 7 (1)  | 0.77 (CI 95%:0.14-0.06) | NA          |



|                                      |                                    |        |                       |        |                       |        |                         |             |
|--------------------------------------|------------------------------------|--------|-----------------------|--------|-----------------------|--------|-------------------------|-------------|
| <b>D<sub>30</sub>-D<sub>60</sub></b> | Switched to other non-MC treatment | 3 (1)  | 0.74 CI 95%:0.25-2.14 | 2 (1)  | 0.56 CI 95%:0.15-2.02 | 5 (1)  | 0.66 (CI 95%:0.09-0.06) | NA          |
| <b>D<sub>30</sub>-D<sub>60</sub></b> | Improved health                    | 2 (0)  | 0.43 CI 95%:0.12-1.54 | 0 (0)  | 0 CI 95%:0-0.94       | 2 (0)  | 0.23 (CI 95%:0-0.03)    | NA          |
| <b>D<sub>30</sub>-D<sub>60</sub></b> | Physician decision temporarily     | 0 (0)  | 0 CI 95%:0-0.9        | 1 (0)  | 0.27 CI 95%:0.05-1.51 | 1 (0)  | 0.13 (CI 95%:0-0.03)    | NA          |
| <b>D<sub>30</sub>-D<sub>60</sub></b> | Immigration                        | 1 (0)  | 0.21 CI 95%:0.04-1.19 | 0 (0)  | 0 CI 95%:0-0.94       | 1 (0)  | 0.11 (CI 95%:0-0.02)    | NA          |
| <b>D<sub>60</sub>-D<sub>90</sub></b> | Ineffectiveness                    | 19 (5) | 5.04 CI 95%:3.25-7.74 | 19 (6) | 5.94 CI 95%:3.83-9.09 | 38 (5) | 5.45 (CI 95%:2.41-0.22) | 0.12 (0.72) |
| <b>D<sub>60</sub>-D<sub>90</sub></b> | Switched to other MC form          | 6 (2)  | 1.68 CI 95%:0.77-3.62 | 12 (4) | 4.1 CI 95%:2.36-7.02  | 18 (3) | 2.77 (CI 95%:0.55-0.15) | 2.65 (0.1)  |
| <b>D<sub>60</sub>-D<sub>90</sub></b> | Other reason                       | 8 (2)  | 2.19 CI 95%:1.11-4.25 | 8 (3)  | 2.58 CI 95%:1.31-5.01 | 16 (2) | 2.37 (CI 95%:0.81-0.14) | 0.01 (0.93) |
| <b>D<sub>60</sub>-D<sub>90</sub></b> | Financial                          | 3 (1)  | 0.75 CI 95%:0.26-2.18 | 7 (2)  | 2.06 CI 95%:1-4.19    | 10 (1) | 1.35 (CI 95%:0.1-0.1)   | NA          |
| <b>D<sub>60</sub>-D<sub>90</sub></b> | Adverse Event                      | 3 (1)  | 0.74 CI 95%:0.25-2.16 | 6 (2)  | 1.71 CI 95%:0.79-3.69 | 9 (1)  | 1.19 (CI 95%:0.1-0.09)  | NA          |
| <b>D<sub>60</sub>-D<sub>90</sub></b> | Physician decision permanently     | 3 (1)  | 0.83 CI 95%:0.28-2.4  | 4 (1)  | 1.31 CI 95%:0.51-3.31 | 7 (1)  | 1.05 (CI 95%:0.13-0.09) | NA          |
| <b>D<sub>60</sub>-D<sub>90</sub></b> | Switched to other non-MC treatment | 3 (1)  | 0.85 CI 95%:0.29-2.46 | 3 (1)  | 1.03 CI 95%:0.35-3    | 6 (1)  | 0.93 (CI 95%:0.14-0.08) | NA          |
| <b>D<sub>60</sub>-D<sub>90</sub></b> | License expired                    | 3 (1)  | 0.8 CI 95%:0.27-2.33  | 2 (1)  | 0.63 CI 95%:0.17-2.26 | 5 (1)  | 0.72 (CI 95%:0.12-0.07) | NA          |
| <b>D<sub>60</sub>-D<sub>90</sub></b> | Deceased                           | 1 (0)  | 0.25 CI 95%:0.04-1.39 | 3 (1)  | 0.86 CI 95%:0.29-2.51 | 4 (1)  | 0.53 (CI 95%:0-0.06)    | NA          |
| <b>D<sub>60</sub>-D<sub>90</sub></b> | Improved health                    | 2 (1)  | 0.51 CI 95%:0.14-1.82 | 1 (0)  | 0.29 CI 95%:0.05-1.65 | 3 (0)  | 0.41 (CI 95%:0-0.05)    | NA          |
| <b>D<sub>60</sub>-D<sub>90</sub></b> | Health Worsening                   | 2 (1)  | 0.5 CI 95%:0.14-1.81  | 0 (0)  | 0 CI 95%:0-1.12       | 2 (0)  | 0.27 (CI 95%:0-0.04)    | NA          |
| <b>D<sub>60</sub>-D<sub>90</sub></b> | Physician decision temporarily     | 0 (0)  | 0 CI 95%:0-1.05       | 1 (0)  | 0.33 CI 95%:0.06-1.83 | 1 (0)  | 0.15 (CI 95%:0-0.03)    | NA          |

|  |                                    |        |                       |        |                       |        |                         |             |
|--|------------------------------------|--------|-----------------------|--------|-----------------------|--------|-------------------------|-------------|
| <b>D<sub>90</sub>-D<sub>120</sub></b>  | Ineffectiveness                    | 12 (4) | 3.59 CI 95%:2.07-6.17 | 12 (4) | 4.48 CI 95%:2.58-7.66 | 24 (4) | 3.99 (CI 95%:1.65-0.2)  | 0.12 (0.73) |
| <b>D<sub>90</sub>-D<sub>120</sub></b>  | Other reason                       | 6 (2)  | 1.83 CI 95%:0.84-3.93 | 7 (3)  | 2.69 CI 95%:1.31-5.45 | 13 (2) | 2.21 (CI 95%:0.65-0.14) | 0.18 (0.67) |
| <b>D<sub>90</sub>-D<sub>120</sub></b>  | Switched to other MC form          | 3 (1)  | 0.93 CI 95%:0.32-2.71 | 7 (3)  | 2.79 CI 95%:1.36-5.64 | 10 (2) | 1.75 (CI 95%:0.18-0.12) | NA          |
| <b>D<sub>90</sub>-D<sub>120</sub></b>  | Financial                          | 3 (1)  | 0.86 CI 95%:0.29-2.5  | 4 (1)  | 1.42 CI 95%:0.55-3.59 | 7 (1)  | 1.11 (CI 95%:0.15-0.09) | NA          |
| <b>D<sub>90</sub>-D<sub>120</sub></b>  | Switched to other non-MC treatment | 3 (1)  | 0.94 CI 95%:0.32-2.74 | 3 (1)  | 1.21 CI 95%:0.41-3.5  | 6 (1)  | 1.06 (CI 95%:0.19-0.09) | NA          |
| <b>D<sub>90</sub>-D<sub>120</sub></b>  | Deceased                           | 2 (1)  | 0.57 CI 95%:0.16-2.05 | 3 (1)  | 1.05 CI 95%:0.36-3.04 | 5 (1)  | 0.78 (CI 95%:0.02-0.08) | NA          |
| <b>D<sub>90</sub>-D<sub>120</sub></b>  | Physician decision permanently     | 2 (1)  | 0.61 CI 95%:0.17-2.21 | 2 (1)  | 0.78 CI 95%:0.21-2.78 | 4 (1)  | 0.68 (CI 95%:0.03-0.07) | NA          |
| <b>D<sub>90</sub>-D<sub>120</sub></b>  | Physician decision temporarily     | 2 (1)  | 0.62 CI 95%:0.17-2.22 | 0 (0)  | 0 CI 95%:0-1.47       | 2 (0)  | 0.34 (CI 95%:0.04-0.05) | NA          |
| <b>D<sub>90</sub>-D<sub>120</sub></b>  | Health Worsening                   | 1 (0)  | 0.29 CI 95%:0.05-1.61 | 1 (0)  | 0.36 CI 95%:0.06-1.99 | 2 (0)  | 0.32 (CI 95%:0-0.05)    | NA          |
| <b>D<sub>90</sub>-D<sub>120</sub></b>  | Adverse Event                      | 1 (0)  | 0.28 CI 95%:0.05-1.59 | 1 (0)  | 0.35 CI 95%:0.06-1.93 | 2 (0)  | 0.31 (CI 95%:0-0.05)    | NA          |
| <b>D<sub>90</sub>-D<sub>120</sub></b>  | Intermittently continued           | 0 (0)  | 0 CI 95%:0-1.14       | 1 (0)  | 0.37 CI 95%:0.07-2.09 | 1 (0)  | 0.17 (CI 95%:0-0.03)    | NA          |
| <b>D<sub>90</sub>-D<sub>120</sub></b>  | Immigration                        | 1 (0)  | 0.29 CI 95%:0.05-1.62 | 0 (0)  | 0 CI 95%:0-1.35       | 1 (0)  | 0.16 (CI 95%:0-0.03)    | NA          |
| <b>D<sub>90</sub>-D<sub>120</sub></b>  | Improved health                    | 0 (0)  | 0 CI 95%:0-1.1        | 1 (0)  | 0.36 CI 95%:0.06-1.99 | 1 (0)  | 0.16 (CI 95%:0-0.03)    | NA          |
| <b>D<sub>120</sub>-D<sub>180</sub></b> | Ineffectiveness                    | 16 (5) | 5.48 CI 95%:3.4-8.71  | 12 (5) | 5.31 CI 95%:3.06-9.05 | 28 (5) | 5.41 (CI 95%:2.93-0.25) | 0 (1)       |
| <b>D<sub>120</sub>-D<sub>180</sub></b> | Other reason                       | 11 (4) | 3.97 CI 95%:2.23-6.97 | 3 (1)  | 1.37 CI 95%:0.47-3.95 | 14 (3) | 2.82 (CI 95%:1.98-0.17) | 2.14 (0.14) |
| <b>D<sub>120</sub>-D<sub>180</sub></b> | Switched to other MC form          | 7 (3)  | 2.66 CI 95%:1.3-5.39  | 9 (4)  | 4.39 CI 95%:2.33-8.13 | 16 (3) | 3.42 (CI 95%:1.19-0.2)  | 0.59 (0.44) |

|  |                                    |       |                       |       |                       |        |                         |          |
|--|------------------------------------|-------|-----------------------|-------|-----------------------|--------|-------------------------|----------|
| <b>D<sub>120</sub>-D<sub>180</sub></b> | Physician decision permanently     | 5 (2) | 1.84 CI 95%:0.79-4.23 | 5 (2) | 2.34 CI 95%:1-5.35    | 10 (2) | 2.06 (CI 95%:0.69-0.15) | 0 (0.95) |
| <b>D<sub>120</sub>-D<sub>180</sub></b> | Switched to other non-MC treatment | 5 (2) | 1.94 CI 95%:0.83-4.46 | 2 (1) | 0.99 CI 95%:0.27-3.52 | 7 (2)  | 1.52 (CI 95%:0.76-0.13) | NA       |
| <b>D<sub>120</sub>-D<sub>180</sub></b> | Improved health                    | 5 (2) | 1.62 CI 95%:0.7-3.74  | 4 (2) | 1.68 CI 95%:0.66-4.24 | 9 (2)  | 1.65 (CI 95%:0.55-0.12) | NA       |
| <b>D<sub>120</sub>-D<sub>180</sub></b> | License expired                    | 4 (1) | 1.39 CI 95%:0.54-3.52 | 3 (1) | 1.35 CI 95%:0.46-3.9  | 7 (1)  | 1.37 (CI 95%:0.43-0.11) | NA       |
| <b>D<sub>120</sub>-D<sub>180</sub></b> | Deceased                           | 2 (1) | 0.63 CI 95%:0.17-2.28 | 2 (1) | 0.82 CI 95%:0.22-2.93 | 4 (1)  | 0.71 (CI 95%:0.04-0.08) | NA       |
| <b>D<sub>120</sub>-D<sub>180</sub></b> | Health Worsening                   | 2 (1) | 0.64 CI 95%:0.18-2.3  | 1 (0) | 0.41 CI 95%:0.07-2.3  | 3 (1)  | 0.54 (CI 95%:0.05-0.07) | NA       |
| <b>D<sub>120</sub>-D<sub>180</sub></b> | Financial                          | 1 (0) | 0.32 CI 95%:0.06-1.78 | 2 (1) | 0.82 CI 95%:0.23-2.95 | 3 (1)  | 0.54 (CI 95%:0-0.07)    | NA       |
| <b>D<sub>120</sub>-D<sub>180</sub></b> | Physician decision temporarily     | 2 (1) | 0.74 CI 95%:0.2-2.66  | 0 (0) | 0 CI 95%:0-1.76       | 2 (0)  | 0.41 (CI 95%:0.09-0.06) | NA       |
| <b>D<sub>120</sub>-D<sub>180</sub></b> | Intermittently continued           | 0 (0) | 0 CI 95%:0-1.3        | 1 (0) | 0.44 CI 95%:0.08-2.47 | 1 (0)  | 0.19 (CI 95%:0-0.04)    | NA       |
| <b>D<sub>120</sub>-D<sub>180</sub></b> | Adverse Event                      | 0 (0) | 0 CI 95%:0-1.19       | 1 (0) | 0.4 CI 95%:0.07-2.26  | 1 (0)  | 0.18 (CI 95%:0-0.04)    | NA       |
| <b>D<sub>180</sub>-D<sub>240</sub></b> | Ineffectiveness                    | 6 (2) | 2.43 CI 95%:1.12-5.2  | 5 (3) | 2.56 CI 95%:1.1-5.86  | 11 (2) | 2.49 (CI 95%:1.07-0.17) | 0 (1)    |
| <b>D<sub>180</sub>-D<sub>240</sub></b> | Switched to other MC form          | 6 (3) | 2.55 CI 95%:1.18-5.46 | 2 (1) | 1.07 CI 95%:0.29-3.82 | 8 (2)  | 1.9 (CI 95%:1.16-0.15)  | NA       |
| <b>D<sub>180</sub>-D<sub>240</sub></b> | License expired                    | 4 (2) | 1.65 CI 95%:0.64-4.16 | 1 (1) | 0.52 CI 95%:0.09-2.86 | 5 (1)  | 1.14 (CI 95%:0.6-0.11)  | NA       |
| <b>D<sub>180</sub>-D<sub>240</sub></b> | Switched to other non-MC treatment | 2 (1) | 0.86 CI 95%:0.24-3.08 | 3 (2) | 1.63 CI 95%:0.56-4.68 | 5 (1)  | 1.2 (CI 95%:0.17-0.12)  | NA       |
| <b>D<sub>180</sub>-D<sub>240</sub></b> | Adverse Event                      | 2 (1) | 0.78 CI 95%:0.21-2.8  | 0 (0) | 0 CI 95%:0-1.86       | 2 (0)  | 0.44 (CI 95%:0.12-0.06) | NA       |
| <b>D<sub>180</sub>-D<sub>240</sub></b> | Financial                          | 2 (1) | 0.79 CI 95%:0.22-2.82 | 0 (0) | 0 CI 95%:0-1.87       | 2 (0)  | 0.44 (CI 95%:0.12-0.07) | NA       |

