Table 1: Univariable analysis of demographic risk factors for being a fast structural progressor

|  | levels | \# of eyes | \# of fast <br> progressors (\%) | OR (95\% CI) | $\begin{array}{r} \mathbf{P} \\ \text { value } \end{array}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Age (years) | <=60 | 304 | 87 (28.62\%) | Ref | 0.304 |
|  | $(60,70]$ | 415 | 122 (29.40\%) | 1.05 (0.75,1.47) |  |
|  | >70 | 609 | 154 (25.29\%) | 0.84 (0.61,1.16) |  |
|  | Missing | 96 | 26 (27.08\%) | - |  |
| Age (per 10 year increase) |  |  |  | 0.88 (0.78,0.99) | 0.033 |
| Sex | Male | 648 | 176 (27.16\%) | Ref | 0.934 |
|  | Female | 772 | 211 (27.33\%) | 1.01 (0.79,1.29) |  |
|  | Missing | 4 | 2 (50.00\%) | - |  |
| BMI group | < 25 | 262 | 72 (27.48\%) | Ref | 0.949 |
|  | 25-30 | 466 | 132 (28.33\%) | 1.04 (0.74,1.47) |  |
|  | >=30 | 563 | 154 (27.35\%) | 0.99 (0.72,1.38) |  |
|  | Missing | 133 | 31 (23.31\%) | - |  |
| BMI (per $1 \mathrm{~kg} / \mathrm{m}^{2}$ increase) |  |  |  | 1.00 (0.98,1.02) | 0.807 |
| Diabetes | No | 735 | 212 (28.84\%) | Ref | 0.266 |
|  | Yes | 558 | 145 (25.99\%) | 0.86 (0.67,1.12) |  |
|  | Missing | 131 | 32 (24.43\%) | - |  |
| Hypertension | No | 228 | 67 (29.39\%) | Ref | 0.509 |
|  | Yes | 1067 | 290 (27.18\%) | 0.90 (0.65,1.23) |  |
|  | Missing | 129 | 32 (24.81\%) | - |  |
| Family glaucoma history | No | 487 | 146 (29.98\%) | Ref | 0.207 |
|  | Yes | 713 | 189 (26.51\%) | $0.84(0.65,1.10)$ |  |
|  | Missing | 224 | 54 (24.11\%) | - |  |
| Alcohol use | No | 569 | 148 (26.01\%) | Ref | 0.264 |
|  | Yes | 661 | 191 (28.90\%) | 1.16 (0.89,1.50) |  |
|  | Missing | 194 | 50 (25.77\%) | - |  |
| Tobacco use | No | 538 | 143 (26.58\%) | Ref | 0.557 |
|  | Yes | 694 | 195 (28.10\%) | 1.08 (0.83,1.40) |  |
|  | Missing | 192 | 51 (26.56\%) | - |  |
| Previous glaucoma surgery | No | 895 | 257 (28.72\%) | Ref | 0.301 |
|  | Yes | 383 | 99 (25.85\%) | 0.86 (0.65,1.15) |  |
|  | Missing | 146 | 33 (22.60\%) | - |  |
| LMX1B | GC | 27 | 8 (29.63\%) | Ref | 0.64 |


|  | GG | 1127 | $297(26.35 \%)$ | 0.85 <br> $(0.45,1.61)$ |  |
| :--- | :--- | :--- | :--- | ---: | ---: |
|  | Missing | 270 | $84(31.11 \%)$ | - |  |
| TRIM66 | TC | 146 | $40(27.40 \%)$ | Ref | 0.83 |
|  | TT | 1004 | $264(26.29 \%)$ | 0.95 |  |
|  |  |  |  | $(0.62,1.46)$ |  |
|  | Missing | 274 | $85(31.02 \%)$ | - |  |

OR=odds ratio; $\mathrm{Cl}=$ confidence interval; $\mathrm{BMI}=$ body mass index

Table 2: Univariable analysis of ocular risk factors for being a fast structural progressor

|  | \# of eyes | \# of fast <br> progressors (\%) | OR (95\% CI) | P value |
| :--- | :--- | :--- | ---: | ---: |
| CCT (per $10 \mu \mathrm{~m} /$ increase) | 1228 | $323(26.30 \%)$ | $1.02(0.98,1.05)$ | 0.318 |
| CDR (per 0.1 increase) | 863 | $217(25.14 \%)$ | $0.76(0.70,0.83)$ | $<.001$ |
| IOP (per 1 mmHg increase) | 1148 | $294(25.61 \%)$ | $1.00(0.98,1.02)$ | 0.940 |
| MD (per 1 dB increase) | 1004 | $243(24.20 \%)$ | $1.08(1.05,1.11)$ | $<.001$ |
| PSD (per 1 dB increase) | 1001 | $242(24.18 \%)$ | $0.84(0.80,0.89)$ | $<.001$ |
| RNFL (per $10 \mu \mathrm{~m} /$ increase) | 1424 | $389(27.32 \%)$ | $2.65(2.35,3.00)$ | $<.001$ |
| VA (per 0.1 logMAR increase) | 727 | $178(24.48 \%)$ | $0.96(0.88,1.06)$ | 0.426 |

