**Supplementary file**

Table S1. Clinical and demographical features of patients based on the centers

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Characteristics | | All patients  n=856 | Isfahan clinic  n=447 | Tehran clinic  n=409 | p value |
| Age, mean±SD | | 40.16±9.42 | 41.27±9.97 | 38.94±8.63 | **<0.001** |
| Age distrubance, n (%) | 15-29 | 104 (12.1) | 53 (11.9) | 51 (12.5) | **0.002** |
| 30-49 | 600 (70.1) | 295 (66.0) | 305 (74.6) |
| 50-76 | 152 (17.8) | 99 (22.1) | 53 (13.0) |
| Age of MS onset, mean±SD | | 29.67±9.04 | 31.07±9.57 | 28.09±8.14 | **<0.001** |
| Sex, female, n (%) | | 714 (83.4) | 394 (88.1) | 320 (78.2) | **<0.001** |
| Education level, advance, n (%) | | 515 (60.2) | 214 (48.0) | 301 (73.8) | **<0.001** |
| Employment status, employed, n (%) | | 369 (43.1) | 148 (33.3) | 221 (54.2) | **<0.001** |
| Disease duration, mean (SD) | | 10.49±5.87 | 10.20±5.53 | 10.81±6.21 | 0.067 |
| EDSS, median (IQR) | | 1.5 (0.0-3.0) | 1.0 (0.0, 2.5) | 2.0 (1.0, 4.0) | **<0.001** |
| Course of MS, n (%) | RRMS | 723 (84.5) | 388 (86.8) | 335 (81.9) | 0.142 |
| SPMS | 111 (13.0) | 49 (11.0) | 62 (15.2) |
| PPMS | 22 (2.6) | 10 (2.2) | 12 (2.9) |
| DMT, n (%) | IFN | 135 (15.8) | 100 (22.4) | 35 (8.6) | **<0.001** |
| GA | 27 (3.2) | 6 (1.3) | 21 (5.1) |
| FNG | 33 (3.9) | 19 (4.3) | 14 (3.4) |
| TRF | 67 (7.8) | 64 (14.3) | 3 (0.7) |
| DMF | 63 (7.4) | 33 (7.4) | 30 (7.3) |
| NTZ | 34 (4.0) | 10 (2.2) | 24 (5.9) |
| RTX | 246 (28.7) | 186 (41.6) | 60 (14.7) |
| OCR | 222 (25.9) | 16 (3.6) | 206 (50.4) |
| No treatment | 29 (3.4) | 13 (2.9) | 16 (3.9) |