|  |                                    |       |                       |       |                       |       |                         |    |
|--|------------------------------------|-------|-----------------------|-------|-----------------------|-------|-------------------------|----|
| <b>D<sub>180</sub>-D<sub>240</sub></b> | Sudden illness temp                | 1 (0) | 0.41 CI 95%:0.07-2.31 | 1 (1) | 0.53 CI 95%:0.09-2.94 | 2 (0) | 0.47 (CI 95%:0-0.07)    | NA |
| <b>D<sub>180</sub>-D<sub>240</sub></b> | Physician decision permanently     | 1 (0) | 0.41 CI 95%:0.07-2.3  | 1 (1) | 0.52 CI 95%:0.09-2.91 | 2 (0) | 0.46 (CI 95%:0-0.07)    | NA |
| <b>D<sub>180</sub>-D<sub>240</sub></b> | Other reason                       | 0 (0) | 0 CI 95%:0-1.56       | 2 (1) | 1.04 CI 95%:0.29-3.72 | 2 (0) | 0.46 (CI 95%:0-0.07)    | NA |
| <b>D<sub>180</sub>-D<sub>240</sub></b> | Improved health                    | 1 (0) | 0.4 CI 95%:0.07-2.2   | 1 (1) | 0.5 CI 95%:0.09-2.78  | 2 (0) | 0.44 (CI 95%:0-0.07)    | NA |
| <b>D<sub>180</sub>-D<sub>240</sub></b> | Deceased                           | 0 (0) | 0 CI 95%:0-1.48       | 1 (0) | 0.5 CI 95%:0.09-2.75  | 1 (0) | 0.22 (CI 95%:0-0.04)    | NA |
| <b>D<sub>180</sub>-D<sub>240</sub></b> | Physician decision temporarily     | 0 (0) | 0 CI 95%:0-1.56       | 1 (1) | 0.53 CI 95%:0.09-2.92 | 1 (0) | 0.23 (CI 95%:0-0.05)    | NA |
| <b>D<sub>180</sub>-D<sub>240</sub></b> | Health Worsening                   | 0 (0) | 0 CI 95%:0-1.49       | 1 (0) | 0.5 CI 95%:0.09-2.76  | 1 (0) | 0.22 (CI 95%:0-0.05)    | NA |
| <b>D<sub>240</sub>-D<sub>360</sub></b> | License expired                    | 7 (3) | 3.21 CI 95%:1.56-6.48 | 1 (1) | 0.56 CI 95%:0.1-3.11  | 8 (2) | 2.02 (CI 95%:1.62-0.16) | NA |
| <b>D<sub>240</sub>-D<sub>360</sub></b> | Switched to other MC form          | 3 (1) | 1.43 CI 95%:0.49-4.12 | 6 (4) | 3.51 CI 95%:1.62-7.44 | 9 (2) | 2.36 (CI 95%:0.51-0.18) | NA |
| <b>D<sub>240</sub>-D<sub>360</sub></b> | Ineffectiveness                    | 4 (2) | 1.78 CI 95%:0.69-4.48 | 4 (2) | 2.23 CI 95%:0.87-5.6  | 8 (2) | 1.98 (CI 95%:0.7-0.16)  | NA |
| <b>D<sub>240</sub>-D<sub>360</sub></b> | Other reason                       | 3 (1) | 1.4 CI 95%:0.48-4.02  | 1 (1) | 0.56 CI 95%:0.1-3.13  | 4 (1) | 1.02 (CI 95%:0.48-0.11) | NA |
| <b>D<sub>240</sub>-D<sub>360</sub></b> | Switched to other non-MC treatment | 3 (1) | 1.45 CI 95%:0.49-4.17 | 0 (0) | 0 CI 95%:0-2.2        | 3 (1) | 0.79 (CI 95%:0.52-0.1)  | NA |
| <b>D<sub>240</sub>-D<sub>360</sub></b> | Improved health                    | 2 (1) | 0.87 CI 95%:0.24-3.13 | 0 (0) | 0 CI 95%:0-2.06       | 2 (0) | 0.49 (CI 95%:0.17-0.07) | NA |
| <b>D<sub>240</sub>-D<sub>360</sub></b> | Financial                          | 1 (0) | 0.43 CI 95%:0.08-2.4  | 1 (1) | 0.55 CI 95%:0.1-3.03  | 2 (0) | 0.48 (CI 95%:0-0.07)    | NA |

|  |                                    |       |                       |       |                       |       |                         |    |
|--|------------------------------------|-------|-----------------------|-------|-----------------------|-------|-------------------------|----|
| <b>D<sub>240</sub>-D<sub>360</sub></b> | Physician decision permanently     | 1 (0) | 0.47 CI 95%:0.08-2.6  | 0 (0) | 0 CI 95%:0-2.12       | 1 (0) | 0.26 (CI 95%:0-0.05)    | NA |
| <b>D<sub>240</sub>-D<sub>360</sub></b> | Physician decision temporarily     | 1 (0) | 0.47 CI 95%:0.08-2.61 | 0 (0) | 0 CI 95%:0-2.12       | 1 (0) | 0.26 (CI 95%:0-0.05)    | NA |
| <b>D<sub>240</sub>-D<sub>360</sub></b> | Immigration                        | 1 (0) | 0.43 CI 95%:0.08-2.41 | 0 (0) | 0 CI 95%:0-2.06       | 1 (0) | 0.24 (CI 95%:0-0.05)    | NA |
| <b>D<sub>360</sub>-D<sub>540</sub></b> | Ineffectiveness                    | 4 (2) | 2.04 CI 95%:0.8-5.13  | 2 (1) | 1.2 CI 95%:0.33-4.29  | 6 (2) | 1.66 (CI 95%:0.91-0.15) | NA |
| <b>D<sub>360</sub>-D<sub>540</sub></b> | Financial                          | 3 (1) | 1.48 CI 95%:0.5-4.25  | 0 (0) | 0 CI 95%:0-2.21       | 3 (1) | 0.8 (CI 95%:0.54-0.1)   | NA |
| <b>D<sub>360</sub>-D<sub>540</sub></b> | License expired                    | 2 (1) | 1.03 CI 95%:0.28-3.68 | 1 (1) | 0.61 CI 95%:0.11-3.35 | 3 (1) | 0.84 (CI 95%:0.29-0.1)  | NA |
| <b>D<sub>360</sub>-D<sub>540</sub></b> | Switched to other MC form          | 2 (1) | 1.06 CI 95%:0.29-3.78 | 0 (0) | 0 CI 95%:0-2.28       | 2 (1) | 0.56 (CI 95%:0.31-0.08) | NA |
| <b>D<sub>360</sub>-D<sub>540</sub></b> | Health Worsening                   | 2 (1) | 1 CI 95%:0.27-3.55    | 0 (0) | 0 CI 95%:0-2.21       | 2 (1) | 0.54 (CI 95%:0.26-0.08) | NA |
| <b>D<sub>360</sub>-D<sub>540</sub></b> | Improved health                    | 1 (1) | 0.5 CI 95%:0.09-2.78  | 2 (1) | 1.19 CI 95%:0.33-4.24 | 3 (1) | 0.82 (CI 95%:0-0.1)     | NA |
| <b>D<sub>360</sub>-D<sub>540</sub></b> | Deceased                           | 1 (0) | 0.49 CI 95%:0.09-2.7  | 1 (1) | 0.59 CI 95%:0.1-3.26  | 2 (1) | 0.53 (CI 95%:0-0.08)    | NA |
| <b>D<sub>360</sub>-D<sub>540</sub></b> | Physician decision temporarily     | 1 (1) | 0.52 CI 95%:0.09-2.91 | 0 (0) | 0 CI 95%:0-2.28       | 1 (0) | 0.28 (CI 95%:0.02-0.06) | NA |
| <b>D<sub>360</sub>-D<sub>540</sub></b> | Other reason                       | 1 (1) | 0.52 CI 95%:0.09-2.88 | 0 (0) | 0 CI 95%:0-2.28       | 1 (0) | 0.28 (CI 95%:0.01-0.06) | NA |
| <b>D<sub>360</sub>-D<sub>540</sub></b> | Physician decision permanently     | 1 (1) | 0.52 CI 95%:0.09-2.89 | 0 (0) | 0 CI 95%:0-2.28       | 1 (0) | 0.28 (CI 95%:0.01-0.06) | NA |
| <b>D<sub>540</sub>-D<sub>720</sub></b> | Health Worsening                   | 2 (1) | 1.07 CI 95%:0.29-3.82 | 1 (1) | 0.61 CI 95%:0.11-3.39 | 3 (1) | 0.86 (CI 95%:0.32-0.11) | NA |
| <b>D<sub>540</sub>-D<sub>720</sub></b> | Physician decision permanently     | 1 (1) | 0.54 CI 95%:0.1-3     | 3 (2) | 1.9 CI 95%:0.65-5.43  | 4 (1) | 1.17 (CI 95%:0.03-0.13) | NA |
| <b>D<sub>540</sub>-D<sub>720</sub></b> | Switched to other non-MC treatment | 1 (1) | 0.54 CI 95%:0.1-3.01  | 1 (1) | 0.64 CI 95%:0.11-3.52 | 2 (1) | 0.59 (CI 95%:0.03-0.09) | NA |

|  |                                    |       |                       |       |                       |       |                         |    |
|--|------------------------------------|-------|-----------------------|-------|-----------------------|-------|-------------------------|----|
| <b>D<sub>540</sub>-D<sub>720</sub></b>   | Ineffectiveness                    | 1 (1) | 0.54 CI 95%:0.09-2.98 | 0 (0) | 0 CI 95%:0-2.32       | 1 (0) | 0.29 (CI 95%:0.03-0.06) | NA |
| <b>D<sub>540</sub>-D<sub>720</sub></b>   | Improved health                    | 0 (0) | 0 CI 95%:0-2.01       | 1 (1) | 0.62 CI 95%:0.11-3.41 | 1 (0) | 0.29 (CI 95%:0-0.06)    | NA |
| <b>D<sub>540</sub>-D<sub>720</sub></b>   | License expired                    | 0 (0) | 0 CI 95%:0-2.02       | 1 (1) | 0.62 CI 95%:0.11-3.43 | 1 (0) | 0.29 (CI 95%:0-0.06)    | NA |
| <b>D<sub>540</sub>-D<sub>720</sub></b>   | Deceased                           | 0 (0) | 0 CI 95%:0-1.99       | 1 (1) | 0.61 CI 95%:0.11-3.37 | 1 (0) | 0.28 (CI 95%:0-0.06)    | NA |
| <b>D<sub>720</sub>-D<sub>900</sub></b>   | License expired                    | 1 (1) | 0.56 CI 95%:0.1-3.08  | 1 (1) | 0.65 CI 95%:0.11-3.56 | 2 (1) | 0.6 (CI 95%:0.04-0.09)  | NA |
| <b>D<sub>720</sub>-D<sub>900</sub></b>   | Improved health                    | 1 (1) | 0.55 CI 95%:0.1-3.05  | 0 (0) | 0 CI 95%:0-2.4        | 1 (0) | 0.3 (CI 95%:0.04-0.06)  | NA |
| <b>D<sub>720</sub>-D<sub>900</sub></b>   | Intermittently continued           | 1 (1) | 0.55 CI 95%:0.1-3.06  | 0 (0) | 0 CI 95%:0-2.4        | 1 (0) | 0.3 (CI 95%:0.04-0.06)  | NA |
| <b>D<sub>720</sub>-D<sub>900</sub></b>   | Financial                          | 1 (1) | 0.55 CI 95%:0.1-3.03  | 0 (0) | 0 CI 95%:0-2.39       | 1 (0) | 0.29 (CI 95%:0.03-0.06) | NA |
| <b>D<sub>720</sub>-D<sub>900</sub></b>   | Physician decision permanently     | 0 (0) | 0 CI 95%:0-2.09       | 1 (1) | 0.65 CI 95%:0.11-3.59 | 1 (0) | 0.3 (CI 95%:0-0.06)     | NA |
| <b>D<sub>720</sub>-D<sub>900</sub></b>   | Health Worsening                   | 0 (0) | 0 CI 95%:0-2.06       | 1 (1) | 0.64 CI 95%:0.11-3.54 | 1 (0) | 0.29 (CI 95%:0-0.06)    | NA |
| <b>D<sub>900</sub>-D<sub>1080</sub></b>  | Improved health                    | 2 (1) | 1.12 CI 95%:0.31-4    | 0 (0) | 0 CI 95%:0-2.48       | 2 (1) | 0.61 (CI 95%:0.38-0.09) | NA |
| <b>D<sub>900</sub>-D<sub>1080</sub></b>  | Health Worsening                   | 0 (0) | 0 CI 95%:0-2.09       | 2 (1) | 1.32 CI 95%:0.36-4.67 | 2 (1) | 0.6 (CI 95%:0-0.09)     | NA |
| <b>D<sub>900</sub>-D<sub>1080</sub></b>  | Switched to other non-MC treatment | 1 (1) | 0.56 CI 95%:0.1-3.13  | 0 (0) | 0 CI 95%:0-2.48       | 1 (0) | 0.3 (CI 95%:0.05-0.06)  | NA |
| <b>D<sub>900</sub>-D<sub>1080</sub></b>  | Immigration                        | 0 (0) | 0 CI 95%:0-2.09       | 1 (1) | 0.66 CI 95%:0.12-3.66 | 1 (0) | 0.3 (CI 95%:0-0.06)     | NA |
| <b>D<sub>1080</sub>-D<sub>1260</sub></b> | Improved health                    | 2 (1) | 1.14 CI 95%:0.31-4.07 | 3 (2) | 2.03 CI 95%:0.69-5.79 | 5 (2) | 1.55 (CI 95%:0.4-0.15)  | NA |
| <b>D<sub>1080</sub>-D<sub>1260</sub></b> | Other reason                       | 1 (1) | 0.57 CI 95%:0.1-3.18  | 0 (0) | 0 CI 95%:0-2.55       | 1 (0) | 0.31 (CI 95%:0.06-0.06) | NA |

|   |                 |       |                 |       |                           |       |                          |    |
|---|-----------------|-------|-----------------|-------|---------------------------|-------|--------------------------|----|
| <b>D<sub>1080</sub>-<br/>D<sub>1260</sub></b> | License expired | 0 (0) | 0 CI 95%:0-2.15 | 1 (1) | 0.68 CI 95%:0.12-<br>3.75 | 1 (0) | 0.31 (CI 95%:0-<br>0.06) | NA |
|---|-----------------|-------|-----------------|-------|---------------------------|-------|--------------------------|----|

MC, Medical cannabis; Numbers does not add to 100% due to concomitant reasons; Only time points with dropout reports are indicated.

