The effect of multimorbidity patterns, and the impact of comorbid anxiety and depression, on primary health service use: the Men Androgen Inflammation Lifestyle Environment and Stress (MAILES) Study (Supplemental Material)

(A) Demographic and lifestyle characteristics of participants

With reference to the RESULTS section (Primary Health Service Use) in the main text, the demographic and lifestyle characteristics of all participants (N=2,039) in the MAILES Stage 2 study and separately for participants with completed or missing information on the annual frequency of GP visits are shown in Supplemental Table S1. Participants who had complete information on GP visits were more likely younger (mean age of 59.6 versus 62.6, p = 0.005), born in Australia (p = 0.016), and employed (p = 0.045). Other demographic and lifestyle characteristics were not different significantly between participants with completed or missing information on GP visits.

(B) Higher level of multimorbidity for participants with 10 or more annual GP visits

With reference to the RESULTS section (Impact of Multimorbidity on Primary Health Service Use) and Table 2 in the main text, Supplemental Figure S1 displays different distributions in multimorbidity levels between participants with zero GP visit (Figure S1a) and 10 or more GP visits (Figure S1b) in a year. The figure shows that participants with 10 or more annual GP visits are more likely to have more comorbid conditions, especially involving CVD or obesity.

(C) Sensitivity analyses regarding the definition of anxiety and depression

With reference to the RESULTS section (Impact of Multimorbidity on Primary Health Service Use) and Table 3 in the main text, Supplemental Tables S2 and S3 present the results of multinomial logistic regression models assessing the impact of anxiety and/or depression defined by formal clinical diagnosis (GAD7 for anxiety; BDI-1a/CES-D for depression) and medications for anxiety and/or depression, respectively. Due to missing data in clinical diagnosis of anxiety or depression, the sample
size available in the regression analyses was much smaller compared to that obtained using self-reported questionnaire. From Table S2, the presence of anxiety or depression further increased the frequency of 10+ GP visits for participants with obesity (adjusted RRR = 3.5; 95% CI: 1.6-7.6), CVD (adjusted RRR = 9.3; 95% CI: 1.8-47), or diabetes (adjusted RRR = 4.1; 95% CI: 1.1-15). The results given in Table S3 obtained using medications for anxiety and/or depression were close to Table 3 obtained by self-reported questionnaire. Table S3 shows that the presence of anxiety or depression further increased the frequency of 10+ GP visits for participants with obesity (adjusted RRR = 3.3; 95% CI: 1.5-7.0), CVD (adjusted RRR = 5.8; 95% CI: 1.2-27), or diabetes (adjusted RRR = 3.8; 95% CI: 1.3-11). The sensitivity analyses indicated the same conclusion as presented in Table 3 that the presence of clinically-diagnosed or medication-based anxiety and/or depression further increased significantly the chance of 10+ GP visits.
Table S1. Demographic and lifestyle characteristics of the MAILES Stage 2 cohort (N=2,039)