Table S2. Prevalence of Comorbidities by Hospital

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Comorbidities | All patients (n=856)  n (percent, 95%CI) | Isfahan (n=447)  n (percent, 95%CI) | Tehran (n=409)  n (percent, 95%CI) | P-value |
| **Any comorbidity** | 329 (38.4, 35.2–41.7) | 158 (35.3, 30.9-39.9) | 171 (41.8, 36.9-46.8) | 0.052 |
| **CVD comorbidities** | 34 (4.0, 2.7–5.3) | 16 (3.6, 2.0-5.7) | 18 (4.4, 2.6-6.9) | 0.539 |
| Valvular diseases | 17 (2.0, 1.1–2.9) | 9 (2.2, 0.9-3.8) | 8 (1.8, 0.8-3.8) | 0.807 |
| Arrhythmia | 5 (0.6, 0.2–1.4) | 3 (0.7, 0.1-1.9) | 2 (0.5, 0.1-1.7) | 1.000 |
| Stroke | 2 (0.2, 0.0–0.8) | 1 (0.2, 0.0-1.2) | 1 (0.2, 0.0-1.3) | 1.000 |
| Ischemic heart disease | 11 (1.3, 0.6–2.3) | 6 (1.3, 0.5-2.9) | 5 (1.2, 0.4-2.8) | 1.000 |
| Cardiomyopathy | 1 (0.1, 0.0–0.6) | 0 | 1 (0.2, 0.0-1.3) | 0.478 |
| Heart failure | 1 (0.1, 0.0–0.6) | 0 | 1 (0.2, 0.0-1.3) | 0.478 |
| **Non-CVD comorbidities** | 253 (29.6, 26.5–32.7) | 124 (27.7, 23.6-32.1) | 129 (31.5, 27.1-36.3) | 0.224 |
| Hypothyroidism | 96 (11.2, 9.2–13.5) | 49 (11.0, 8.2-14.2) | 47 (11.5, 8.6-14.9) | 0.806 |
| Migraine | 14 (1.6, 0.9–2.7) | 5 (1.1, 0.4-2.6) | 9 (2.2, 1.0-4.1) | 0.283 |
| Anemia | 37 (4.3, 3.0–5.9) | 20 (4.5, 2.7-6.8) | 17 (4.2, 2.4-6.6) | 0.819 |
| Hyperthyroidism | 5 (0.6, 0.2–1.4) | 0 | 5 (1.2, 0.4-2.8) | **0.025** |
| Thalassemia | 14 (1.6, 0.9–2.7) | 5 (1.1, 0.4-2.6) | 9 (2.2, 1.0-4.1) | 0.283 |
| Fatty liver | 14 (1.6, 0.9–2.7) | 3 (0.7, 0.1-1.9) | 11 (2.7, 1.3-4.8) | **0.028** |
| Gastrointestinal and other liver disorders | 13 (1.5, 0.8–2.6) | 5 (1.1, 0.4-2.6) | 8 (2.0, 0.8-3.8) | 0.405 |
| Asthma | 12 (1.4, 0.7–2.4) | 7 (1.6, 0.6-3.2) | 5 (1.2, 0.4-2.8) | 0.776 |
| Pulmonary embolism/ Deep vein thrombosis | 5 (0.6, 0.2–1.4) | 3 (0.7, 0.1-1.9) | 2 (0.5, 0.1-1.7) | 1.000 |
| Renal diseases | 3 (0.4, 0.0–1.0) | 2 (0.4, 0.0-1.6) | 1 (0.2, 0.0-1.3) | 1.000 |
| Polycystic Ovary Syndrome | 3 (0.4, 0.0–1.0) | 2 (0.4, 0.0-1.6) | 1 (0.2, 0.0-1.3) | 1.000 |
| Endometrioses | 4 (0.5, 0.1–1.2) | 3 (0.7, 0.1-1.9) | 1 (0.2, 0.0-1.3) | 0.626 |
| Epilepsy | 6 (0.7, 0.2–1.5) | 4 (0.9, 0.2-2.3) | 2 (0.5, 0.1-1.7) | 0.688 |
| Infertility | 1 (0.1, 0.0–0.6) | 0 | 1 (0.2, 0.0-1.3) | 0.478 |