**Table S4: Specific sample etiologies/diagnoses for treatment**

| <b>Pain diagnosis etiology</b> | <b>Women<br/>n=607<br/>N (%)</b> | <b>Women proportion<br/>(CI 95%)</b> | <b>Men<br/>n=513<br/>N (%)</b> | <b>Men proportional<br/>(CI 95%)</b> | <b>Overall<br/>sample<br/>N=1120<br/>N (%)</b> | <b>Overall proportion<br/>(CI 95%)</b> | <b>Wilson's <math>X^2</math><br/>test<br/>(p-value)</b> |
|--------------------------------|----------------------------------|--------------------------------------|--------------------------------|--------------------------------------|--|--|---|
| <b>Chronic pain</b>            | 512<br>(84)                      | 84.35 (CI 95%:<br>81.24-87.02)       | 407<br>(79)                    | 79.34 (CI 95%:<br>75.62-82.62)       | 919 (82)                                       | 82.05 (CI 95%:<br>79.81-84.3)          | 4.41 (0.04)   |
| <b>Neuropathic pain</b>        | 345<br>(57)                      | 56.84 (CI 95%:<br>52.87-60.72)       | 353<br>(69)                    | 68.81 (CI 95%:<br>64.67-72.67)       | 698 (62)                                       | 62.32 (CI 95%:<br>59.48-65.16)         | 16.47<br>(<0.001)                                       |
| Lumbar Herniated Disc          | 187<br>(31)                      | 30.81 (CI 95%:<br>27.26-34.59)       | 160<br>(31)                    | 31.19 (CI 95%:<br>27.33-35.33)       | 347 (31)                                       | 30.98 (CI 95%:<br>28.27-33.69)         | 0.01 (0.94)   |
| Cervical radicular pain        | 40 (7)                           | 6.59 (CI 95%: 4.88-<br>8.85)         | 45 (9)                         | 8.77 (CI 95%: 6.62-<br>11.54)        | 85 (8)   | 7.59 (CI 95%: 6.04-<br>9.14)           | 1.59 (0.21)   |
| Complex regional pain syndrome | 31 (5)                           | 5.11 (CI 95%: 3.62-<br>7.16)         | 24 (5)                         | 4.68 (CI 95%: 3.16-<br>6.87)         | 55 (5)   | 4.91 (CI 95%: 3.65-<br>6.18)           | 0.04 (0.85)   |
| Diabetic Neuropathy Pain       | 25 (4)                           | 4.12 (CI 95%: 2.81-<br>6.01)         | 34 (7)                         | 6.63 (CI 95%: 4.78-<br>9.12)         | 59 (5)   | 5.27 (CI 95%: 3.96-<br>6.58)           | 3.02 (0.08)   |
| Nerve injury                   | 21 (3)                           | 3.46 (CI 95%: 2.27-<br>5.23)         | 43 (8)                         | 8.38 (CI 95%: 6.28-<br>11.1)         | 64 (6)   | 5.71 (CI 95%: 4.35-<br>7.07)           | 11.6<br>(<0.001)  |
| MS related neuropathic pain    | 12 (2)                           | 1.98 (CI 95%: 1.13-<br>3.42)         | 5 (1)                          | 0.97 (CI 95%: 0.42-<br>2.26)         | 17 (2)   | 1.52 (CI 95%: 0.8-<br>2.23)            | 1.26 (0.26)   |



|   |        |                          |        |                          |        |                          |             |
|---|--------|--------------------------|--------|--------------------------|--------|--------------------------|-------------|
| Post herpetic neuralgia                           | 9 (1)  | 1.48 (CI 95%: 0.78-2.79) | 10 (2) | 1.95 (CI 95%: 1.06-3.55) | 19 (2) | 1.7 (CI 95%: 0.94-2.45)  | 0.14 (0.71) |
| Chemotherapy induced neuropathic pain             | 10 (2) | 1.65 (CI 95%: 0.9-3.01)  | 5 (1)  | 0.97 (CI 95%: 0.42-2.26) | 15 (1) | 1.34 (CI 95%: 0.67-2.01) | 0.51 (0.48) |
| Trigeminal neuralgia                              | 9 (1)  | 1.48 (CI 95%: 0.78-2.79) | 1 (0)  | 0.19 (CI 95%: 0.03-1.1)  | 10 (1) | 0.89 (CI 95%: 0.34-1.44) | NA          |
| Idiopathic peripheral neuropathy                  | 8 (1)  | 1.32 (CI 95%: 0.67-2.58) | 9 (2)  | 1.75 (CI 95%: 0.93-3.3)  | 17 (2) | 1.52 (CI 95%: 0.8-2.23)  | 0.12 (0.73) |
| Spinal cord injury                                | 8 (1)  | 1.32 (CI 95%: 0.67-2.58) | 8 (2)  | 1.56 (CI 95%: 0.79-3.05) | 16 (1) | 1.43 (CI 95%: 0.73-2.12) | 0.01 (0.93) |
| Phantom limb pain                                 | 4 (1)  | 0.66 (CI 95%: 0.26-1.68) | 20 (4) | 3.9 (CI 95%: 2.54-5.94)  | 24 (2) | 2.14 (CI 95%: 1.29-2.99) | NA          |
| Small fiber neuropathy                            | 3 (0)  | 0.49 (CI 95%: 0.17-1.44) | 6 (1)  | 1.17 (CI 95%: 0.54-2.53) | 9 (1)  | 0.8 (CI 95%: 0.28-1.33)  | NA          |
| Facial nerve injury                               | 3 (0)  | 0.49 (CI 95%: 0.17-1.44) | 4 (1)  | 0.78 (CI 95%: 0.3-1.99)  | 7 (1)  | 0.62 (CI 95%: 0.16-1.09) | NA          |
| CVA related pain                                  | 3 (0)  | 0.49 (CI 95%: 0.17-1.44) | 3 (1)  | 0.58 (CI 95%: 0.2-1.71)  | 6 (1)  | 0.54 (CI 95%: 0.11-0.96) | NA          |
| Carpal tunnel syndrome                            | 4 (1)  | 0.66 (CI 95%: 0.26-1.68) | 1 (0)  | 0.19 (CI 95%: 0.03-1.1)  | 5 (0)  | 0.45 (CI 95%: 0.06-0.84) | NA          |
| Parkinson's disease related peripheral neuropathy | 3 (0)  | 0.49 (CI 95%: 0.17-1.44) | 1 (0)  | 0.19 (CI 95%: 0.03-1.1)  | 4 (0)  | 0.36 (CI 95%: 0.01-0.71) | NA          |

|  |          |                             |          |                           |          |                           |             |
|--|----------|-----------------------------|----------|---------------------------|----------|---------------------------|-------------|
| Post mastectomy pain                       | 4 (1)    | 0.66 (CI 95%: 0.26-1.68)    | 0 (0)    | 0 (CI 95%: 0-0.74)        | 4 (0)    | 0.36 (CI 95%: 0.01-0.71)  | NA          |
| Failed back surgery pain                   | 2 (0)    | 0.33 (CI 95%: 0.09-1.19)    | 4 (1)    | 0.78 (CI 95%: 0.3-1.99)   | 6 (1)    | 0.54 (CI 95%: 0.11-0.96)  | NA          |
| Cancer related neuropathic pain            | 2 (0)    | 0.33 (CI 95%: 0.09-1.19)    | 0 (0)    | 0 (CI 95%: 0-0.74)        | 2 (0)    | 0.18 (CI 95%: -0.07-0.43) | NA          |
| Post lumpectomy pain                       | 2 (0)    | 0.33 (CI 95%: 0.09-1.19)    | 0 (0)    | 0 (CI 95%: 0-0.74)        | 2 (0)    | 0.18 (CI 95%: -0.07-0.43) | NA          |
| Berger's disease                           | 1 (0)    | 0.16 (CI 95%: 0.03-0.93)    | 2 (0)    | 0.39 (CI 95%: 0.11-1.41)  | 3 (0)    | 0.27 (CI 95%: -0.03-0.57) | NA          |
| Radiation therapy related neuropathic pain | 1 (0)    | 0.16 (CI 95%: 0.03-0.93)    | 2 (0)    | 0.39 (CI 95%: 0.11-1.41)  | 3 (0)    | 0.27 (CI 95%: -0.03-0.57) | NA          |
| Transverse Myelitis                        | 1 (0)    | 0.16 (CI 95%: 0.03-0.93)    | 2 (0)    | 0.39 (CI 95%: 0.11-1.41)  | 3 (0)    | 0.27 (CI 95%: -0.03-0.57) | NA          |
| <b>Musculoskeletal pain</b>                | 197 (32) | 32.45 (CI 95%: 28.85-36.28) | 139 (27) | 27.1 (CI 95%: 23.43-31.1) | 336 (30) | 30 (CI 95%: 27.32-32.68)  | 3.55 (0.06) |
| Osteoarthritis                             | 45 (7)   | 7.41 (CI 95%: 5.59-9.78)    | 14 (3)   | 2.73 (CI 95%: 1.63-4.53)  | 59 (5)   | 5.27 (CI 95%: 3.96-6.58)  | 11.3 (0)    |
| Rheumatoid Arthritis                       | 38 (6)   | 6.26 (CI 95%: 4.59-8.48)    | 10 (2)   | 1.95 (CI 95%: 1.06-3.55)  | 48 (4)   | 4.29 (CI 95%: 3.1-5.47)   | 11.6 (0)    |
| Spinal stenosis                            | 22 (4)   | 3.62 (CI 95%: 2.41-5.43)    | 19 (4)   | 3.7 (CI 95%: 2.38-5.71)   | 41 (4)   | 3.66 (CI 95%: 2.56-4.76)  | 0 (1)       |

|                              |        |                          |        |                          |        |                          |             |
|------------------------------|--------|--------------------------|--------|--------------------------|--------|--------------------------|-------------|
| Low back pain                | 17 (3) | 2.8 (CI 95%: 1.76-4.44)  | 11 (2) | 2.14 (CI 95%: 1.2-3.8)   | 28 (3) | 2.5 (CI 95%: 1.59-3.41)  | 0.26 (0.61) |
| Tendon tear                  | 14 (2) | 2.31 (CI 95%: 1.38-3.83) | 14 (3) | 2.73 (CI 95%: 1.63-4.53) | 28 (3) | 2.5 (CI 95%: 1.59-3.41)  | 0.07 (0.8)  |
| Unknown origin shoulder pain | 9 (1)  | 1.48 (CI 95%: 0.78-2.79) | 10 (2) | 1.95 (CI 95%: 1.06-3.55) | 19 (2) | 1.7 (CI 95%: 0.94-2.45)  | 0.14 (0.71) |
| Unknown origin knee pain     | 8 (1)  | 1.32 (CI 95%: 0.67-2.58) | 8 (2)  | 1.56 (CI 95%: 0.79-3.05) | 16 (1) | 1.43 (CI 95%: 0.73-2.12) | 0.01 (0.93) |
| Bones cancer pain            | 8 (1)  | 1.32 (CI 95%: 0.67-2.58) | 5 (1)  | 0.97 (CI 95%: 0.42-2.26) | 13 (1) | 1.16 (CI 95%: 0.53-1.79) | 0.06 (0.8)  |
| Psoriatic arthritis          | 8 (1)  | 1.32 (CI 95%: 0.67-2.58) | 4 (1)  | 0.78 (CI 95%: 0.3-1.99)  | 12 (1) | 1.07 (CI 95%: 0.47-1.67) | NA          |
| Scoliosis related pain       | 6 (1)  | 0.99 (CI 95%: 0.45-2.14) | 3 (1)  | 0.58 (CI 95%: 0.2-1.71)  | 9 (1)  | 0.8 (CI 95%: 0.28-1.33)  | NA          |
| Ankylosing spondylitis       | 5 (1)  | 0.82 (CI 95%: 0.35-1.91) | 6 (1)  | 1.17 (CI 95%: 0.54-2.53) | 11 (1) | 0.98 (CI 95%: 0.4-1.56)  | 0.08 (0.78) |
| Multi trauma related pain    | 5 (1)  | 0.82 (CI 95%: 0.35-1.91) | 4 (1)  | 0.78 (CI 95%: 0.3-1.99)  | 9 (1)  | 0.8 (CI 95%: 0.28-1.33)  | NA          |
| Hip replacement pain         | 5 (1)  | 0.82 (CI 95%: 0.35-1.91) | 1 (0)  | 0.19 (CI 95%: 0.03-1.1)  | 6 (1)  | 0.54 (CI 95%: 0.11-0.96) | NA          |
| Unknown origin hip pain      | 3 (0)  | 0.49 (CI 95%: 0.17-1.44) | 5 (1)  | 0.97 (CI 95%: 0.42-2.26) | 8 (1)  | 0.71 (CI 95%: 0.22-1.21) | NA          |

|                            |       |                          |       |                          |       |                           |    |
|----------------------------|-------|--------------------------|-------|--------------------------|-------|---------------------------|----|
| Post traumatic pain        | 4 (1) | 0.66 (CI 95%: 0.26-1.68) | 4 (1) | 0.78 (CI 95%: 0.3-1.99)  | 8 (1) | 0.71 (CI 95%: 0.22-1.21)  | NA |
| Unknown origin neck pain   | 4 (1) | 0.66 (CI 95%: 0.26-1.68) | 4 (1) | 0.78 (CI 95%: 0.3-1.99)  | 8 (1) | 0.71 (CI 95%: 0.22-1.21)  | NA |
| Knee replacement pain      | 3 (0) | 0.49 (CI 95%: 0.17-1.44) | 3 (1) | 0.58 (CI 95%: 0.2-1.71)  | 6 (1) | 0.54 (CI 95%: 0.11-0.96)  | NA |
| Pathologic fracture        | 3 (0) | 0.49 (CI 95%: 0.17-1.44) | 2 (0) | 0.39 (CI 95%: 0.11-1.41) | 5 (0) | 0.45 (CI 95%: 0.06-0.84)  | NA |
| Kyphosis related pain      | 3 (0) | 0.49 (CI 95%: 0.17-1.44) | 1 (0) | 0.19 (CI 95%: 0.03-1.1)  | 4 (0) | 0.36 (CI 95%: 0.01-0.71)  | NA |
| Unknown origin Pelvic pain | 3 (0) | 0.49 (CI 95%: 0.17-1.44) | 0 (0) | 0 (CI 95%: 0-0.74)       | 3 (0) | 0.27 (CI 95%: -0.03-0.57) | NA |
| Osteomyelitis              | 2 (0) | 0.33 (CI 95%: 0.09-1.19) | 0 (0) | 0 (CI 95%: 0-0.74)       | 2 (0) | 0.18 (CI 95%: -0.07-0.43) | NA |
| Unknown origin joint pain  | 1 (0) | 0.16 (CI 95%: 0.03-0.93) | 7 (1) | 1.36 (CI 95%: 0.66-2.79) | 8 (1) | 0.71 (CI 95%: 0.22-1.21)  | NA |
| Parkinson related pain     | 1 (0) | 0.16 (CI 95%: 0.03-0.93) | 2 (0) | 0.39 (CI 95%: 0.11-1.41) | 3 (0) | 0.27 (CI 95%: -0.03-0.57) | NA |
| Unknown origin legs pain   | 1 (0) | 0.16 (CI 95%: 0.03-0.93) | 2 (0) | 0.39 (CI 95%: 0.11-1.41) | 3 (0) | 0.27 (CI 95%: -0.03-0.57) | NA |
| FMF arthritis              | 1 (0) | 0.16 (CI 95%: 0.03-0.93) | 0 (0) | 0 (CI 95%: 0-0.74)       | 1 (0) | 0.09 (CI 95%: -0.09-0.26) | NA |

|                             |          |                             |        |                          |          |                             |                 |
|-----------------------------|----------|-----------------------------|--------|--------------------------|----------|-----------------------------|-----------------|
| Gout                        | 0 (0)    | 0 (CI 95%: 0-0.63)          | 5 (1)  | 0.97 (CI 95%: 0.42-2.26) | 5 (0)    | 0.45 (CI 95%: 0.06-0.84)    | NA              |
| <b>Nociplastic pain</b>     | 131 (22) | 21.58 (CI 95%: 18.49-25.03) | 29 (6) | 5.65 (CI 95%: 3.96-8)    | 160 (14) | 14.29 (CI 95%: 12.24-16.34) | 56.315 (<0.001) |
| Fibromyalgia                | 130 (21) | 21.42 (CI 95%: 18.34-24.85) | 28 (5) | 5.46 (CI 95%: 3.8-7.78)  | 158 (14) | 14.11 (CI 95%: 12.07-16.15) | 57.1 (<0.001)   |
| <b>Visceral pain</b>        | 76 (13)  | 12.52 (CI 95%: 10.12-15.39) | 8 (2)  | 1.56 (CI 95%: 0.79-3.05) | 84 (8)   | 7.5 (CI 95%: 5.96-9.04)     | 46.583 (<0.001) |
| Endometriosis               | 56 (9)   | 9.23 (CI 95%: 7.17-11.79)   | NA     | NA                       | 56 (5)   | 5 (CI 95%: 3.72-6.28)       | NA              |
| Adenomyosis                 | 5 (1)    | 0.82 (CI 95%: 0.35-1.91)    | 0 (0)  | 0 (CI 95%: 0-0.74)       | 5 (0)    | 0.45 (CI 95%: 0.06-0.84)    | NA              |
| Interstitial cystitis       | 3 (0)    | 0.49 (CI 95%: 0.17-1.44)    | 0 (0)  | 0 (CI 95%: 0-0.74)       | 3 (0)    | 0.27 (CI 95%: 0-0.57)       | NA              |
| Post abdominal surgery pain | 2 (0)    | 0.33 (CI 95%: 0.09-1.19)    | 1 (0)  | 0.19 (CI 95%: 0.03-1.1)  | 3 (0)    | 0.27 (CI 95%: 0-0.57)       | NA              |
| Ascites related pain        | 2 (0)    | 0.33 (CI 95%: 0.09-1.19)    | 0 (0)  | 0 (CI 95%: 0-0.74)       | 2 (0)    | 0.18 (CI 95%: 0-0.43)       | NA              |
| Perianal pain               | 1 (0)    | 0.16 (CI 95%: 0.03-0.93)    | 2 (0)  | 0.39 (CI 95%: 0.11-1.41) | 3 (0)    | 0.27 (CI 95%: 0-0.57)       | NA              |
| IBD related abdominal pain  | 1 (0)    | 0.16 (CI 95%: 0.03-0.93)    | 1 (0)  | 0.19 (CI 95%: 0.03-1.1)  | 2 (0)    | 0.18 (CI 95%: 0-0.43)       | NA              |