OR=odds ratio; $\mathrm{Cl}=$ confidence interval; CCT=central corneal thickness; CDR=cup-to-disc ratio; IOP=intraocular pressure; MD=mean deviation; PSD=pattern standard deviation; RNFL=retinal nerve fiber layer thickness; VA=visual acuity

Table 3: Univariable analysis of qualitative phenotype risk factors for being a fast structural progressor

|  |  | \# of eyes | \# of fast progressors (\%) | OR (95\% CI) | $\begin{array}{r} P \\ \text { value } \end{array}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Disc shape | Round | 243 | 60 (24.69\%) | Reference | 0.402 |
|  | Oval | 237 | 72 (30.38\%) | 1.34 (0.88,2.04) |  |
|  | Missing | 944 | 257 (27.22\%) | 1.13 (0.81,1.58) |  |
| Disc Size | Recorded | 482 | 132 (27.39\%) | Reference | 0.907 |
|  | Missing | 942 | 257 (27.28\%) | 0.98 (0.76,1.27) |  |
| Shape of cup | Conical | 156 | 47 (30.13\%) | Reference | 0.438 |
|  | Cylindrical | 256 | 69 (26.95\%) | 0.86 (0.54,1.35) |  |
|  | Bean Pot | 62 | 12 (19.35\%) | 0.57 (0.28,1.15) |  |
|  | Missing | 950 | 261 (27.47\%) | 0.87 (0.59,1.27) |  |
| Cup Depth | Shallow | 54 | 16 (29.63\%) | Reference | 0.702 |
|  | Moderate | 315 | 89 (28.25\%) | 0.93 (0.48,1.77) |  |
|  | deep | 110 | 25 (22.73\%) | 0.71 (0.34,1.48) |  |
|  | Missing | 945 | 259 (27.41\%) | 0.88 (0.47,1.67) |  |
| Rim plane position constant through 360 | No | 69 | 16 (23.19\%) | Reference | 0.657 |
|  | Yes | 410 | 114 (27.80\%) | 1.33 (0.70,2.52) |  |
|  | Missing | 945 | 259 (27.41\%) | 1.28 (0.70,2.35) |  |
| Beta PPA | No | 157 | 36 (22.93\%) | Reference | 0.239 |
|  | Yes | 325 | 96 (29.54\%) | 1.43 (0.93,2.20) |  |
|  | Missing | 942 | 257 (27.28\%) | 1.26 (0.85, 1.87) |  |
| Tilted disc | No | 441 | 121 (27.44\%) | Reference | 0.984 |
|  | Yes | 41 | 11 (26.83\%) | 0.95 (0.44,2.06) |  |
|  | Missing | 942 | 257 (27.28\%) | 0.98 (0.75,1.28) |  |
| Disc hemorrhage | No | 475 | 130 (27.37\%) | Reference | 0.993 |
|  | Yes | 7 | 2 (28.57\%) | 1.03 (0.19,5.70) |  |
|  | Missing | 942 | 257 (27.28\%) | 0.99 (0.76,1.28) |  |
| Arteriole narrowing | No | 473 | 131 (27.70\%) | Reference | 0.389 |
|  | Yes | 9 | 1 (11.11\%) | 0.31 (0.03,2.84) |  |
|  | Missing | 942 | 257 (27.28\%) | 0.97 (0.75,1.26) |  |
| Venule narrowing | No | 475 | 129 (27.16\%) | Reference | 0.730 |
|  | Yes | 7 | 3 (42.86\%) | 1.99 (0.44,8.95) |  |
|  | Missing | 942 | 257 (27.28\%) | 1.00 (0.77,1.29) |  |