| Thyroid nodules | 3 (0.4, 0.0–1.0) | 2 (0.4, 0.0-1.6) | 1 (0.2, 0.0-1.3) | 1.000 |
| Parkinson's disease | 1 (0.1, 0.0–0.6) | 0 | 1 (0.2, 0.0-1.3) | 0.478 |
| Becker muscular dystrophy | 4 (0.5, 0.1–1.2) | 2 (0.4, 0.0-1.6) | 2 (0.5, 0.1-1.7) | 1.000 |
| Charcot-Marrie-Tooth | 2 (0.2, 0.0–0.8) | 0 | 2 (0.5, 0.1-1.7) | 0.228 |
| Discopathy | 3 (0.4, 0.0–1.0) | 1 (0.2, 0.0-1.2) | 2 (0.5, 0.1-1.7) | 0.609 |
| Gout | 2 (0.2, 0.0–0.8) | 0 | 2 (0.5, 0.1-1.7) | 0.228 |
| Avascular necrosis | 1 (0.1, 0.0–0.6) | 0 | 1 (0.2, 0.0-1.3) | 0.478 |
| Detachment of retina | 1 (0.1, 0.0–0.6) | 0 | 1 (0.2, 0.0-1.3) | 0.478 |
| Dystrophy | 1 (0.1, 0.0–0.6) | 0 | 1 (0.2, 0.0-1.3) | 0.478 |
| Systemic Lupus Erythematosus | 1 (0.1, 0.0–0.6) | 1 (0.2, 0.0-1.2) | 0 | 1.000 |
| Rheumatoid Arthritis | 4 (0.5, 0.1–1.2) | 2 (0.4, 0.0-1.6) | 2 (0.5, 0.1-1.7) | 1.000 |
| Immune Thrombocytopenic Purpura | 1 (0.1, 0.0–0.6) | 0 | 1 (0.2, 0.0-1.3) | 0.478 |
| Hashimoto Thyroiditis | 1 (0.1, 0.0–0.6) | 1 (0.2, 0.0-1.2) | 0 | 1.000 |
| Lichen Planus | 2 (0.2, 0.0–0.8) | 2 (0.4, 0.0-1.6) | 0 | 0.500 |
| Vitiligo | 1 (0.1, 0.0–0.4) | 0 | 1 (0.2, 0.0-1.3) | 0.478 |
| Psoriasis | 4 (0.5, 0.1–1.2) | 3 (0.7, 0.1-1.9) | 1 (0.2, 0.0-1.3) | 0.626 |
| Cancer | 7 (0.8, 0.3-1.7) | 6 (1.3, 0.5-2.9) | 1 (0.2, 0.0-1.3) | 0.126 |
| Major depression disorder | 29 (3.4, 2.3-4.8) | 17 (3.8, 2.2-6.0) | 12 (2.9, 1.5-5.1) | 0.483 |
| Obsessive-compulsive disorder | 3 (0.4, 0.0–1.0) | 2 (0.4, 0.0-1.6) | 1 (0.2, 0.0-1.3) | 1.000 |
| Other psychiatric disorders | 7 (0.8, 0.3-1.7) | 3 (0.7, 0.1-1.9) | 4 (1.0, 0.3-2.5) | 0.715 |
| **CVD-related comorbidities** |  |  |  |  |
| Hypertension | 52 (5.6, 4.6-7.9) | 20 (4.5, 2.7-6.8) | 32 (7.8, 5.4-10.9) | **0.040** |
| Hyperlipidemia | 44 (5.1, 3.8-6.8) | 11 (2.5, 1.2-4.4) | 33 (8.1, 5.6-11.1) | **<0.001** |
| Diabetes mellitus type II | 27 (3.2, 2.0-4.6) | 11 (2.5, 1.2-4.4) | 16 (3.9, 2.2-6.3) | 0.245 |
| **Adverse health factors** |  |  |  |  |
| History of smoking | 248 (29.0, 25.9-32.1) | 125 (28.0, 23.8-32.4) | 123 (30.1, 25.7-34.8) | 0.497 |
| Current smoker | 88 (10.3, 8.3-12.5) | 39 (8.7, 6.3-11.7) | 49 (12.0, 9.0-15.5) | 0.117 |
| Obesity | 91 (10.6, 8.6-12.9) | 38 (8.5, 6.0-11.5) | 53 (13.0, 9.9-16.6) | 0.036 |