|                               |        |                          |        |                          |        |                          |               |
|-------------------------------|--------|--------------------------|--------|--------------------------|--------|--------------------------|---------------|
| Achalasia                     | 1 (0)  | 0.16 (CI 95%: 0.03-0.93) | 0 (0)  | 0 (CI 95%: 0-0.74)       | 1 (0)  | 0.09 (CI 95%: 0-0.26)    | NA            |
| Anal pain                     | 1 (0)  | 0.16 (CI 95%: 0.03-0.93) | 0 (0)  | 0 (CI 95%: 0-0.74)       | 1 (0)  | 0.09 (CI 95%: 0-0.26)    | NA            |
| Cancer related abdominal pain | 1 (0)  | 0.16 (CI 95%: 0.03-0.93) | 0 (0)  | 0 (CI 95%: 0-0.74)       | 1 (0)  | 0.09 (CI 95%: 0-0.26)    | NA            |
| <b>Headaches</b>              | 45 (7) | 7.41 (CI 95%: 5.59-9.78) | 22 (4) | 4.29 (CI 95%: 2.85-6.41) | 67 (6) | 5.98 (CI 95%: 4.59-7.37) | 4.29 (0.04)   |
| Migraine                      | 22 (4) | 3.62 (CI 95%: 2.41-5.43) | 3 (1)  | 0.58 (CI 95%: 0.2-1.71)  | 25 (2) | 2.23 (CI 95%: 1.37-3.1)  | 10.4 (<0.001) |
| Other                         | 7 (1)  | 1.15 (CI 95%: 0.56-2.36) | 3 (1)  | 0.58 (CI 95%: 0.2-1.71)  | 10 (1) | 0.89 (CI 95%: 0.34-1.44) | 0.47 (0.49)   |
| Post-surgical headache        | 3 (0)  | 0.49 (CI 95%: 0.17-1.44) | 3 (1)  | 0.58 (CI 95%: 0.2-1.71)  | 6 (1)  | 0.54 (CI 95%: 0.11-0.96) | NA            |
| Hemangioma related headache   | 3 (0)  | 0.49 (CI 95%: 0.17-1.44) | 1 (0)  | 0.19 (CI 95%: 0.03-1.1)  | 4 (0)  | 0.36 (CI 95%: 0.01-0.71) | NA            |
| Cervicogenic headache         | 2 (0)  | 0.33 (CI 95%: 0.09-1.19) | 3 (1)  | 0.58 (CI 95%: 0.2-1.71)  | 5 (0)  | 0.45 (CI 95%: 0.06-0.84) | NA            |
| Post-concussion headache      | 1 (0)  | 0.16 (CI 95%: 0.03-0.93) | 4 (1)  | 0.78 (CI 95%: 0.3-1.99)  | 5 (0)  | 0.45 (CI 95%: 0.06-0.84) | NA            |
| Tension headache              | 1 (0)  | 0.16 (CI 95%: 0.03-0.93) | 3 (1)  | 0.58 (CI 95%: 0.2-1.71)  | 4 (0)  | 0.36 (CI 95%: 0.01-0.71) | NA            |

|                      |        |                          |        |                           |        |                          |             |
|----------------------|--------|--------------------------|--------|---------------------------|--------|--------------------------|-------------|
| Trigeminal neuralgia | 1 (0)  | 0.16 (CI 95%: 0.03-0.93) | 1 (0)  | 0.19 (CI 95%: 0.03-1.1)   | 2 (0)  | 0.18 (CI 95%: 0-0.43)    | NA          |
| Cluster headache     | 1 (0)  | 0.16 (CI 95%: 0.03-0.93) | 0 (0)  | 0 (CI 95%: 0-0.74)        | 1 (0)  | 0.09 (CI 95%: 0-0.26)    | NA          |
| <b>Oncology</b>      | 43 (7) | 7.08 (CI 95%: 5.3-9.41)  | 47 (9) | 9.16 (CI 95%: 6.96-11.97) | 90 (8) | 8.04 (CI 95%: 6.44-9.63) | 1.36 (0.24) |
| Breast               | 10 (2) | 1.65 (CI 95%: 0.9-3.01)  | 1 (0)  | 0.19 (CI 95%: 0.03-1.1)   | 11 (1) | 0.98 (CI 95%: 0.4-1.56)  | NA          |
| Other                | 8 (1)  | 1.32 (CI 95%: 0.67-2.58) | 4 (1)  | 0.78 (CI 95%: 0.3-1.99)   | 12 (1) | 1.07 (CI 95%: 0.47-1.67) | NA          |
| Pancreas             | 3 (0)  | 0.49 (CI 95%: 0.17-1.44) | 8 (2)  | 1.56 (CI 95%: 0.79-3.05)  | 11 (1) | 0.98 (CI 95%: 0.4-1.56)  | NA          |
| Colon                | 3 (0)  | 0.49 (CI 95%: 0.17-1.44) | 5 (1)  | 0.97 (CI 95%: 0.42-2.26)  | 8 (1)  | 0.71 (CI 95%: 0.22-1.21) | NA          |
| Multiple myeloma     | 3 (0)  | 0.49 (CI 95%: 0.17-1.44) | 4 (1)  | 0.78 (CI 95%: 0.3-1.99)   | 7 (1)  | 0.62 (CI 95%: 0.16-1.09) | NA          |
| Lungs                | 4 (1)  | 0.66 (CI 95%: 0.26-1.68) | 3 (1)  | 0.58 (CI 95%: 0.2-1.71)   | 7 (1)  | 0.62 (CI 95%: 0.16-1.09) | NA          |
| Endometrium          | 4 (1)  | 0.66 (CI 95%: 0.26-1.68) | NA     | NA                        | 4 (0)  | 0.36 (CI 95%: 0.01-0.71) | NA          |
| Leukemia             | 2 (0)  | 0.33 (CI 95%: 0.09-1.19) | 2 (0)  | 0.39 (CI 95%: 0.11-1.41)  | 4 (0)  | 0.36 (CI 95%: 0.01-0.71) | NA          |

|                                    |        |                          |        |                          |        |                          |             |
|------------------------------------|--------|--------------------------|--------|--------------------------|--------|--------------------------|-------------|
| Lymphoma                           | 2 (0)  | 0.33 (CI 95%: 0.09-1.19) | 2 (0)  | 0.39 (CI 95%: 0.11-1.41) | 4 (0)  | 0.36 (CI 95%: 0.01-0.71) | NA          |
| Bladder                            | 1 (0)  | 0.16 (CI 95%: 0.03-0.93) | 2 (0)  | 0.39 (CI 95%: 0.11-1.41) | 3 (0)  | 0.27 (CI 95%: 0-0.57)    | NA          |
| Kidney                             | 1 (0)  | 0.16 (CI 95%: 0.03-0.93) | 2 (0)  | 0.39 (CI 95%: 0.11-1.41) | 3 (0)  | 0.27 (CI 95%: 0-0.57)    | NA          |
| Skin                               | 1 (0)  | 0.16 (CI 95%: 0.03-0.93) | 0 (0)  | 0 (CI 95%: 0-0.74)       | 1 (0)  | 0.09 (CI 95%: 0-0.26)    | NA          |
| Stomach                            | 1 (0)  | 0.16 (CI 95%: 0.03-0.93) | 0 (0)  | 0 (CI 95%: 0-0.74)       | 1 (0)  | 0.09 (CI 95%: 0-0.26)    | NA          |
| Liver                              | 0 (0)  | 0 (CI 95%: 0-0.63)       | 1 (0)  | 0.19 (CI 95%: 0.03-1.1)  | 1 (0)  | 0.09 (CI 95%: 0-0.26)    | NA          |
| Mouth and neck                     | 0 (0)  | 0 (CI 95%: 0-0.63)       | 1 (0)  | 0.19 (CI 95%: 0.03-1.1)  | 1 (0)  | 0.09 (CI 95%: 0-0.26)    | NA          |
| Thyroid                            | 0 (0)  | 0 (CI 95%: 0-0.63)       | 1 (0)  | 0.19 (CI 95%: 0.03-1.1)  | 1 (0)  | 0.09 (CI 95%: 0-0.26)    | NA          |
| Prostate                           | NA     | NA                       | 11 (2) | 2.14 (CI 95%: 1.2-3.8)   | 11 (1) | 0.98 (CI 95%: 0.4-1.56)  | NA          |
| <b>inflammatory bowel diseases</b> | 27 (4) | 4.45 (CI 95%: 3.07-6.39) | 10 (2) | 1.95 (CI 95%: 1.06-3.55) | 37 (3) | 3.3 (CI 95%: 2.26-4.35)  | 4.68 (0.03) |
| Crohn's Disease                    | 16 (3) | 2.64 (CI 95%: 1.63-4.24) | 7 (1)  | 1.36 (CI 95%: 0.66-2.79) | 23 (2) | 2.05 (CI 95%: 1.22-2.88) | 1.65 (0.2)  |



|                    |        |                          |        |                          |        |                          |             |
|--------------------|--------|--------------------------|--------|--------------------------|--------|--------------------------|-------------|
| IBS                | 6 (1)  | 0.99 (CI 95%: 0.45-2.14) | 1 (0)  | 0.19 (CI 95%: 0.03-1.1)  | 7 (1)  | 0.62 (CI 95%: 0.16-1.09) | NA          |
| Ulcerative Colitis | 5 (1)  | 0.82 (CI 95%: 0.35-1.91) | 2 (0)  | 0.39 (CI 95%: 0.11-1.41) | 7 (1)  | 0.62 (CI 95%: 0.16-1.09) | NA          |
| Colon prolapse     | 1 (0)  | 0.16 (CI 95%: 0.03-0.93) | 0 (0)  | 0 (CI 95%: 0-0.74)       | 1 (0)  | 0.09 (CI 95%: 0-0.26)    | NA          |
| Reflux             | 1 (0)  | 0.16 (CI 95%: 0.03-0.93) | 0 (0)  | 0 (CI 95%: 0-0.74)       | 1 (0)  | 0.09 (CI 95%: 0-0.26)    | NA          |
| <b>Neurology</b>   | 39 (6) | 6.43 (CI 95%: 4.74-8.66) | 34 (7) | 6.63 (CI 95%: 4.78-9.12) | 73 (7) | 6.52 (CI 95%: 5.07-7.96) | 0 (0.99)    |
| MS                 | 26 (4) | 4.28 (CI 95%: 2.94-6.2)  | 12 (2) | 2.34 (CI 95%: 1.34-4.04) | 38 (3) | 3.39 (CI 95%: 2.33-4.45) | 2.64 (0.1)  |
| Parkinson disease  | 24 (4) | 3.95 (CI 95%: 2.67-5.82) | 15 (3) | 2.92 (CI 95%: 1.78-4.77) | 39 (3) | 3.48 (CI 95%: 2.41-4.56) | 0.6 (0.44)  |
| Other              | 5 (1)  | 0.82 (CI 95%: 0.35-1.91) | 11 (2) | 2.14 (CI 95%: 1.2-3.8)   | 16 (1) | 1.43 (CI 95%: 0.73-2.12) | 2.57 (0.11) |
| Epilepsy           | 3 (0)  | 0.49 (CI 95%: 0.17-1.44) | 2 (0)  | 0.39 (CI 95%: 0.11-1.41) | 5 (0)  | 0.45 (CI 95%: 0.06-0.84) | NA          |
| Essential tremor   | 4 (1)  | 0.66 (CI 95%: 0.26-1.68) | 0 (0)  | 0 (CI 95%: 0-0.74)       | 4 (0)  | 0.36 (CI 95%: 0.01-0.71) | NA          |
| Dementia           | 1 (0)  | 0.16 (CI 95%: 0.03-0.93) | 2 (0)  | 0.39 (CI 95%: 0.11-1.41) | 3 (0)  | 0.27 (CI 95%: 0-0.57)    | NA          |

|                                       |       |                          |        |                          |        |                          |               |
|---------------------------------------|-------|--------------------------|--------|--------------------------|--------|--------------------------|---------------|
| Neurofibromatosis                     | 1 (0) | 0.16 (CI 95%: 0.03-0.93) | 2 (0)  | 0.39 (CI 95%: 0.11-1.41) | 3 (0)  | 0.27 (CI 95%: 0-0.57)    | NA            |
| Tourette syndrome                     | 1 (0) | 0.16 (CI 95%: 0.03-0.93) | 3 (1)  | 0.58 (CI 95%: 0.2-1.71)  | 4 (0)  | 0.36 (CI 95%: 0.01-0.71) | NA            |
| Post CVA spasticity                   | 1 (0) | 0.16 (CI 95%: 0.03-0.93) | 1 (0)  | 0.19 (CI 95%: 0.03-1.1)  | 2 (0)  | 0.18 (CI 95%: 0-0.43)    | NA            |
| ALS                                   | 1 (0) | 0.16 (CI 95%: 0.03-0.93) | 0 (0)  | 0 (CI 95%: 0-0.74)       | 1 (0)  | 0.09 (CI 95%: 0-0.26)    | NA            |
| <b>Post-traumatic stress disorder</b> | 5 (1) | 0.82 (CI 95%: 0.35-1.91) | 31 (6) | 6.04 (CI 95%: 4.29-8.45) | 36 (3) | 3.21 (CI 95%: 2.18-4.25) | 22.7 (<0.001) |
| <b>Palliative conditions</b>          | 7 (1) | 1.15 (CI 95%: 0.56-2.36) | 8 (2)  | 1.56 (CI 95%: 0.79-3.05) | 15 (1) | 1.34 (CI 95%: 0.67-2.01) | 0.11 (0.74)   |

ALS, amyotrophic lateral sclerosis; CVA, cerebrovascular accident; FMF, familial Mediterranean fever; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; MS, multiple sclerosis; NA, not applicable; Numbers does not add up to 100% due to concomitant diagnoses.