| Characteristics | All participants (N=2,039) | Participants with complete information on annual frequency of GP visits (n=1,904) | Participants with missing information on annual frequency of GP visits (n=135) |
|-----------------|----------------------------|---------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Age*            | 59.8 (11.6) | 59.6 (11.5) | 62.6 (12.4) |
| Marital status  |                                            |                                                                                 |                                                                          |
| Married         | 1520 (77.8%) | 1465 (77.7%) | 55 (80.9%)  |
| Separated/widowed | 314 (16.1%) | 303 (16.1%) | 11 (16.2%)  |
| Never married   | 119 (6.1%)  | 117 (6.2%)  | 2 (2.9%)    |
| missing         | 86          | 19          | 67          |
| Country of birth* |                                        |                                                                                 |                                                                          |
| Australia       | 1365 (67.0%) | 1288 (67.7%) | 77 (57.5%)  |
| UK/Ireland      | 386 (19.0%)  | 358 (18.8%)  | 28 (20.9%)  |
| Europe          | 205 (10.1%)  | 187 (9.8%)   | 18 (13.4%)  |
| Asia/Other      | 81 (4.0%)    | 70 (3.7%)    | 11 (8.2%)   |
| missing         | 2           | 1           | 1           |
| Household income|                                            |                                                                                 |                                                                          |
| Up to $20K      | 261 (14.0%)  | 253 (14.0%)  | 8 (12.5%)   |
| $20 - $60K      | 825 (44.2%)  | 797 (44.2%)  | 28 (43.8%)  |
| $60 - $80K      | 262 (14.0%)  | 255 (14.2%)  | 7 (10.9%)   |
| >$80K           | 518 (27.8%)  | 497 (27.6%)  | 21 (32.8%)  |
| missing         | 173         | 102         | 71          |
| Education Qualification |                                    |                                                                                 |                                                                          |
| High school     | 578 (28.6%)  | 529 (28.0%)  | 49 (37.7%)  |
| Trade           | 483 (23.9%)  | 452 (23.9%)  | 31 (23.9%)  |
| Cert./Diploma   | 661 (32.7%)  | 629 (33.3%)  | 32 (24.6%)  |
| Degree          | 298 (14.8%)  | 280 (14.8%)  | 18 (13.9%)  |
| missing         | 16          | 14          | 2           |
| Work status*    |                                            |                                                                                 |                                                                          |
| Employed        | 1085 (55.4%) | 1051 (55.6%) | 34 (50.8%)  |
| Unemployed      | 37 (1.9%)    | 35 (1.9%)    | 2 (3.0%)    |
| Retired         | 722 (36.9%)  | 691 (36.6%)  | 31 (46.3%)  |
| Other           | 113 (5.8%)   | 113 (6.0%)   | 0 (0%)      |
| missing         | 82          | 14          | 68          |
| Smoking         |                                            |                                                                                 |                                                                          |
| Yes/Occasionally | 291 (15.0%) | 270 (14.8%) | 21 (18.8%) |
| No              | 1649 (85.0%) | 1558 (85.2%) | 91 (81.3%)  |
| missing         | 99          | 76          | 23          |
| Alcohol         |                                            |                                                                                 |                                                                          |
| <2 drinks       | 1511 (79.7%) | 1434 (79.5%) | 77 (83.7%)  |
| 3-4 drinks      | 209 (11.0%)  | 197 (10.9%)  | 12 (13.0%)  |
| 5-8 drinks      | 113 (6.0%)   | 111 (6.2%)   | 2 (2.2%)    |
| >8 drinks       | 63 (3.3%)    | 62 (3.4%)    | 1 (1.1%)    |
| missing         | 143         | 100         | 43          |

* Test for differences in frequencies among the four categories using chi-square/Fisher’s exact tests; test for differences in means using independent-sample t-test.
* Significant differences between participants with complete and missing information on annual frequency of GP visits (p<0.05).
Figure S1. Characteristics of comorbid conditions between participants with (a) zero GP visit; (b) 10+ GP visits
Table S2. Multinomial logistic regression on GP visits (clinically diagnosed anxiety/depression)