Table S3. Age-Standardized Prevalence of Comorbidities

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Comorbidity | All  N=856 | 15-29  N= 104 | 30-49  N=600 | 50-76  N=152 | Age-standardized  (Ref. MS population) | |
| USA 1 | UK 2 |
| All comorbidities | 329 (38.4) | 25 (24.0) | 224 (37.3) | 80 (52.6) | 47.3 | 54.5 |
| Non-CVD | 253 (29.6) | 22 (21.2) | 182 (30.3) | 49 (32.2) | 30.2 | 32 |
| CVD | 34 (4.0) | 1 (1.0) | 23 (3.8) | 10 (6.6) | 5.9 | 3.9 |
| HTN | 52 (6.1) | 0 (0) | 24 (4.0) | 28 (18.4) | 15 | 27.3 |
| HLP | 44 (5.1) | 3 (2.9) | 28 (4.7) | 13 (8.6) | 9.6 | 13.3 |
| DM | 27 (3.2) | 2 (1.9) | 13 (2.2) | 12 (7.9) | 6.7 | 11.2 |
| Cancer | 7 (0.8) | 0 (0) | 5 (0.8) | 2 (1.3) | 0.6 | 0.6 |
| Psychiatric | 39 (4.6) | 5 (4.8) | 28 (4.7) | 6 (3.9) | 4.3 | 3.4 |
| Autoimmune | 14 (1.6) | 0 | 11 (1.8) | 3 (2.0) | 1.7 | 1 |