**Table S5: Specific comorbidities diagnoses**

| <b>Disease</b>                               | <b>Women<br/>n=607<br/>N (%)</b> | <b>Women<br/>proportion<br/>(CI 95%)</b> | <b>Men<br/>n=513<br/>N (%)</b> | <b>Men<br/>proportional<br/>(CI 95%)</b> | <b>Overall sample<br/>N=1120<br/>N (%)</b> | <b>Overall<br/>proportion<br/>(CI 95%)</b> | <b>Wilson's <math>X^2</math><br/>test<br/>(p-value)</b> |
|--|----------------------------------|--|--------------------------------|--|--|--|---|
| <b>Comorbidity<br/>diagnoses at baseline</b> |                                  |  |                                |  |  |  |   |
| Yes  | 435 (72)                         | 71.66 (CI<br>95%:67.95 -<br>75.1)        | 358 (70)                       | 69.79 (CI<br>95%:65.68 -<br>73.6)        | 793 (71)                                   | 70.8 (CI<br>95%:68.07 -<br>73.39)          | 0.39 (0.53)   |
| No   | 159 (26)                         | 26.19 (CI<br>95%:22.85 -<br>29.83)       | 147 (29)                       | 28.65 (CI<br>95%:24.91 -<br>32.71)       | 306 (27)                                   | 27.32 (CI<br>95%:24.79 -<br>30.01)         | 0.73 (0.39)   |
| <b>Specific diagnoses</b>                    |                                  |  |                                |  |  |  |   |
| HTN  | 232 (38)                         | 38.22 (CI<br>95%: 34.44 -<br>42.15)      | 209 (41)                       | 40.74 (CI<br>95%: 36.57 -<br>45.05)      | 441 (39)                                   | 39.38 (CI<br>95%: 36.55 -<br>42.27)        | 0.64 (0.42)   |
| Diabetes                                     | 97 (16)                          | 15.98 (CI<br>95%: 13.28 -<br>19.11)      | 128 (25)                       | 24.95 (CI<br>95%: 21.4 -<br>28.87)       | 225 (20)                                   | 20.09 (CI<br>95%: 17.84 -<br>22.54)        | 13.4 (<0.001)   |
| Psychiatric                                  | 91 (15)                          | 14.99 (CI<br>95%: 12.37 -<br>18.05)      | 56 (11)                        | 10.92 (CI<br>95%: 8.5 -<br>13.91)        | 147 (13)                                   | 13.13 (CI<br>95%: 11.27 -<br>15.23)        | 3.7 (0.05)  |
| Hypothyroidism                               | 73 (12)                          | 12.03 (CI<br>95%: 9.67 -<br>14.86)       | 26 (5)                         | 5.07 (CI 95%:<br>3.48 -7.32)             | 99 (9)                                     | 8.84 (CI 95%:<br>7.31 -10.65)              | 15.9 (<0.001)   |
| Hyperlipidemia                               | 72 (12)                          | 11.86 (CI<br>95%: 9.53 -<br>14.68)       | 95 (19)                        | 18.52 (CI<br>95%: 15.4 -<br>22.11)       | 167 (15)                                   | 14.91 (CI<br>95%: 12.94 -<br>17.12)        | 9.19 (<0.005)   |

|                 |        |                                  |         |                                    |          |                                 |               |
|-----------------|--------|----------------------------------|---------|------------------------------------|----------|---------------------------------|---------------|
| Respiratory     | 56 (9) | 9.23 (CI 95%:<br>7.17 -11.79)    | 33 (6)  | 6.43 (CI 95%:<br>4.62 -8.9)        | 89 (8)   | 7.95 (CI 95%:<br>6.5 -9.68)     | 2.6 (0.11)    |
| Depression      | 55 (9) | 9.06 (CI<br>95%:7.03 -<br>11.61) | 28 (5)  | 5.46 (CI<br>95%:3.8 -7.78)         | 83 (7)   | 7.41 (CI<br>95%:6.01 -<br>9.1)  | 4.75 (0.03)   |
| Cardiac disease | 50 (8) | 8.24 (CI 95%:<br>6.3 -10.7)      | 71 (14) | 13.84 (CI<br>95%: 11.12 -<br>17.1) | 121 (11) | 10.8 (CI 95%:<br>9.11 -12.76)   | 8.49 (<0.005) |
| Osteoporosis    | 41 (7) | 6.75 (CI 95%:<br>5.02 -9.04)     | 9 (2)   | 1.75 (CI 95%:<br>0.93 -3.3)        | 50 (4)   | 4.46 (CI 95%:<br>3.39 -5.85)    | 15.1 (<0.001) |
| Asthma          | 33 (5) | 5.44(CI<br>95%:3.9 -<br>7.54)    | 11 (2)  | 2.14(CI<br>95%:1.2 -3.8)           | 44 (4)   | 3.93(CI<br>95%:2.93 -<br>5.24)  | 7.14(<0.01)   |
| Anxiety         | 27 (4) | 4.45 (CI<br>95%:3.07 -<br>6.39)  | 13 (3)  | 2.53 (CI<br>95%:1.49 -<br>4.29)    | 40 (4)   | 3.57 (CI<br>95%:2.62 -<br>4.84) | 2.43 (0.12)   |
| IHD             | 11 (2) | 1.81(CI<br>95%:1.01 -<br>3.22)   | 28 (5)  | 5.46(CI<br>95%:3.8 -7.78)          | 39 (3)   | 3.48(CI<br>95%:2.55 -<br>4.74)  | 9.94(<0.005)  |
| AF              | 9 (1)  | 1.48(CI<br>95%:0.78 -<br>2.79)   | 8 (2)   | 1.56(CI<br>95%:0.79 -<br>3.05)     | 17 (2)   | 1.52(CI<br>95%:0.93 -<br>2.44)  | 0(1)          |
| CRF             | 8 (1)  | 1.32 (CI 95%:<br>0.67 -2.58)     | 9 (2)   | 1.75 (CI 95%:<br>0.93 -3.3)        | 17 (2)   | 1.52 (CI 95%:<br>0.93 -2.44)    | 0.12 (0.73)   |
| ADHD            | 7 (1)  | 1.15 (CI 95%:<br>0.56 -2.36)     | 8 (2)   | 1.56 (CI 95%:<br>0.79 -3.05)       | 15 (1)   | 1.34 (CI 95%:<br>0.79 -2.22)    | 0.11 (0.74)   |
| COPD            | 7 (1)  | 1.15(CI<br>95%:0.56 -<br>2.36)   | 6 (1)   | 1.17(CI<br>95%:0.54 -<br>2.53)     | 13 (1)   | 1.16(CI<br>95%:0.66 -2)         | 0(1)          |

|                            |       |                                |       |                                |        |                                |       |
|----------------------------|-------|--------------------------------|-------|--------------------------------|--------|--------------------------------|-------|
| S/P CVA                    | 6 (1) | 0.99 (CI 95%:<br>0.45 -2.14)   | 6 (1) | 1.17 (CI 95%:<br>0.54 -2.53)   | 12 (1) | 1.07 (CI 95%:<br>0.59 -1.89)   | 0 (1) |
| Anemia                     | 6 (1) | 0.99 (CI 95%:<br>0.45 -2.14)   | 3 (1) | 0.58 (CI 95%:<br>0.2 -1.71)    | 9 (1)  | 0.8 (CI 95%:<br>0.4 -1.55)     | NA    |
| Sarcoidosis                | 6 (1) | 0.99(CI<br>95%:0.45 -<br>2.14) | 2 (0) | 0.39(CI<br>95%:0.11 -<br>1.41) | 8 (1)  | 0.71(CI<br>95%:0.34 -<br>1.43) | NA    |
| Glaucoma                   | 5 (1) | 0.82 (CI 95%:<br>0.35 -1.91)   | 4 (1) | 0.78 (CI 95%:<br>0.3 -1.99)    | 9 (1)  | 0.8 (CI 95%:<br>0.4 -1.55)     | NA    |
| Urine incontineneces       | 5 (1) | 0.82 (CI 95%:<br>0.35 -1.91)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74)        | 5 (0)  | 0.45 (CI 95%:<br>0.16 -1.07)   | NA    |
| Arrhythmia                 | 4 (1) | 0.66(CI<br>95%:0.26 -<br>1.68) | 6 (1) | 1.17(CI<br>95%:0.54 -<br>2.53) | 10 (1) | 0.89(CI<br>95%:0.46 -<br>1.66) | NA    |
| Thrombophilia              | 3 (0) | 0.49 (CI 95%:<br>0.17 -1.44)   | 4 (1) | 0.78 (CI 95%:<br>0.3 -1.99)    | 7 (1)  | 0.63 (CI 95%:<br>0.27 -1.31)   | NA    |
| Cardiac pacemaker          | 3 (0) | 0.49(CI<br>95%:0.17 -<br>1.44) | 2 (0) | 0.39(CI<br>95%:0.11 -<br>1.41) | 5 (0)  | 0.45(CI<br>95%:0.16 -<br>1.07) | NA    |
| Hashimoto's<br>thyroiditis | 4 (1) | 0.66 (CI 95%:<br>0.26 -1.68)   | 1 (0) | 0.19 (CI 95%:<br>0.03 -1.1)    | 5 (0)  | 0.45 (CI 95%:<br>0.16 -1.07)   | NA    |
| Reflux                     | 4 (1) | 0.66 (CI 95%:<br>0.26 -1.68)   | 1 (0) | 0.19 (CI 95%:<br>0.03 -1.1)    | 5 (0)  | 0.45 (CI 95%:<br>0.16 -1.07)   | NA    |
| Overactive bladder         | 3 (0) | 0.49 (CI 95%:<br>0.17 -1.44)   | 1 (0) | 0.19 (CI 95%:<br>0.03 -1.1)    | 4 (0)  | 0.36 (CI 95%:<br>0.1 -0.95)    | NA    |
| DVT                        | 4 (1) | 0.66 (CI 95%:<br>0.26 -1.68)   | 1 (0) | 0.19 (CI 95%:<br>0.03 -1.1)    | 5 (0)  | 0.45 (CI 95%:<br>0.16 -1.07)   | NA    |
| Cataract                   | 3 (0) | 0.49 (CI 95%:<br>0.17 -1.44)   | 1 (0) | 0.19 (CI 95%:<br>0.03 -1.1)    | 4 (0)  | 0.36 (CI 95%:<br>0.1 -0.95)    | NA    |

|                               |       |                                |       |                                |       |                                |    |
|-------------------------------|-------|--------------------------------|-------|--------------------------------|-------|--------------------------------|----|
| Diaphragmatic hernia          | 3 (0) | 0.49 (CI 95%:<br>0.17 -1.44)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74)        | 3 (0) | 0.27 (CI 95%:<br>0.05 -0.82)   | NA |
| S/P breast cancer             | 3 (0) | 0.49 (CI 95%:<br>0.17 -1.44)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74)        | 3 (0) | 0.27 (CI 95%:<br>0.05 -0.82)   | NA |
| Spinal stenosis               | 3 (0) | 0.49 (CI 95%:<br>0.17 -1.44)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74)        | 3 (0) | 0.27 (CI 95%:<br>0.05 -0.82)   | NA |
| Scoliosis                     | 3 (0) | 0.49 (CI 95%:<br>0.17 -1.44)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74)        | 3 (0) | 0.27 (CI 95%:<br>0.05 -0.82)   | NA |
| Mitral valve<br>insufficiency | 3 (0) | 0.49(CI<br>95%:0.17 -<br>1.44) | 0 (0) | 0(CI 95%:0 -<br>0.74)          | 3 (0) | 0.27(CI<br>95%:0.05 -<br>0.82) | NA |
| Aortic stenosis               | 3 (0) | 0.49(CI<br>95%:0.17 -<br>1.44) | 0 (0) | 0(CI 95%:0 -<br>0.74)          | 3 (0) | 0.27(CI<br>95%:0.05 -<br>0.82) | NA |
| CHF                           | 2 (0) | 0.33(CI<br>95%:0.09 -<br>1.19) | 5 (1) | 0.97(CI<br>95%:0.42 -<br>2.26) | 7 (1) | 0.63(CI<br>95%:0.27 -<br>1.31) | NA |
| PVD                           | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)   | 2 (0) | 0.39 (CI 95%:<br>0.11 -1.41)   | 4 (0) | 0.36 (CI 95%:<br>0.1 -0.95)    | NA |
| Gastritis                     | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)   | 3 (1) | 0.58 (CI 95%:<br>0.2 -1.71)    | 5 (0) | 0.45 (CI 95%:<br>0.16 -1.07)   | NA |
| Sarcoidosis                   | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)   | 2 (0) | 0.39 (CI 95%:<br>0.11 -1.41)   | 4 (0) | 0.36 (CI 95%:<br>0.1 -0.95)    | NA |
| Pulmonary<br>hypertension     | 2 (0) | 0.33(CI<br>95%:0.09 -<br>1.19) | 2 (0) | 0.39(CI<br>95%:0.11 -<br>1.41) | 4 (0) | 0.36(CI<br>95%:0.1 -<br>0.95)  | NA |
| Hypokalemia                   | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)   | 1 (0) | 0.19 (CI 95%:<br>0.03 -1.1)    | 3 (0) | 0.27 (CI 95%:<br>0.05 -0.82)   | NA |

|                                  |       |                                 |       |                             |       |                                 |    |
|----------------------------------|-------|---------------------------------|-------|-----------------------------|-------|---------------------------------|----|
| FMF                              | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)    | 1 (0) | 0.19 (CI 95%:<br>0.03 -1.1) | 3 (0) | 0.27 (CI 95%:<br>0.05 -0.82)    | NA |
| Psoriasis                        | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)    | 1 (0) | 0.19 (CI 95%:<br>0.03 -1.1) | 3 (0) | 0.27 (CI 95%:<br>0.05 -0.82)    | NA |
| HCV                              | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)    | 1 (0) | 0.19 (CI 95%:<br>0.03 -1.1) | 3 (0) | 0.27 (CI 95%:<br>0.05 -0.82)    | NA |
| Aortic valve<br>replacement      | 2 (0) | 0.33(CI<br>95%:0.09 -<br>1.19)  | 1 (0) | 0.19(CI<br>95%:0.03 -1.1)   | 3 (0) | 0.27(CI<br>95%:0.05 -<br>0.82)  | NA |
| PE                               | 2 (0) | 0.33(CI<br>95%:0.09 -<br>1.19)  | 1 (0) | 0.19(CI<br>95%:0.03 -1.1)   | 3 (0) | 0.27(CI<br>95%:0.05 -<br>0.82)  | NA |
| Bipolar disorder                 | 2 (0) | 0.33 (CI<br>95%:0.09 -<br>1.19) | 1 (0) | 0.19 (CI<br>95%:0.03 -1.1)  | 3 (0) | 0.27 (CI<br>95%:0.05 -<br>0.82) | NA |
| Amyloidosis                      | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)    | 0 (0) | 0 (CI 95%: 0 -<br>0.74)     | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)       | NA |
| Anal fissure                     | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)    | 0 (0) | 0 (CI 95%: 0 -<br>0.74)     | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)       | NA |
| Fatty liver                      | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)    | 0 (0) | 0 (CI 95%: 0 -<br>0.74)     | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)       | NA |
| Retinal detachment               | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)    | 0 (0) | 0 (CI 95%: 0 -<br>0.74)     | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)       | NA |
| Esophageal reflux                | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)    | 0 (0) | 0 (CI 95%: 0 -<br>0.74)     | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)       | NA |
| Vertigo                          | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)    | 0 (0) | 0 (CI 95%: 0 -<br>0.74)     | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)       | NA |
| S/P breast cancer-<br>lumpectomy | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)    | 0 (0) | 0 (CI 95%: 0 -<br>0.74)     | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)       | NA |