| Characteristics                  | Zero GP visit (n=54) versus 1-4 GP visits (n=368) | 5-9 GP visits (n=150) versus 1-4 GP visits (n=368) | 10+ GP visits (n=99) versus 1-4 GP visits (n=368) |
|----------------------------------|---------------------------------------------------|--------------------------------------------------|--------------------------------------------------|
| **Condition A (for Obesity)***   |                                                   |                                                  |                                                  |
| Obesity effect for participants  | 0.8 (0.4-1.7)                                     | 1.0 (0.6-1.8)                                    | 1.3 (0.5-3.5)                                    |
| without anx or dep               |                                                   |                                                  |                                                  |
| Extra effect from anx, dep, or both for participants with obesity | 1.0 (0.4-2.5)                                     | 1.3 (0.7-2.2)                                    | 3.5* (1.6-7.6)                                   |
| Age                              | 1.0 (0.9-1.0)                                     | 1.0 (1.0-1.0)                                    | 1.1* (1.0-1.1)                                   |
| Household income                 |                                                   |                                                  |                                                  |
| Up to $20K                       | Reference                                         | Reference                                        | Reference                                        |
| $20 - $60K                       | 3.1 (0.4-25)                                      | 0.9 (0.5-1.9)                                    | 0.5 (0.3-1.1)                                    |
| $60 - $80K                       | 4.1 (0.5-36)                                      | 1.0 (0.4-2.3)                                    | 0.5 (0.2-1.4)                                    |
| >$80K                            | 3.0 (0.4-26)                                      | 0.6 (0.3-1.3)                                    | 0.2* (0.1-0.7)                                   |
| Work status                      |                                                   |                                                  |                                                  |
| Employed                         | Reference                                         | Reference                                        | Reference                                        |
| Unemployed                       | ---                                              | 1.2 (0.3-4.8)                                    | 1.5 (0.3-8.5)                                    |
| Retired                          | 1.0 (0.3-3.3)                                     | 2.4* (1.2-4.8)                                   | 1.6 (0.7-3.9)                                    |
| Other                            | 1.2 (0.2-5.5)                                     | 2.7* (1.1-6.4)                                   | 15.2* (6.3-36)                                   |
| **Condition B (for CVD)***       |                                                   |                                                  |                                                  |
| CVD effect for participants      | N/A                                               |                                                  |                                                  |
| without anx or dep               |                                                   |                                                  |                                                  |
| Extra effect from anx, dep, or both for participants with CVD | 2.5 (0.7-9.1)                                     | 9.3* (1.8-47)                                   |
| Age                              | 1.0 (1.0-1.0)                                     | 1.1* (1.0-1.1)                                   |
| Household income                 |                                                   |                                                  |                                                  |
| Up to $20K                       | Reference                                         | Reference                                        | Reference                                        |
| $20 - $60K                       | 0.9 (0.5-1.8)                                     | 0.5 (0.3-1.1)                                    |                                                  |
| $60 - $80K                       | 1.0 (0.4-2.3)                                     | 0.5 (0.2-1.4)                                    |                                                  |
| >$80K                            | 0.6 (0.3-1.3)                                     | 0.2* (0.1-0.7)                                   |                                                  |
| Work status                      |                                                   |                                                  |                                                  |
| Employed                         | Reference                                         | Reference                                        | Reference                                        |
| Unemployed                       | 1.2 (0.3-4.8)                                     | 1.5 (0.3-8.5)                                    |                                                  |
| Retired                          | 2.3* (1.2-4.5)                                    | 1.6 (0.6-3.9)                                    |                                                  |
| Other                            | 2.6* (1.1-6.2)                                    | 15.4* (6.4-37)                                   |                                                  |
| **Condition C (for Diabetes)***  |                                                   |                                                  |                                                  |
| Diabetes effect for participants | 2.2 (0.7-6.6)                                     | 1.8 (0.8-4.1)                                    | 1.4 (0.4-5.2)                                    |
| without anx or dep               |                                                   |                                                  |                                                  |
| Extra effect from anx, dep, or both for participants with diabetes | 0.4 (0.1-1.8)                                     | 0.5 (0.2-1.5)                                    | 4.1* (1.1-15)                                    |
| Age                              | 1.0 (1.0-1.0)                                     | 1.0 (1.0-1.1)                                    | 1.1* (1.0-1.1)                                   |
| Household income                 |                                                   |                                                  |                                                  |
| Up to $20K                       | Reference                                         | Reference                                        | Reference                                        |
| $20 - $60K                       | 1.8 (0.4-9.0)                                     | 0.9 (0.5-1.8)                                    | 0.6 (0.3-1.2)                                    |
| $60 - $80K                       | 2.5 (0.5-13)                                      | 1.0 (0.4-2.3)                                    | 0.6 (0.2-1.6)                                    |
| >$80K                            | 1.7 (0.3-8.9)                                     | 0.6 (0.3-1.3)                                    | 0.2* (0.1-0.7)                                   |
| Work status                      |                                                   |                                                  |                                                  |
| Employed                         | Reference                                         | Reference                                        | Reference                                        |
| Unemployed                       | 1.2 (0.1-11)                                      | 1.1 (0.3-4.6)                                    | 1.4 (0.2-7.9)                                    |
| Retired                          | 0.7 (0.2-2.5)                                     | 2.2* (1.1-4.3)                                   | 1.5 (0.6-3.6)                                    |
| Other                            | 1.1 (0.2-5.2)                                     | 2.6* (1.1-6.2)                                   | 15.2* (6.4-36)                                   |

Data are adjusted relative risk ratios (RRRs) with 95% CI (significant results marked with an *).
N/A for Model B because there are no participants with comorbid conditions involving CVD in the category of zero GP visit. Other work status includes student and people with home duties.