Table S4. Difference in paramedical profile across age groups

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Dependent Variable | (I) Age group | (J) Age groups | Mean Difference (I-J) | Std. Error | Sig. | 95% Confidence Interval | |
| Lower Bound | Upper Bound |
| SBP | 15-29 | 30-49 | -1.6315 | 1.3543 | .451 | -4.811 | 1.548 |
| 50-76 | -9.3941\* | 1.6185 | .000 | -13.194 | -5.594 |
| 30-49 | 15-29 | 1.6315 | 1.3543 | .451 | -1.548 | 4.811 |
| 50-76 | -7.7626\* | 1.1502 | .000 | -10.463 | -5.062 |
| 50-76 | 15-29 | 9.3941\* | 1.6185 | .000 | 5.594 | 13.194 |
| 30-49 | 7.7626\* | 1.1502 | .000 | 5.062 | 10.463 |
| DBP | 15-29 | 30-49 | -1.357 | 1.039 | .392 | -3.80 | 1.08 |
| 50-76 | -5.677\* | 1.241 | .000 | -8.59 | -2.76 |
| 30-49 | 15-29 | 1.357 | 1.039 | .392 | -1.08 | 3.80 |
| 50-76 | -4.320\* | .879 | .000 | -6.38 | -2.26 |
| 50-76 | 15-29 | 5.677\* | 1.241 | .000 | 2.76 | 8.59 |
| 30-49 | 4.320\* | .879 | .000 | 2.26 | 6.38 |
| BMI | 15-29 | 30-49 | -.28533 | .45028 | .802 | -1.3425 | .7719 |
| 50-76 | -2.10972\* | .54020 | .000 | -3.3780 | -.8414 |
| 30-49 | 15-29 | .28533 | .45028 | .802 | -.7719 | 1.3425 |
| 50-76 | -1.82439\* | .38596 | .000 | -2.7306 | -.9182 |
| 50-76 | 15-29 | 2.10972\* | .54020 | .000 | .8414 | 3.3780 |
| 30-49 | 1.82439\* | .38596 | .000 | .9182 | 2.7306 |
| FBS | 15-29 | 30-49 | -4.0659 | 2.4285 | .217 | -9.791 | 1.660 |
| 50-76 | -9.7087\* | 2.8311 | .002 | -16.383 | -3.034 |
| 30-49 | 15-29 | 4.0659 | 2.4285 | .217 | -1.660 | 9.791 |
| 50-76 | -5.6427\* | 1.8952 | .009 | -10.111 | -1.174 |
| 50-76 | 15-29 | 9.7087\* | 2.8311 | .002 | 3.034 | 16.383 |
| 30-49 | 5.6427\* | 1.8952 | .009 | 1.174 | 10.111 |
| TG | 15-29 | 30-49 | -9.4286 | 12.3308 | .725 | -38.500 | 19.643 |
| 50-76 | -43.7545\* | 14.3749 | .007 | -77.646 | -9.863 |
| 30-49 | 15-29 | 9.4286 | 12.3308 | .725 | -19.643 | 38.500 |
| 50-76 | -34.3259\* | 9.6231 | .001 | -57.014 | -11.638 |
| 50-76 | 15-29 | 43.7545\* | 14.3749 | .007 | 9.863 | 77.646 |
| 30-49 | 34.3259\* | 9.6231 | .001 | 11.638 | 57.014 |
| LDL | 15-29 | 30-49 | -2.8077 | 6.1896 | .893 | -17.401 | 11.785 |
| 50-76 | -14.7758 | 7.2158 | .103 | -31.788 | 2.236 |
| 30-49 | 15-29 | 2.8077 | 6.1896 | .893 | -11.785 | 17.401 |
| 50-76 | -11.9681\* | 4.8305 | .037 | -23.357 | -.580 |
| 50-76 | 15-29 | 14.7758 | 7.2158 | .103 | -2.236 | 31.788 |
| 30-49 | 11.9681\* | 4.8305 | .037 | .580 | 23.357 |
| HDL | 15-29 | 30-49 | -2.3407 | 2.4457 | .605 | -8.107 | 3.425 |
| 50-76 | -2.0974 | 2.8511 | .743 | -8.819 | 4.625 |
| 30-49 | 15-29 | 2.3407 | 2.4457 | .605 | -3.425 | 8.107 |
| 50-76 | .2433 | 1.9087 | .991 | -4.257 | 4.743 |
| 50-76 | 15-29 | 2.0974 | 2.8511 | .743 | -4.625 | 8.819 |
| 30-49 | -.2433 | 1.9087 | .991 | -4.743 | 4.257 |
| Cholesterol | 15-29 | 30-49 | -11.4945 | 7.0258 | .232 | -28.059 | 5.070 |
| 50-76 | -34.3298\* | 8.1905 | .000 | -53.640 | -15.020 |
| 30-49 | 15-29 | 11.4945 | 7.0258 | .232 | -5.070 | 28.059 |
| 50-76 | -22.8353\* | 5.4830 | .000 | -35.762 | -9.908 |
| 50-76 | 15-29 | 34.3298\* | 8.1905 | .000 | 15.020 | 53.640 |
| 30-49 | 22.8353\* | 5.4830 | .000 | 9.908 | 35.762 |
| Insulin | 15-29 | 30-49 | .20451 | 1.70070 | .992 | -3.8051 | 4.2142 |
| 50-76 | -4.61257 | 1.98264 | .054 | -9.2869 | .0618 |
| 30-49 | 15-29 | -.20451 | 1.70070 | .992 | -4.2142 | 3.8051 |
| 50-76 | -4.81708\* | 1.32725 | .001 | -7.9463 | -1.6879 |
| 50-76 | 15-29 | 4.61257 | 1.98264 | .054 | -.0618 | 9.2869 |
| 30-49 | 4.81708\* | 1.32725 | .001 | 1.6879 | 7.9463 |
| HOMA-IR | 15-29 | 30-49 | -.04243 | .40369 | .994 | -.9942 | .9093 |
| 50-76 | -1.36852\* | .47061 | .011 | -2.4781 | -.2590 |
| 30-49 | 15-29 | .04243 | .40369 | .994 | -.9093 | .9942 |
| 50-76 | -1.32610\* | .31504 | .000 | -2.0689 | -.5833 |
| 50-76 | 15-29 | 1.36852\* | .47061 | .011 | .2590 | 2.4781 |
| 30-49 | 1.32610\* | .31504 | .000 | .5833 | 2.0689 |