|                           |       |                                |       |                                |       |                                |    |
|---------------------------|-------|--------------------------------|-------|--------------------------------|-------|--------------------------------|----|
| Thrombocytopenia          | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74)        | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)      | NA |
| Celiac                    | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74)        | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)      | NA |
| Menopause symptoms        | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74)        | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)      | NA |
| Ehlers-Danlos<br>syndrome | 2 (0) | 0.33 (CI 95%:<br>0.09 -1.19)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74)        | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)      | NA |
| S/P SVT Post ablation     | 2 (0) | 0.33(CI<br>95%:0.09 -<br>1.19) | 0 (0) | 0(CI 95%:0 -<br>0.74)          | 2 (0) | 0.18(CI<br>95%:0 -0.69)        | NA |
| Chronic bronchitis        | 2 (0) | 0.33(CI<br>95%:0.09 -<br>1.19) | 0 (0) | 0(CI 95%:0 -<br>0.74)          | 2 (0) | 0.18(CI<br>95%:0 -0.69)        | NA |
| S/P MI                    | 1 (0) | 0.16(CI<br>95%:0.03 -<br>0.93) | 7 (1) | 1.36(CI<br>95%:0.66 -<br>2.79) | 8 (1) | 0.71(CI<br>95%:0.34 -<br>1.43) | NA |
| S/P PTCA                  | 1 (0) | 0.16(CI<br>95%:0.03 -<br>0.93) | 5 (1) | 0.97(CI<br>95%:0.42 -<br>2.26) | 6 (1) | 0.54(CI<br>95%:0.22 -<br>1.19) | NA |
| OSA                       | 2 (0) | 0.33(CI<br>95%:0.09 -<br>1.19) | 6 (1) | 1.17(CI<br>95%:0.54 -<br>2.53) | 8 (1) | 0.71(CI<br>95%:0.34 -<br>1.43) | NA |
| Dry eyes                  | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)   | 2 (0) | 0.39 (CI 95%:<br>0.11 -1.41)   | 3 (0) | 0.27 (CI 95%:<br>0.05 -0.82)   | NA |
| Dialysis                  | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)   | 2 (0) | 0.39 (CI 95%:<br>0.11 -1.41)   | 3 (0) | 0.27 (CI 95%:<br>0.05 -0.82)   | NA |
| Renal transplant          | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)   | 2 (0) | 0.39 (CI 95%:<br>0.11 -1.41)   | 3 (0) | 0.27 (CI 95%:<br>0.05 -0.82)   | NA |



|                                 |       |                                 |       |                                |       |                                |    |
|---------------------------------|-------|---------------------------------|-------|--------------------------------|-------|--------------------------------|----|
| Gout                            | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)    | 2 (0) | 0.39 (CI 95%:<br>0.11 -1.41)   | 3 (0) | 0.27 (CI 95%:<br>0.05 -0.82)   | NA |
| Osteopenia                      | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)    | 2 (0) | 0.39 (CI 95%:<br>0.11 -1.41)   | 3 (0) | 0.27 (CI 95%:<br>0.05 -0.82)   | NA |
| CHD                             | 1 (0) | 0.16(CI<br>95%:0.03 -<br>0.93)  | 2 (0) | 0.39(CI<br>95%:0.11 -<br>1.41) | 3 (0) | 0.27(CI<br>95%:0.05 -<br>0.82) | NA |
| Bowel syndrome                  | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)    | 1 (0) | 0.19 (CI 95%:<br>0.03 -1.1)    | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)      | NA |
| S/P spontaneous<br>pneumothorax | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)    | 1 (0) | 0.19 (CI 95%:<br>0.03 -1.1)    | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)      | NA |
| Obesity                         | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)    | 1 (0) | 0.19 (CI 95%:<br>0.03 -1.1)    | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)      | NA |
| Vasculitis                      | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)    | 1 (0) | 0.19 (CI 95%:<br>0.03 -1.1)    | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)      | NA |
| Tinnitus                        | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)    | 1 (0) | 0.19 (CI 95%:<br>0.03 -1.1)    | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)      | NA |
| Nephrolithiasis                 | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)    | 1 (0) | 0.19 (CI 95%:<br>0.03 -1.1)    | 2 (0) | 0.18 (CI 95%:<br>0 -0.69)      | NA |
| AV block                        | 1 (0) | 0.16(CI<br>95%:0.03 -<br>0.93)  | 1 (0) | 0.19(CI<br>95%:0.03 -1.1)      | 2 (0) | 0.18(CI<br>95%:0 -0.69)        | NA |
| Pulmonary fibrosis              | 1 (0) | 0.16(CI<br>95%:0.03 -<br>0.93)  | 1 (0) | 0.19(CI<br>95%:0.03 -1.1)      | 2 (0) | 0.18(CI<br>95%:0 -0.69)        | NA |
| Schizophrenia                   | 1 (0) | 0.16 (CI<br>95%:0.03 -<br>0.93) | 1 (0) | 0.19 (CI<br>95%:0.03 -1.1)     | 2 (0) | 0.18 (CI<br>95%:0 -0.69)       | NA |

|                      |       |                              |       |                         |       |                               |    |
|----------------------|-------|------------------------------|-------|-------------------------|-------|-------------------------------|----|
| Cholelithiasis       | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Hiatus hernia        | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| GERD                 | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Stomach polyp        | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Melanoma             | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Macular degeneration | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Lupus                | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Thalassemia minor    | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Gall bladder stones  | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Duodenal ulcer       | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Biliary Atresia      | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Goiter               | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Kyphosis             | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Benign tumor         | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |

|                                 |       |                              |       |                         |       |                               |    |
|---------------------------------|-------|------------------------------|-------|-------------------------|-------|-------------------------------|----|
| ITP                             | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Urticaria                       | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Polycystic ovaries<br>removal   | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| S/P colon and thyroid<br>cancer | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Diverticulitis                  | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Bladder problems                | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Hemodialysis                    | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Dwarfism                        | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Femoral-facial<br>syndrome      | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Chronic sinusitis               | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Ovarian cyst                    | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Post nasal drip                 | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Arachnoiditis                   | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Polio                           | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93) | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |

|                               |       |                                |       |                         |       |                               |    |
|-------------------------------|-------|--------------------------------|-------|-------------------------|-------|-------------------------------|----|
| Aphasia                       | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Polycythemia                  | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| APLA                          | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| White robe syndrome           | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Keratoconjunctivitis          | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Kidney stones                 | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Helicobacter Pylori           | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| BRCA2 carrier                 | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Narcolepsy                    | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Past sarcoma                  | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| S/P non-Hodgkin's<br>lymphoma | 1 (0) | 0.16 (CI 95%:<br>0.03 -0.93)   | 0 (0) | 0 (CI 95%: 0 -<br>0.74) | 1 (0) | 0.09 (CI 95%:<br>-0.04 -0.56) | NA |
| Valve replacement             | 1 (0) | 0.16(CI<br>95%:0.03 -<br>0.93) | 0 (0) | 0(CI 95%:0 -<br>0.74)   | 1 (0) | 0.09(CI 95%:-<br>0.04 -0.56)  | NA |
| Bradycardia                   | 1 (0) | 0.16(CI<br>95%:0.03 -<br>0.93) | 0 (0) | 0(CI 95%:0 -<br>0.74)   | 1 (0) | 0.09(CI 95%:-<br>0.04 -0.56)  | NA |

|                            |       |                           |        |                           |        |                            |    |
|----------------------------|-------|---------------------------|--------|---------------------------|--------|----------------------------|----|
| Blood circulation disorder | 1 (0) | 0.16(CI 95%:0.03 - 0.93)  | 0 (0)  | 0(CI 95%:0 - 0.74)        | 1 (0)  | 0.09(CI 95%:-0.04 -0.56)   | NA |
| S/P Myocarditis            | 1 (0) | 0.16(CI 95%:0.03 - 0.93)  | 0 (0)  | 0(CI 95%:0 - 0.74)        | 1 (0)  | 0.09(CI 95%:-0.04 -0.56)   | NA |
| POTS                       | 1 (0) | 0.16(CI 95%:0.03 - 0.93)  | 0 (0)  | 0(CI 95%:0 - 0.74)        | 1 (0)  | 0.09(CI 95%:-0.04 -0.56)   | NA |
| RT Carotid full block      | 1 (0) | 0.16(CI 95%:0.03 - 0.93)  | 0 (0)  | 0(CI 95%:0 - 0.74)        | 1 (0)  | 0.09(CI 95%:-0.04 -0.56)   | NA |
| Radiation treatment AE     | 1 (0) | 0.16(CI 95%:0.03 - 0.93)  | 0 (0)  | 0(CI 95%:0 - 0.74)        | 1 (0)  | 0.09(CI 95%:-0.04 -0.56)   | NA |
| Emphysema                  | 1 (0) | 0.16(CI 95%:0.03 - 0.93)  | 0 (0)  | 0(CI 95%:0 - 0.74)        | 1 (0)  | 0.09(CI 95%:-0.04 -0.56)   | NA |
| Lung GVHD                  | 1 (0) | 0.16(CI 95%:0.03 - 0.93)  | 0 (0)  | 0(CI 95%:0 - 0.74)        | 1 (0)  | 0.09(CI 95%:-0.04 -0.56)   | NA |
| Hypomania                  | 1 (0) | 0.16 (CI 95%:0.03 - 0.93) | 0 (0)  | 0 (CI 95%:0 - 0.74)       | 1 (0)  | 0.09 (CI 95%:-0.04 - 0.56) | NA |
| Addiction                  | 1 (0) | 0.16 (CI 95%:0.03 - 0.93) | 0 (0)  | 0 (CI 95%:0 - 0.74)       | 1 (0)  | 0.09 (CI 95%:-0.04 - 0.56) | NA |
| BPH                        | 0 (0) | 0 (CI 95%: 0 - 0.63)      | 37 (7) | 7.21 (CI 95%: 5.28 -9.78) | 37 (3) | 3.3 (CI 95%: 2.39 -4.53)   | NA |

|                     |       |                      |       |                           |       |                            |    |
|---------------------|-------|----------------------|-------|---------------------------|-------|----------------------------|----|
| Coronary stent      | 0 (0) | 0(CI 95%:0 - 0.63)   | 4 (1) | 0.78(CI 95%:0.3 -1.99)    | 4 (0) | 0.36(CI 95%:0.1 - 0.95)    | NA |
| Dry mouth           | 0 (0) | 0 (CI 95%: 0 - 0.63) | 2 (0) | 0.39 (CI 95%: 0.11 -1.41) | 2 (0) | 0.18 (CI 95%: 0 -0.69)     | NA |
| Cirrhosis           | 0 (0) | 0 (CI 95%: 0 - 0.63) | 2 (0) | 0.39 (CI 95%: 0.11 -1.41) | 2 (0) | 0.18 (CI 95%: 0 -0.69)     | NA |
| Hernia              | 0 (0) | 0 (CI 95%: 0 - 0.63) | 2 (0) | 0.39 (CI 95%: 0.11 -1.41) | 2 (0) | 0.18 (CI 95%: 0 -0.69)     | NA |
| Irritable bladder   | 0 (0) | 0 (CI 95%: 0 - 0.63) | 2 (0) | 0.39 (CI 95%: 0.11 -1.41) | 2 (0) | 0.18 (CI 95%: 0 -0.69)     | NA |
| Hyperparathyroidism | 0 (0) | 0 (CI 95%: 0 - 0.63) | 2 (0) | 0.39 (CI 95%: 0.11 -1.41) | 2 (0) | 0.18 (CI 95%: 0 -0.69)     | NA |
| Bypass surgery      | 0 (0) | 0(CI 95%:0 - 0.63)   | 3 (1) | 0.58(CI 95%:0.2 -1.71)    | 3 (0) | 0.27(CI 95%:0.05 - 0.82)   | NA |
| Cardiomyopathy      | 0 (0) | 0(CI 95%:0 - 0.63)   | 2 (0) | 0.39(CI 95%:0.11 - 1.41)  | 2 (0) | 0.18(CI 95%:0 -0.69)       | NA |
| OCD                 | 0 (0) | 0 (CI 95%:0 - 0.63)  | 3 (1) | 0.58 (CI 95%:0.2 -1.71)   | 3 (0) | 0.27 (CI 95%:0.05 - 0.82)  | NA |
| Parathyroidectomy   | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1)  | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| S/P Knee surgeries  | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1)  | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| S/P B cell lymphoma | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1)  | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |

|                                   |       |                      |       |                          |       |                            |    |
|-----------------------------------|-------|----------------------|-------|--------------------------|-------|----------------------------|----|
| S/P complicated bariatric surgery | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Churg-Strauss syndrome            | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Addison's disease                 | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Alzheimer's disease               | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Lobectomy                         | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Lung cancer                       | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Chronic prostatitis               | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Uveitis                           | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Drop foot                         | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| S/P Lymphoma                      | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Meniere's disease                 | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Astigmatism                       | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Infertility                       | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Splenomegaly                      | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |

|                        |       |                      |       |                          |       |                            |    |
|------------------------|-------|----------------------|-------|--------------------------|-------|----------------------------|----|
| Hypogonadism           | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Pre-dialysis           | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Hydronephrotic         | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Brain metastases       | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Gilbert's Syndrome     | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| Spinal fracture        | 0 (0) | 0 (CI 95%: 0 - 0.63) | 1 (0) | 0.19 (CI 95%: 0.03 -1.1) | 1 (0) | 0.09 (CI 95%: -0.04 -0.56) | NA |
| VF                     | 0 (0) | 0(CI 95%:0 - 0.63)   | 1 (0) | 0.19(CI 95%:0.03 -1.1)   | 1 (0) | 0.09(CI 95%:-0.04 -0.56)   | NA |
| Aortic dilatation      | 0 (0) | 0(CI 95%:0 - 0.63)   | 1 (0) | 0.19(CI 95%:0.03 -1.1)   | 1 (0) | 0.09(CI 95%:-0.04 -0.56)   | NA |
| Aortic regurgitation   | 0 (0) | 0(CI 95%:0 - 0.63)   | 1 (0) | 0.19(CI 95%:0.03 -1.1)   | 1 (0) | 0.09(CI 95%:-0.04 -0.56)   | NA |
| Pulmonary edema        | 0 (0) | 0(CI 95%:0 - 0.63)   | 1 (0) | 0.19(CI 95%:0.03 -1.1)   | 1 (0) | 0.09(CI 95%:-0.04 -0.56)   | NA |
| S/P Pulmonary effusion | 0 (0) | 0(CI 95%:0 - 0.63)   | 1 (0) | 0.19(CI 95%:0.03 -1.1)   | 1 (0) | 0.09(CI 95%:-0.04 -0.56)   | NA |
| Myasthenia Gravis      | 0 (0) | 0(CI 95%:0 - 0.63)   | 1 (0) | 0.19(CI 95%:0.03 -1.1)   | 1 (0) | 0.09(CI 95%:-0.04 -0.56)   | NA |
| Lung injury            | 0 (0) | 0(CI 95%:0 - 0.63)   | 1 (0) | 0.19(CI 95%:0.03 -1.1)   | 1 (0) | 0.09(CI 95%:-0.04 -0.56)   | NA |
| Smoking lung damage    | 0 (0) | 0(CI 95%:0 - 0.63)   | 1 (0) | 0.19(CI 95%:0.03 -1.1)   | 1 (0) | 0.09(CI 95%:-0.04 -0.56)   | NA |



|                      |       |                     |       |                         |       |                            |    |
|----------------------|-------|---------------------|-------|-------------------------|-------|----------------------------|----|
| Tonsil's enlargement | 0 (0) | 0(CI 95%:0 - 0.63)  | 1 (0) | 0.19(CI 95%:0.03 -1.1)  | 1 (0) | 0.09(CI 95%:-0.04 -0.56)   | NA |
| Suicidal ideation    | 0 (0) | 0 (CI 95%:0 - 0.63) | 1 (0) | 0.19 (CI 95%:0.03 -1.1) | 1 (0) | 0.09 (CI 95%:-0.04 - 0.56) | NA |
|                      |       |                     |       |                         |       |                            |    |

ADHD, attention deficit hyperactivity disorder; AE, adverse event; AF, atrial fibrillation; AV block, atrioventricular block; BPH, benign prostatic hyperplasia; CHD coronary heart disease; CHF chronic heart failure; COPD chronic obstructive pulmonary disease; CRF chronic renal failure; CVA, cerebrovascular accident; DVT, deep vein thrombosis; FMF, familial Mediterranean fever; GERD, gastro-esophageal reflux disease; HTN, hypertension; HCV, hepatitis C virus; IHD, ischemic heart disease; ITP, immune thrombocytopenic purpura; OCD, obsessive compulsive disorder; OSA, obstructive sleep apnea; PE, pulmonary emboli; PTCA, percutaneous transluminal coronary angioplasty; POTS, postural tachycardia syndrome; PVD, peripheral vascular disease; S/P status post; SVT, supraventricular tachycardia; NA, not applicable; Numbers do not add up to 100% due to concomitant diagnoses.