* Number of medications was not adjusted in the models; see text for details.
Table S3. Multinomial logistic regression on GP visits (medications for anxiety/depression)

| Characteristics | Zero GP visit (n=149) versus 1-4 GP visits (n=1006) | 5-9 GP visits (n=386) versus 1-4 GP visits (n=1006) | 10+ GP visits (n=225) versus 1-4 GP visits (n=1006) |
|-----------------|---------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| Condition A (for Obesity)\(^a\) | | | |
| Obesity effect for participants without anx or dep | 0.7 (0.5-1.1) | 1.5* (1.1-1.9) | 2.4* (1.6-3.4) |
| Extra effect from anx, dep, or both for participants with obesity | 1.8 (0.4-8.5) | 1.6 (0.7-3.5) | 3.3* (1.5-7.0) |
| Age | 0.9* (0.9-1.0) | 1.0 (1.0-1.0) | 1.1* (1.0-1.1) |
| Household income | | | |
| Up to $20K | Reference | Reference | Reference |
| $20 - $60K | 0.8 (0.3-2.1) | 0.8 (0.6-1.2) | 0.7 (0.5-1.1) |
| $60 - $80K | 0.9 (0.3-2.4) | 1.1 (0.7-1.8) | 0.6 (0.3-1.2) |
| >$80K | 0.9 (0.4-2.4) | 0.6* (0.4-1.0) | 0.3* (0.1-0.5) |
| Work status | | | |
| Employed | | | |
| Unemployed | 1.3 (0.4-4.3) | 0.9 (0.3-2.6) | 1.0 (0.2-3.7) |
| Retired | 0.6 (0.3-1.4) | 2.1* (1.4-3.2) | 1.4 (0.8-2.4) |
| Other | 0.7 (0.3-1.8) | 1.6 (0.9-2.9) | 7.8* (4.4-14) |
| Condition B (for CVD)\(^a\) | | | |
| CVD effect for participants without anx or dep | N/A | 1.8* (1.2-2.7) | 4.2* (2.7-6.5) |
| Extra effect from anx, dep, or both for participants with CVD | | 1.3 (0.2-7.9) | 5.8* (1.2-27) |
| Age | | 1.0 (1.0-1.0) | 1.0* (1.0-1.1) |
| Household income | | | |
| Up to $20K | | Reference | Reference |
| $20 - $60K | 0.8 (0.6-1.2) | 0.6* (0.4-1.0) | |
| $60 - $80K | 1.0 (0.6-1.7) | 0.5* (0.3-1.0) | |
| >$80K | 0.5* (0.3-0.9) | 0.2* (0.1-0.4) | |
| Work status | | | |
| Employed | | Reference | Reference |
| Unemployed | 0.8 (0.3-2.3) | 1.1 (0.3-4.0) | |
| Retired | 2.1* (1.5-3.2) | 1.3 (0.8-2.2) | |
| Other | 1.6 (0.9-2.8) | 7.2* (4.1-13) | |
| Condition C (for Diabetes)\(^a\) | | | |
| Diabetes effect for participants without anx or dep | 0.8 (0.4-1.5) | 1.7* (1.2-2.3) | 2.9* (2.0-4.2) |
| Extra effect from anx, dep, or both for participants with diabetes | 3.3 (0.3-34) | 1.5 (0.5-5.0) | 3.8* (1.3-11) |
| Age | 0.9* (0.9-1.0) | 1.0 (1.0-1.0) | 1.1* (1.0-1.1) |
| Household income | | | |
| Up to $20K | | Reference | Reference |
| $20 - $60K | 0.8 (0.3-1.9) | 0.8 (0.6-1.2) | 0.7 (0.5-1.1) |
| $60 - $80K | 0.9 (0.3-2.2) | 1.1 (0.7-1.8) | 0.6 (0.3-1.2) |
| >$80K | 0.9 (0.4-2.1) | 0.6* (0.4-0.9) | 0.3* (0.1-0.6) |
| Work status | | | |
| Employed | | Reference | Reference |
| Unemployed | 1.6 (0.5-4.6) | 0.8 (0.3-2.4) | 0.9 (0.2-3.4) |
| Retired | 0.6 (0.3-1.4) | 2.0* (1.4-3.0) | 1.3 (0.8-2.2) |
| Other | 0.6 (0.2-1.7) | 1.6 (0.9-3.0) | 7.4* (4.2-13) |

Data are adjusted relative risk ratios (RRRs) with 95% CI (significant results marked with an *).
N/A for Model B because there are no participants with comorbid conditions involving CVD in the category of zero GP visit. Other work status includes student and people with home duties.

\(^a\) Number of medications was not adjusted in the models; see text for details.