Note. HOMA-IR: Homeostatic Model Assessment for Insulin Resistance; FBS: fasting blood sugar; SBP: systolic blood pressure; DBP: diastolic blood pressure TG: triglycerides; LDL: low-density lipoprotein-cholesterol; HDL: high-density lipoprotein-cholesterol

Table S5. Difference in paramedical profile across age groups in females

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Dependent Variable | (I) Age  group | (J)  Age groups | Mean Difference (I-J) | Std. Error | Sig. | 95% Confidence Interval | |
| Lower Bound | Upper Bound |
| SBP | 15-29 | 30-49 | -1.9176 | 1.4655 | .391 | -5.360 | 1.524 |
| 50-76 | -10.6902\* | 1.7371 | .000 | -14.770 | -6.610 |
| 30-49 | 15-29 | 1.9176 | 1.4655 | .391 | -1.524 | 5.360 |
| 50-76 | -8.7726\* | 1.2008 | .000 | -11.593 | -5.952 |
| 50-76 | 15-29 | 10.6902\* | 1.7371 | .000 | 6.610 | 14.770 |
| 30-49 | 8.7726\* | 1.2008 | .000 | 5.952 | 11.593 |
| DBP | 15-29 | 30-49 | -.319 | 1.185 | .961 | -3.10 | 2.47 |
| 50-76 | -5.213\* | 1.405 | .001 | -8.51 | -1.91 |
| 30-49 | 15-29 | .319 | 1.185 | .961 | -2.47 | 3.10 |
| 50-76 | -4.894\* | .971 | .000 | -7.18 | -2.61 |
| 50-76 | 15-29 | 5.213\* | 1.405 | .001 | 1.91 | 8.51 |
| 30-49 | 4.894\* | .971 | .000 | 2.61 | 7.18 |
| BMI | 15-29 | 30-49 | .02954 | .50095 | .998 | -1.1470 | 1.2061 |
| 50-76 | -2.14833\* | .59643 | .001 | -3.5491 | -.7475 |
| 30-49 | 15-29 | -.02954 | .50095 | .998 | -1.2061 | 1.1470 |
| 50-76 | -2.17786\* | .41484 | .000 | -3.1522 | -1.2036 |
| 50-76 | 15-29 | 2.14833\* | .59643 | .001 | .7475 | 3.5491 |
| 30-49 | 2.17786\* | .41484 | .000 | 1.2036 | 3.1522 |
| FBS | 15-29 | 30-49 | -4.5321 | 2.7861 | .237 | -11.111 | 2.047 |
| 50-76 | -11.3401\* | 3.1947 | .001 | -18.884 | -3.796 |
| 30-49 | 15-29 | 4.5321 | 2.7861 | .237 | -2.047 | 11.111 |
| 50-76 | -6.8080\* | 2.0598 | .003 | -11.672 | -1.944 |
| 50-76 | 15-29 | 11.3401\* | 3.1947 | .001 | 3.796 | 18.884 |
| 30-49 | 6.8080\* | 2.0598 | .003 | 1.944 | 11.672 |
| TG | 15-29 | 30-49 | -2.3434 | 12.3614 | .980 | -31.532 | 26.846 |
| 50-76 | -40.0337\* | 14.1747 | .014 | -73.504 | -6.563 |
| 30-49 | 15-29 | 2.3434 | 12.3614 | .980 | -26.846 | 31.532 |
| 50-76 | -37.6904\* | 9.1390 | .000 | -59.270 | -16.110 |
| 50-76 | 15-29 | 40.0337\* | 14.1747 | .014 | 6.563 | 73.504 |
| 30-49 | 37.6904\* | 9.1390 | .000 | 16.110 | 59.270 |
| LDL | 15-29 | 30-49 | .2505 | 7.1581 | .999 | -16.652 | 17.153 |
| 50-76 | -14.8327 | 8.2081 | .170 | -34.214 | 4.549 |
| 30-49 | 15-29 | -.2505 | 7.1581 | .999 | -17.153 | 16.652 |
| 50-76 | -15.0831\* | 5.2921 | .013 | -27.579 | -2.587 |
| 50-76 | 15-29 | 14.8327 | 8.2081 | .170 | -4.549 | 34.214 |
| 30-49 | 15.0831\* | 5.2921 | .013 | 2.587 | 27.579 |
| HDL | 15-29 | 30-49 | -3.0751 | 2.8215 | .521 | -9.738 | 3.587 |
| 50-76 | -2.9784 | 3.2354 | .628 | -10.618 | 4.661 |
| 30-49 | 15-29 | 3.0751 | 2.8215 | .521 | -3.587 | 9.738 |
| 50-76 | .0967 | 2.0860 | .999 | -4.829 | 5.022 |
| 50-76 | 15-29 | 2.9784 | 3.2354 | .628 | -4.661 | 10.618 |
| 30-49 | -.0967 | 2.0860 | .999 | -5.022 | 4.829 |
| Cholesterol | 15-29 | 30-49 | -11.3459 | 8.4957 | .377 | -31.407 | 8.715 |
| 50-76 | -34.4170\* | 9.7419 | .001 | -57.421 | -11.413 |
| 30-49 | 15-29 | 11.3459 | 8.4957 | .377 | -8.715 | 31.407 |
| 50-76 | -23.0711\* | 6.2810 | .001 | -37.902 | -8.240 |
| 50-76 | 15-29 | 34.4170\* | 9.7419 | .001 | 11.413 | 57.421 |
| 30-49 | 23.0711\* | 6.2810 | .001 | 8.240 | 37.902 |
| Insulin | 15-29 | 30-49 | .60062 | 1.69075 | .933 | -3.3917 | 4.5930 |
| 50-76 | -3.91271 | 1.93875 | .110 | -8.4907 | .6653 |
| 30-49 | 15-29 | -.60062 | 1.69075 | .933 | -4.5930 | 3.3917 |
| 50-76 | -4.51334\* | 1.25000 | .001 | -7.4650 | -1.5617 |
| 50-76 | 15-29 | 3.91271 | 1.93875 | .110 | -.6653 | 8.4907 |
| 30-49 | 4.51334\* | 1.25000 | .001 | 1.5617 | 7.4650 |
| HOMA-IR | 15-29 | 30-49 | .01646 | .41896 | .999 | -.9728 | 1.0058 |
| 50-76 | -1.28526\* | .48042 | .022 | -2.4197 | -.1508 |
| 30-49 | 15-29 | -.01646 | .41896 | .999 | -1.0058 | .9728 |
| 50-76 | -1.30172\* | .30975 | .000 | -2.0331 | -.5703 |
| 50-76 | 15-29 | 1.28526\* | .48042 | .022 | .1508 | 2.4197 |
| 30-49 | 1.30172\* | .30975 | .000 | .5703 | 2.0331 |