**Supplement Table 6: Patients' reported treatment-related specific AEs by sex**

|                                 | Analyzed population<br>N=1249            |  |                              | Statistic                           |
|---------------------------------|--|--|------------------------------|-------------------------------------|
| Adverse events by SOC           | Proportion in Women<br>(CI 95%)<br>N=666 | Proportion in Men<br>(CI 95%)<br>N=582 | Total<br>(CI 95%)<br>N=1248  | Wilson's $\chi^2$ test<br>(p-value) |
| Any (at least 1 AE)             | 10.02 (CI 95%: 8.47 - 11.81)             | 9.76 (CI 95%: 7.73 - 12.25)            | 10.31 (CI 95%: 8.09 - 13.05) | 0.05(0.82)                          |
| <b>Nervous System Disorders</b> |  |  |                              |                                     |
| Dizziness (Excl Vertigo)        | 4.49 (CI 95%: 3.47 - 5.78)               | 3.3 (CI 95%: 2.19 - 4.95)              | 3.95 (CI 95%: 2.65 - 5.86)   | 0.21(0.65)                          |
| Headache                        | 3.12 (CI 95%: 2.29 - 4.24)               | 2.25 (CI 95%: 1.37 - 3.68)             | 2.75 (CI 95%: 1.7 - 4.42)    | 0.15(0.7)                           |
| Weakness Of Limbs               | 0.88 (CI 95%: 0.49 - 1.57)               | 0.9 (CI 95%: 0.41 - 1.95)              | 0.86 (CI 95%: 0.37 - 2)      | 0(1)                                |
| Memory Impairment               | 0.32 (CI 95%: 0.12 - 0.82)               | 0.45 (CI 95%: 0.15 - 1.32)             | 0.17 (CI 95%: 0.03 - 0.97)   | 0.14(0.71)                          |
| Balance Impaired Nos            | 0.24 (CI 95%: 0.08 - 0.7)                | 0.3 (CI 95%: 0.08 - 1.09)              | 0.17 (CI 95%: 0.03 - 0.97)   | 0(1)                                |
| Blurred Vision                  | 0.16 (CI 95%: 0.04 - 0.58)               | 0.15 (CI 95%: 0.03 - 0.85)             | 0.17 (CI 95%: 0.03 - 0.97)   | 0(1)                                |
| Burning Sensation In Face       | 0.08 (CI 95%: 0.01 - 0.45)               | 0.15 (CI 95%: 0.03 - 0.85)             | 0 (CI 95%: 0 - 0.66)         | 0(1)                                |
| Hyperalgesia                    | 0.24 (CI 95%: 0.08 - 0.7)                | 0.15 (CI 95%: 0.03 - 0.85)             | 0.34 (CI 95%: 0.09 - 1.24)   | 0.01(0.91)                          |
| Burning Sensation Of Lower Limb | 0.08 (CI 95%: 0.01 - 0.45)               | 0.15 (CI 95%: 0.03 - 0.85)             | 0 (CI 95%: 0 - 0.66)         | 0(1)                                |
| Tremor                          | 0.08 (CI 95%: 0.01 - 0.45)               | 0.15 (CI 95%: 0.03 - 0.85)             | 0 (CI 95%: 0 - 0.66)         | 0(1)                                |

|   | Analyzed population<br>N=1249            |  |                             | Statistic                        |
|---|--|--|-----------------------------|----------------------------------|
| Adverse events by SOC                                       | Proportion in Women<br>(CI 95%)<br>N=666 | Proportion in Men<br>(CI 95%)<br>N=582 | Total<br>(CI 95%)<br>N=1248 | Wilson's $X^2$ test<br>(p-value) |
| Bad Taste   | 0.16 (CI 95%: 0.04 - 0.58)               | 0 (CI 95%: 0 - 0.57)                   | 0.34 (CI 95%: 0.09 - 1.24)  | 0.65(0.42)                       |
| Other Speech Disturbance                                    | 0.08 (CI 95%: 0.01 - 0.45)               | 0 (CI 95%: 0 - 0.57)                   | 0.17 (CI 95%: 0.03 - 0.97)  | 0(0.95)                          |
| Ringing in Ears   | 0.08 (CI 95%: 0.01 - 0.45)               | 0 (CI 95%: 0 - 0.57)                   | 0.17 (CI 95%: 0.03 - 0.97)  | 0(0.95)                          |
| <b>Gastrointestinal Disorders</b>                           |  |  |                             |                                  |
| Sore Throat   | 2.24 (CI 95%: 1.56 - 3.22)               | 2.7 (CI 95%: 1.72 - 4.23)              | 1.2 (CI 95%: 0.58 - 2.46)   | 2.84(0.09)                       |
| Nausea  | 1.12 (CI 95%: 0.67 - 1.87)               | 1.5 (CI 95%: 0.82 - 2.74)              | 0.34 (CI 95%: 0.09 - 1.24)  | 3.24(0.07)                       |
| Dry Mouth   | 1.04 (CI 95%: 0.61 - 1.77)               | 0.75 (CI 95%: 0.32 - 1.75)             | 1.03 (CI 95%: 0.47 - 2.23)  | 0.05(0.82)                       |
| Vomiting  | 0.4 (CI 95%: 0.17 - 0.93)                | 0.45 (CI 95%: 0.15 - 1.32)             | 0.17 (CI 95%: 0.03 - 0.97)  | 0.14(0.71)                       |
| Heartburn   | 0.4 (CI 95%: 0.17 - 0.93)                | 0.45 (CI 95%: 0.15 - 1.32)             | 0.34 (CI 95%: 0.09 - 1.24)  | 0(1)                             |
| Abdominal Pain Nos  | 0.08 (CI 95%: 0.01 - 0.45)               | 0.15 (CI 95%: 0.03 - 0.85)             | 0 (CI 95%: 0 - 0.66)        | 0(1)                             |
| <b>General Disorders and Administration Site Conditions</b> |  |  |                             |                                  |
| Sleepiness  | 2.4 (CI 95%: 1.69 - 3.41)                | 2.85 (CI 95%: 1.83 - 4.41)             | 1.37 (CI 95%: 0.7 - 2.69)   | 2.55(0.11)                       |
| Diplopia  | 0.08 (CI 95%: 0.01 - 0.45)               | 0 (CI 95%: 0 - 0.57)                   | 0.17 (CI 95%: 0.03 - 0.97)  | 0(0.95)                          |

|  | Analyzed population<br>N=1249            |  |                             | Statistic                        |
|--|--|--|-----------------------------|----------------------------------|
| Adverse events by SOC                                  | Proportion in Women<br>(CI 95%)<br>N=666 | Proportion in Men<br>(CI 95%)<br>N=582 | Total<br>(CI 95%)<br>N=1248 | Wilson's $X^2$ test<br>(p-value) |
| Thirst   | 0.08 (CI 95%: 0.01 - 0.45)               | 0 (CI 95%: 0 - 0.57)                   | 0.17 (CI 95%: 0.03 - 0.97)  | 0(0.95)                          |
| <b>Respiratory, Thoracic and Mediastinal Disorders</b> |  |  |                             |                                  |
| Cough  | 2.72 (CI 95%: 1.96 - 3.78)               | 2.7 (CI 95%: 1.72 - 4.23)              | 2.41 (CI 95%: 1.44 - 4)     | 0.02(0.88)                       |
| Difficulty Breathing                                   | 0.32 (CI 95%: 0.12 - 0.82)               | 0.45 (CI 95%: 0.15 - 1.32)             | 0.17 (CI 95%: 0.03 - 0.97)  | 0.14(0.71)                       |
| Dyspnea  | 0.32 (CI 95%: 0.12 - 0.82)               | 0.45 (CI 95%: 0.15 - 1.32)             | 0.17 (CI 95%: 0.03 - 0.97)  | 0.14(0.71)                       |
| <b>Psychiatric Disorders</b>                           |  |  |                             |                                  |
| Abnormal Sleep-Related Events                          | 0.64 (CI 95%: 0.33 - 1.26)               | 0.9 (CI 95%: 0.41 - 1.95)              | 0.17 (CI 95%: 0.03 - 0.97)  | 1.8(0.18)                        |
| Poor Quality Sleep                                     | 0.64 (CI 95%: 0.33 - 1.26)               | 0.9 (CI 95%: 0.41 - 1.95)              | 0.17 (CI 95%: 0.03 - 0.97)  | 1.8(0.18)                        |
| Night Sweats   | 0.64 (CI 95%: 0.33 - 1.26)               | 0.9 (CI 95%: 0.41 - 1.95)              | 0.17 (CI 95%: 0.03 - 0.97)  | 1.8(0.18)                        |
| Anxiety  | 0.72 (CI 95%: 0.38 - 1.36)               | 0.6 (CI 95%: 0.23 - 1.53)              | 0.52 (CI 95%: 0.18 - 1.5)   | 0(1)                             |
| Impairment of Attention                                | 0.16 (CI 95%: 0.04 - 0.58)               | 0.15 (CI 95%: 0.03 - 0.85)             | 0.17 (CI 95%: 0.03 - 0.97)  | 0(1)                             |
| Bad Mood   | 0.08 (CI 95%: 0.01 - 0.45)               | 0.15 (CI 95%: 0.03 - 0.85)             | 0 (CI 95%: 0 - 0.66)        | 0(1)                             |
| Disrupted Thoughts                                     | 0.16 (CI 95%: 0.04 - 0.58)               | 0.15 (CI 95%: 0.03 - 0.85)             | 0.17 (CI 95%: 0.03 - 0.97)  | 0(1)                             |

|  | Analyzed population<br>N=1249            |  |                             | Statistic                        |
|--|--|--|-----------------------------|----------------------------------|
| Adverse events by SOC                                  | Proportion in Women<br>(CI 95%)<br>N=666 | Proportion in Men<br>(CI 95%)<br>N=582 | Total<br>(CI 95%)<br>N=1248 | Wilson's $X^2$ test<br>(p-value) |
| Nervousness  | 0.56 (CI 95%: 0.27 - 1.15)               | 0.15 (CI 95%: 0.03 - 0.85)             | 0.86 (CI 95%: 0.37 - 2)     | 1.95(0.16)                       |
| Euphoria   | 0.08 (CI 95%: 0.01 - 0.45)               | 0 (CI 95%: 0 - 0.57)                   | 0.17 (CI 95%: 0.03 - 0.97)  | 0(0.95)                          |
| Confusion  | 0.4 (CI 95%: 0.17 - 0.93)                | 0 (CI 95%: 0 - 0.57)                   | 0.69 (CI 95%: 0.27 - 1.75)  | 2.69(0.1)                        |
| <b>Cardiac Disorders</b>                               |  |  |                             |                                  |
| Palpitations   | 0.72 (CI 95%: 0.38 - 1.36)               | 0.45 (CI 95%: 0.15 - 1.32)             | 0.86 (CI 95%: 0.37 - 2)     | 0.3(0.58)                        |
| <b>Musculoskeletal and Connective Tissue Disorders</b> |  |  |                             |                                  |
| Motor Dysfunction Nos                                  | 0.08 (CI 95%: 0.01 - 0.45)               | 0 (CI 95%: 0 - 0.57)                   | 0.17 (CI 95%: 0.03 - 0.97)  | 0(0.95)                          |
| <b>Skin and Subcutaneous Tissue Disorders</b>          |  |  |                             |                                  |
| Sweaty   | 0.08 (CI 95%: 0.01 - 0.45)               | 0 (CI 95%: 0 - 0.57)                   | 0.17 (CI 95%: 0.03 - 0.97)  | 0(0.95)                          |
| <b>Vascular Disorders</b>                              |  |  |                             |                                  |
| Hypotension  | 0.16 (CI 95%: 0.04 - 0.58)               | 0 (CI 95%: 0 - 0.57)                   | 0.34 (CI 95%: 0.09 - 1.24)  | 0.65(0.42)                       |

AEs, Adverse events; CI, Confidence interval; PT, Preferred term; SOC, System organ classification; Numbers do not add up to 100% due to concomitant AEs.

### Results S1: Pain reduction response comparison by sex

For the general sample, at the end of the up-titration phase, no significant differences were found between women and men in treatment effectiveness. At D<sub>30</sub>, when pain reduction started to plateau, 348 patients (68%) reported a reduction in pain intensity of at least one numerical pain scale point (of them, n=202, 58% were women and n=146, 42% were men), 135 patients (26%) reported no change (of them, n=71, 53% were women and n=64, 47% were men), and 28 patients (5%) reported an increase in pain intensity (of them, n=14, 50% were women and n=14, 50% were men) ( $\chi^2_{(1)}=1.60$ ,  $p=0.44$ ). In addition, At D<sub>30</sub>, there were no significant differences in the magnitude of pain intensity reduction between women and men. Overall, 132 patients (26%) reported a reduction of  $\geq 30\%$  (n=67, 23% for women and n=65, 29% for men;  $\chi^2_{(1)}=1.90$ ,  $p=0.17$ ) and 54 patients (11%) reported a reduction of  $\geq 50\%$  from D<sub>0</sub> (n=27, 9% for women and n=27, 12% for men;  $\chi^2_{(1)}=0.70$ ,  $p=0.40$ ). Thus, no clinical difference in the response to the treatment have been found between the sexes.

Among the 28 patients who reported an increase in pain intensity following a 30-days treatment period with the MDI, 12 (44%) patients provided data on the following secondary outcomes: sleep duration, sleep quality, McGill score and health-related quality of life score. From these patients, nine (32%) reported sleep duration improvement, six (22%) patients reported sleep quality improvement, four (14%) reported quality of life improvement, three reported McGill total score reduction (affective and sensory pain intensities) and two (7%) patients reported pain catastrophizing score improvement at D<sub>30</sub> in comparison to D<sub>0</sub>. The remaining 16 patients did not provide any additional information for the outcome measures other than weekly average pain intensity.

Among the 45 patients who reported their pain intensity at D<sub>30</sub> and at D<sub>240</sub> (i.e., study endpoint), by means of mixed linear regression analysis, pain intensity measured by NPS decreased by 1.58 (95% CI, -3.02 to -0.15;  $p<0.05$ ), from  $7.4 \pm 2.0$  at baseline to  $5.7 \pm 1.7$  at D<sub>240</sub> following treatment initiation (27% mean pain reduction) with no sex differences apparent. For sensitivity analysis, LOCF was performed on that measure, increasing the number of reports at D<sub>240</sub> to 145 instead of 45. Mixed linear regression analysis showed that the pain intensity measured by NPS decreased by 2.60 (95% CI, -2.91 to -2.30;  $p<0.001$ ) at D<sub>240</sub>.