Note. HOMA-IR: Homeostatic Model Assessment for Insulin Resistance; FBS: fasting blood sugar; SBP: systolic blood pressure; DBP: diastolic blood pressure TG: triglycerides; LDL: low-density lipoprotein-cholesterol; HDL: high-density lipoprotein-cholesterol

Table S6. Difference in paramedical profile across age groups in males

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Dependent Variable | (I) Age group | (J) Age  groups | Mean Difference (I-J) | Std. Error | Sig. | 95% Confidence Interval | |
| Lower Bound | Upper Bound |
| SBP | 15-29 | 30-49 | -4.7945 | 2.9483 | .238 | -11.782 | 2.193 |
| 50-76 | -6.1571 | 3.6197 | .209 | -14.736 | 2.422 |
| 30-49 | 15-29 | 4.7945 | 2.9483 | .238 | -2.193 | 11.782 |
| 50-76 | -1.3625 | 2.8580 | .882 | -8.136 | 5.411 |
| 50-76 | 15-29 | 6.1571 | 3.6197 | .209 | -2.422 | 14.736 |
| 30-49 | 1.3625 | 2.8580 | .882 | -5.411 | 8.136 |
| DBP | 15-29 | 30-49 | -6.817\* | 1.949 | .002 | -11.44 | -2.20 |
| 50-76 | -7.584\* | 2.380 | .005 | -13.22 | -1.94 |
| 30-49 | 15-29 | 6.817\* | 1.949 | .002 | 2.20 | 11.44 |
| 50-76 | -.767 | 1.858 | .910 | -5.17 | 3.64 |
| 50-76 | 15-29 | 7.584\* | 2.380 | .005 | 1.94 | 13.22 |
| 30-49 | .767 | 1.858 | .910 | -3.64 | 5.17 |
| BMI | 15-29 | 30-49 | -2.17382 | .99477 | .077 | -4.5305 | .1829 |
| 50-76 | -1.99199 | 1.22128 | .236 | -4.8853 | .9013 |
| 30-49 | 15-29 | 2.17382 | .99477 | .077 | -.1829 | 4.5305 |
| 50-76 | .18183 | .96551 | .981 | -2.1055 | 2.4692 |
| 50-76 | 15-29 | 1.99199 | 1.22128 | .236 | -.9013 | 4.8853 |
| 30-49 | -.18183 | .96551 | .981 | -2.4692 | 2.1055 |
| FBS | 15-29 | 30-49 | -3.1120 | 5.0851 | .814 | -15.402 | 9.178 |
| 50-76 | -3.3214 | 6.3852 | .862 | -18.754 | 12.111 |
| 30-49 | 15-29 | 3.1120 | 5.0851 | .814 | -9.178 | 15.402 |
| 50-76 | -.2095 | 4.8104 | .999 | -11.836 | 11.417 |
| 50-76 | 15-29 | 3.3214 | 6.3852 | .862 | -12.111 | 18.754 |
| 30-49 | .2095 | 4.8104 | .999 | -11.417 | 11.836 |
| Triglyceride | 15-29 | 30-49 | -37.2046 | 33.2682 | .508 | -117.611 | 43.202 |
| 50-76 | -61.9107 | 41.7738 | .308 | -162.875 | 39.053 |
| 30-49 | 15-29 | 37.2046 | 33.2682 | .508 | -43.202 | 117.611 |
| 50-76 | -24.7061 | 31.4712 | .714 | -100.769 | 51.357 |
| 50-76 | 15-29 | 61.9107 | 41.7738 | .308 | -39.053 | 162.875 |
| 30-49 | 24.7061 | 31.4712 | .714 | -51.357 | 100.769 |
| LDL | 15-29 | 30-49 | -8.9691 | 11.4951 | .717 | -36.752 | 18.814 |
| 50-76 | -4.0536 | 14.4341 | .957 | -38.940 | 30.832 |