**Table S7: Descriptive sample etiologies**

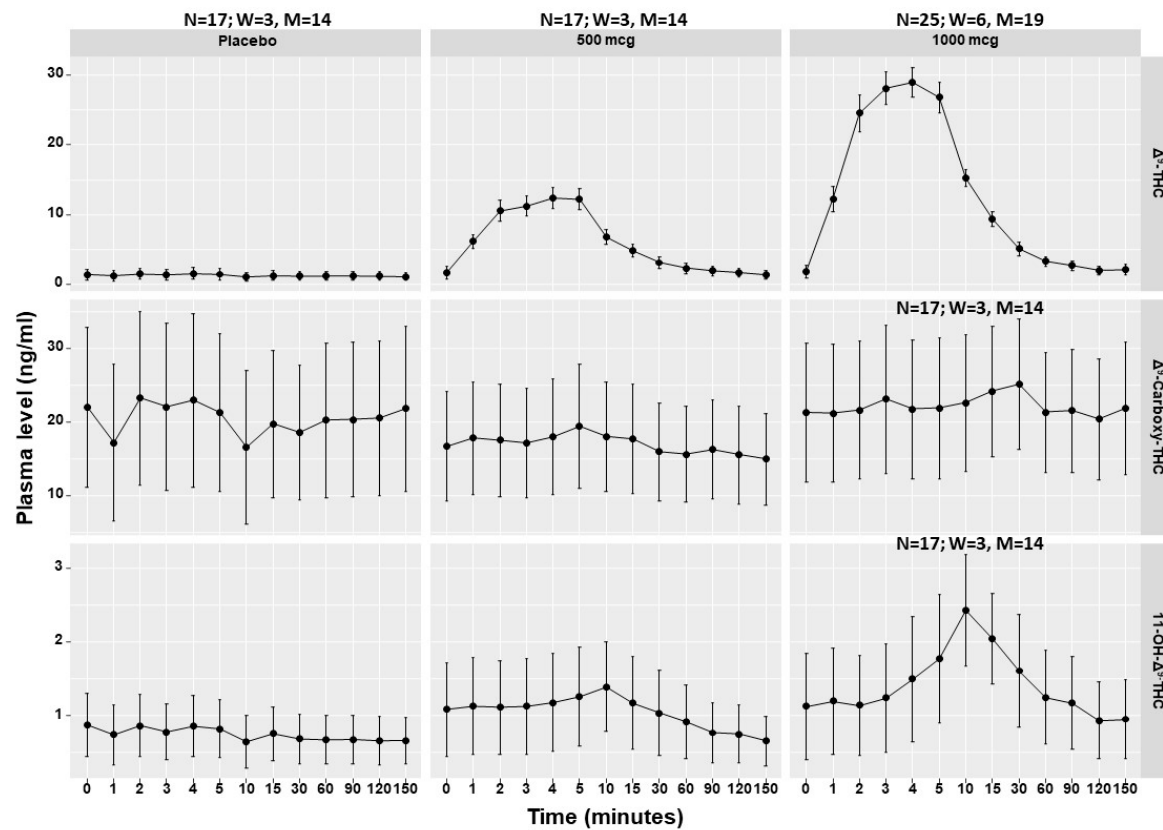
| Study arm                        | Placebo<br>N=17   |                    | 500 mcg THC<br>N=17 |                    | 1,000 mcg THC<br>N=25 |                    | 1,500 mcg THC<br>N=3 |                   | Total<br>N=25 |
|----------------------------------|-------------------|--------------------|---------------------|--------------------|-----------------------|--------------------|----------------------|-------------------|---------------|
| Pain diagnosis etiology          | W<br>N=3<br>n (%) | M<br>N=14<br>n (%) | W<br>N=3<br>n (%)   | M<br>N=14<br>n (%) | W<br>N=6<br>n (%)     | M<br>N=19<br>n (%) | W<br>N=2<br>n (%)    | M<br>N=1<br>n (%) | n (%)         |
| <b>Chronic pain</b>              | 3 (100)           | 14 (100)           | 3 (100)             | 14 (100)           | 6 (100)               | 19 (100)           | 2 (100)              | 1 (100)           | 25 (100)      |
| <b>Neuropathic pain</b>          | 3 (100)           | 14 (100)           | 3 (100)             | 14 (100)           | 6 (100)               | 19 (100)           | 2 (100)              | 1 (100)           | 25 (100)      |
| Lumbar radicular pain            | 0                 | 3 (21)             | 0                   | 3 (21)             | 1 (17)                | 4 (21)             | NA                   | NA                | 5 (20)        |
| Complex regional pain syndrome   | 0                 | 4 (29)             | 0                   | 4 (29)             | 1 (17)                | 3 (16)             | 0                    | 1 (100)           | 4 (16)        |
| Painful diabetic peripheral pain | 0                 | 3 (21)             | 0                   | 3 (21)             | 0                     | 3 (16)             | NA                   | NA                | 3 (12)        |
| Phantom limb pain                | 0                 | 1 (7)              | 0                   | 1 (7)              | 0                     | 1 (5)              | NA                   | NA                | 1 (4)         |
| Nerve injury                     | NA                | NA                 | NA                  | NA                 | 1 (17)                | 0                  | 1 (50)               | 0                 | 1 (4)         |
| Cervical radicular pain          | NA                | NA                 | NA                  | NA                 | 1 (17)                | 0                  | NA                   | NA                | 1 (4)         |
| Berger's disease                 | 0                 | 1 (7)              | 0                   | 1 (7)              | 0                     | 1 (5)              | NA                   | NA                | 1 (4)         |
| Idiopathic peripheral neuropathy | 1 (33)            | 1 (7)              | 1 (33)              | 1 (7)              | 1 (17)                | 1 (5)              | 1 (50)               | 0                 | 2 (8)         |
| Failed back surgery pain         | 0                 | 1 (7)              | 0                   | 1 (7)              | 1 (17)                | 1 (5)              | NA                   | NA                | 2 (8)         |
| <b>Musculoskeletal pain</b>      | NA                | NA                 | NA                  | NA                 | 0                     | 1 (5)              | NA                   | NA                | 1 (4)         |
| Sacroiliitis                     | NA                | NA                 | NA                  | NA                 | 0                     | 1 (5)              | NA                   | NA                | 1 (4)         |

|                                    |        |       |        |       |        |       |        |    |        |
|------------------------------------|--------|-------|--------|-------|--------|-------|--------|----|--------|
| <b>Headaches</b>                   | 0      | 1 (7) | 0      | 1 (7) | 0      | 1 (5) | NA     | NA | 1 (4)  |
| Cluster headache                   | 0      | 1 (7) | 0      | 1 (7) | 0      | 1 (5) | NA     | NA | 1 (4)  |
| <b>inflammatory bowel diseases</b> | 1 (33) | 1 (7) | 1 (33) | 1 (7) | 2 (34) | 1 (5) | 1 (50) | 0  | 3 (12) |
| Crohn's disease                    | 1 (33) | 1 (7) | 1 (33) | 1 (7) | 1 (17) | 1 (5) | 1 (50) | 0  | 2 (8)  |
| Ulcerative colitis                 | NA     | NA    | NA     | NA    | 1 (17) | 0     | NA     | NA | 1 (4)  |

W, women; M, men; NA, not applicable; Numbers do not add up to 100% due to concomitant diagnoses.

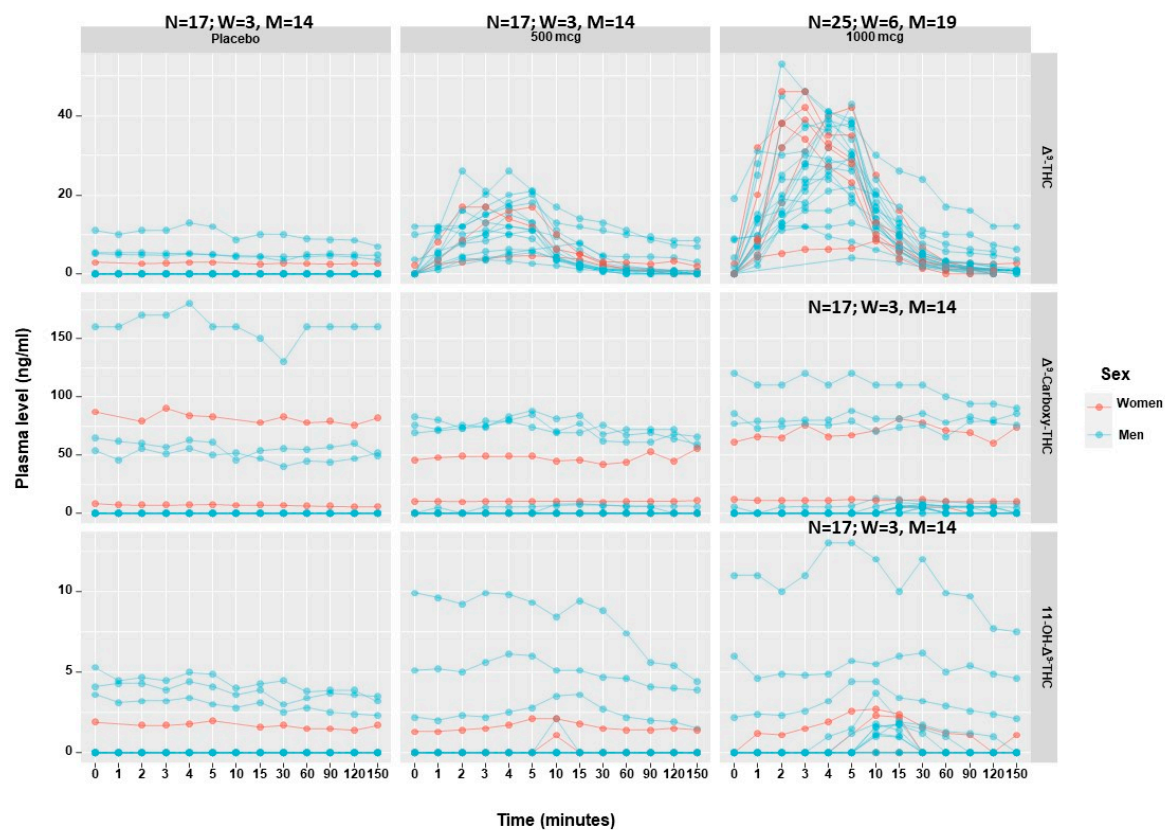


**FigureS1:  $\Delta^9$ -THC and its metabolites pharmacokinetics**



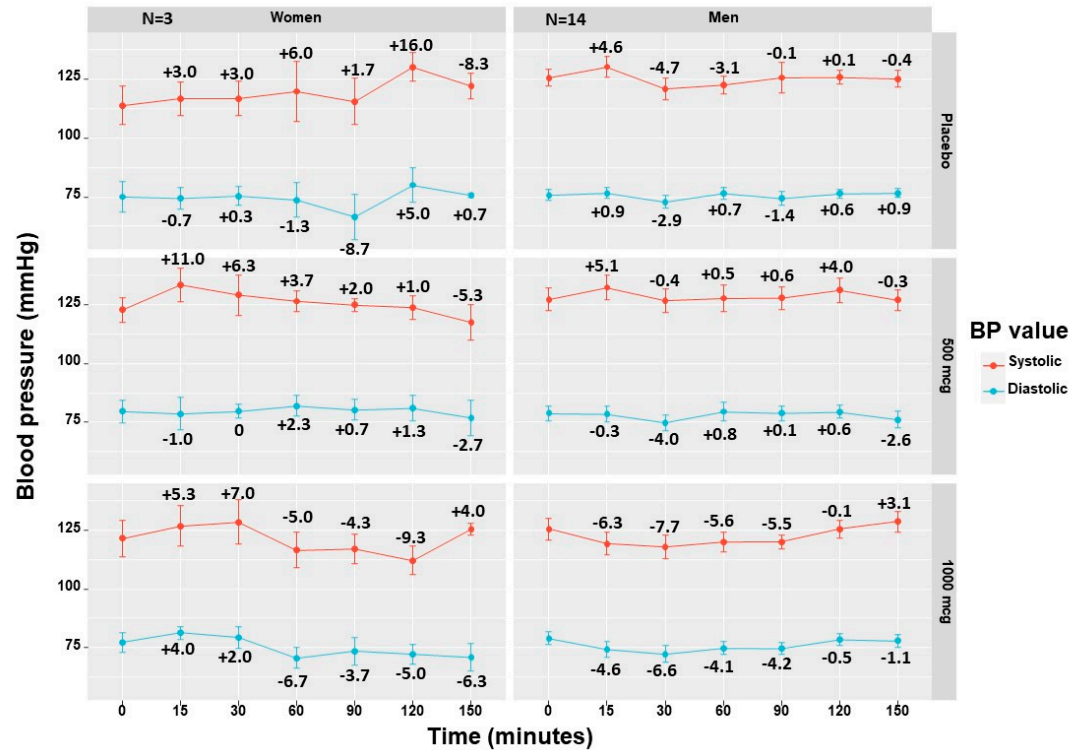
$\Delta^9$ -THC, Tetrahydrocannabinol; 11-Nor-9-carboxy- $\Delta^9$ -tetrahydrocannabinol; 11-OH- $\Delta^9$ -THC, 11-Nor-9-carboxy- $\Delta^9$ -tetrahydrocannabinol; M, Men; W, Women, error bars represent standard deviation.

**FigureS2: Individualized sex differences in  $\Delta^9$ -THC and its metabolites pharmacokinetics**



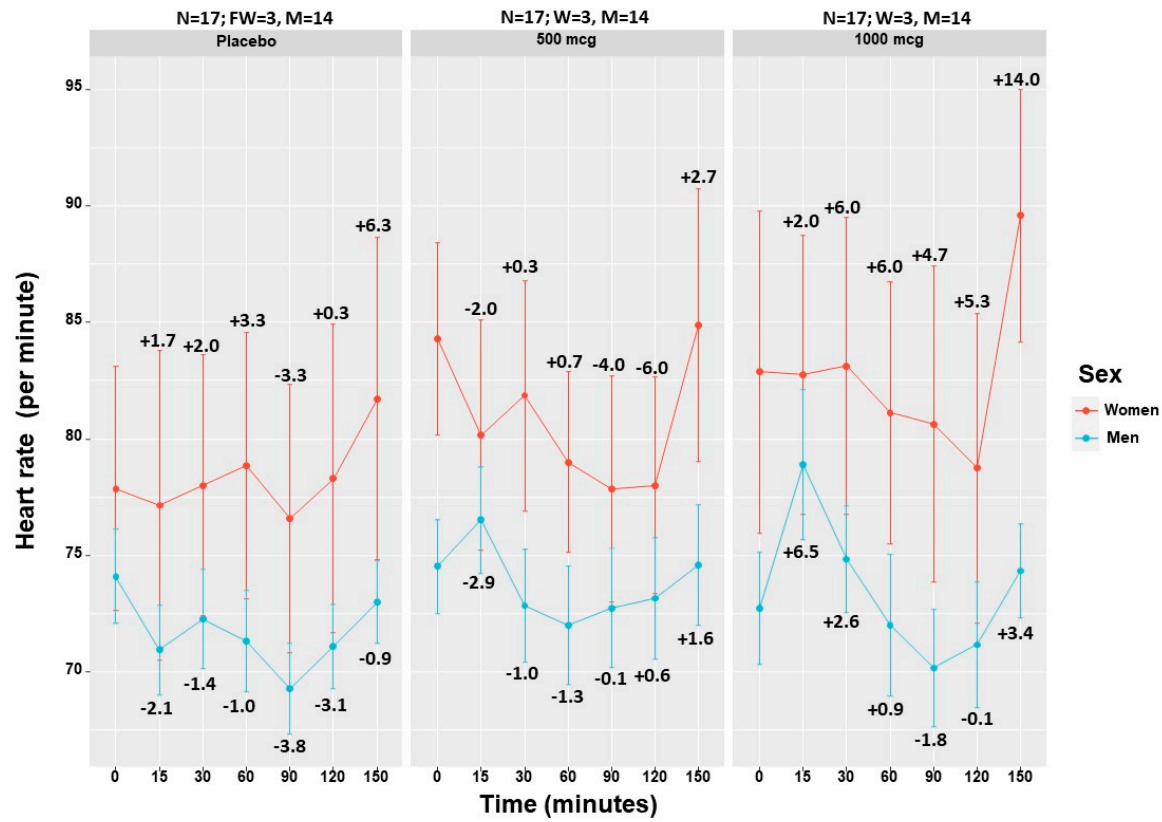
$\Delta^9$ -THC, Tetrahydrocannabinol; 11-Nor-9-carboxy- $\Delta^9$ -tetrahydrocannabinol; 11-OH- $\Delta^9$ -THC, 11-Nor-9-carboxy- $\Delta^9$ -tetrahydrocannabinol; M, Men; W, Women. Notably, neither of the sexes exhibited outlier behavior that might have impacted the results of the comparison.

FigureS3: Sex comparison of blood pressure following a single inhalation



BP, Blood pressure, error bars represent standard deviation.

**FigureS4: Sex comparison of heart rate following a single inhalation**



M, Men; W, Women, error bars represent standard deviation.