| 30-49 | 15-29 | 8.9691 | 11.4951 | .717 | -18.814 | 36.752 |
| 50-76 | 4.9155 | 10.8742 | .894 | -21.367 | 31.198 |
| 50-76 | 15-29 | 4.0536 | 14.4341 | .957 | -30.832 | 38.940 |
| 30-49 | -4.9155 | 10.8742 | .894 | -31.198 | 21.367 |
| HDL | 15-29 | 30-49 | 1.4131 | 4.3237 | .943 | -9.037 | 11.863 |
| 50-76 | 3.7679 | 5.4291 | .768 | -9.354 | 16.890 |
| 30-49 | 15-29 | -1.4131 | 4.3237 | .943 | -11.863 | 9.037 |
| 50-76 | 2.3547 | 4.0901 | .834 | -7.531 | 12.240 |
| 50-76 | 15-29 | -3.7679 | 5.4291 | .768 | -16.890 | 9.354 |
| 30-49 | -2.3547 | 4.0901 | .834 | -12.240 | 7.531 |
| Cholesterol | 15-29 | 30-49 | -11.7915 | 11.8433 | .583 | -40.416 | 16.833 |
| 50-76 | -33.3929 | 14.8713 | .074 | -69.336 | 2.550 |
| 30-49 | 15-29 | 11.7915 | 11.8433 | .583 | -16.833 | 40.416 |
| 50-76 | -21.6014 | 11.2036 | .142 | -48.680 | 5.477 |
| 50-76 | 15-29 | 33.3929 | 14.8713 | .074 | -2.550 | 69.336 |
| 30-49 | 21.6014 | 11.2036 | .142 | -5.477 | 48.680 |
| Insulin | 15-29 | 30-49 | -2.07297 | 4.50485 | .890 | -12.9609 | 8.8149 |
| 50-76 | -9.32500 | 5.65660 | .235 | -22.9966 | 4.3466 |
| 30-49 | 15-29 | 2.07297 | 4.50485 | .890 | -8.8149 | 12.9609 |
| 50-76 | -7.25203 | 4.26152 | .215 | -17.5518 | 3.0477 |
| 50-76 | 15-29 | 9.32500 | 5.65660 | .235 | -4.3466 | 22.9966 |
| 30-49 | 7.25203 | 4.26152 | .215 | -3.0477 | 17.5518 |
| HOMA-IR | 15-29 | 30-49 | -.46865 | 1.00959 | .888 | -2.9088 | 1.9715 |
| 50-76 | -2.12498 | 1.26772 | .224 | -5.1889 | .9390 |
| 30-49 | 15-29 | .46865 | 1.00959 | .888 | -1.9715 | 2.9088 |
| 50-76 | -1.65633 | .95506 | .203 | -3.9646 | .6520 |
| 50-76 | 15-29 | 2.12498 | 1.26772 | .224 | -.9390 | 5.1889 |
| 30-49 | 1.65633 | .95506 | .203 | -.6520 | 3.9646 |

Note. HOMA-IR: Homeostatic Model Assessment for Insulin Resistance; FBS: fasting blood sugar; SBP: systolic blood pressure; DBP: diastolic blood pressure TG: triglycerides; LDL: low-density lipoprotein-cholesterol; HDL: high-density lipoprotein-cholesterol

References

1. Hittle M, Culpepper WJ, Langer-Gould A, et al. Population-based estimates for the prevalence of multiple sclerosis in the United States by race, ethnicity, age, sex, and geographic region. *JAMA neurology*. 2023;80(7):693-701.

2. Multiple sclerosis: prevalence, incidence and smoking status - data briefing. Accessed 01 June, 2025. <https://www.gov.uk/government/publications/multiple-sclerosis-prevalence-incidence-and-smoking-status/multiple-sclerosis-prevalence-incidence-and-smoking-status-data-briefing>