| Baring of the lamina cribrosa | No | 128 | 50 (39.06\%) | Reference | 0.007 |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  | Yes | 354 | 82 (23.16\%) | 0.48 (0.32,0.73) |  |
|  | Missing | 942 | 257 (27.28\%) | 0.59 (0.40,0.86) |  |
| Baring of the circumlinear vessels | No | 340 | 90 (26.47\%) | Reference | 0.843 |
|  | Yes | 141 | 41 (29.08\%) | 1.14 (0.73,1.79) |  |
|  | Missing | 943 | 258 (27.36\%) | 1.04 (0.77,1.39) |  |
| Vessels overpass | No | 471 | 129 (27.39\%) | Reference | 0.654 |
|  | Yes | 7 | 1 (14.29\%) | 0.43 (0.05,3.97) |  |
|  | Missing | 946 | 259 (27.38\%) | 0.99 (0.76,1.28) |  |
| Bayonetting | No | 319 | 91 (28.53\%) | Reference | 0.648 |
|  | Yes | 134 | 31 (23.13\%) | 0.76 (0.47, 1.21) |  |
|  | 2 | 26 | 8 (30.77\%) | 1.15 (0.48,2.74) |  |
|  | Missing | 945 | 259 (27.41\%) | 0.94 (0.70,1.26) |  |
| Nasalization of the vessels | No | 308 | 95 (30.84\%) | Reference | 0.067 |
|  | Yes | 174 | 37 (21.26\%) | 0.61 (0.39,0.93) |  |
|  | Missing | 942 | 257 (27.28\%) | 0.83 (0.62,1.11) |  |
| Cilio-retinal vessels | No | 381 | 110 (28.87\%) | Reference | 0.298 |
|  | Yes | 101 | 22 (21.78\%) | 0.68 (0.41,1.13) |  |
|  | Missing | 942 | 257 (27.28\%) | 0.91 (0.70,1.20) |  |
| Gray crescent | No | 445 | 124 (27.87\%) | Reference | 0.722 |
|  | Yes | 37 | 8 (21.62\%) | 0.72 (0.32,1.66) |  |
|  | Missing | 942 | 257 (27.28\%) | 0.96 (0.74,1.25) |  |
| Conus pigmentosus | No | 434 | 122 (28.11\%) | Reference | 0.440 |
|  | Yes | 48 | 10 (20.83\%) | 0.67 (0.35,1.29) |  |
|  | Missing | 942 | 257 (27.28\%) | 0.95 (0.73,1.24) |  |
| Notching of neural rim | No | 449 | 126 (28.06\%) | Reference | 0.111 |
|  | Yes | 30 | 4 (13.33\%) | 0.39 (0.13,1.14) |  |
|  | Missing | 945 | 259 (27.41\%) | 0.96 (0.74,1.24) |  |
| Pallor of the neural rim | No | 475 | 131 (27.58\%) | Reference | 0.727 |
|  | Yes | 7 | 1 (14.29\%) | 0.48 (0.06,3.67) |  |
|  | Missing | 942 | 257 (27.28\%) | 0.98 (0.75,1.26) |  |

OR=odds ratio; $\mathrm{Cl}=$ confidence interval

Table 4: Univariable analysis for demographic risk factors for increasing RNFL progression rate

|  | Levels | \# of eyes | Rate of RNFL progression ( $\mu \mathrm{m} / \mathrm{y}$ ) Mean (SE) | Difference (95\% CI) | $P$-value |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Age group | <=60 | 304 | -1.71 (0.09) | Reference | 0.83 |
|  | (60,70] | 415 | -1.65 (0.05) | 0.06 (-0.15,0.27) |  |
|  | >70 | 609 | -1.65 (0.05) | 0.06 (-0.14,0.26) |  |
|  | missing | 96 | - | - |  |
| Age at enrollment (per 1 year increase) |  |  |  | 0.00 (-0.00,0.01) | 0.44 |
| sex | Male | 648 | -1.71 (0.07) | Reference | 0.32 |
|  | Female | 772 | -1.64 (0.03) | 0.08 (-0.07,0.22) |  |
|  | NA | 4 | - | - |  |
| BMI group (kg/m²) | <25 | 262 | -1.64 (0.07) | Reference | 0.16 |
|  | 25-30 | 466 | -1.60 (0.04) | 0.03 (-0.12,0.19) |  |
|  | >=30 | 563 | -1.75 (0.06) | -0.11(-0.29,0.06) |  |
|  | missing | 133 | - | - |  |
| BMI (per $1 \mathrm{~kg} / \mathrm{m}^{2}$ increase) |  |  |  | -0.01 (-0.02,0.00) | 0.22 |
| Diabetes | No | 735 | -1.69 (0.05) | Reference | 0.44 |
|  | Yes | 558 | -1.64 (0.05) | 0.05 (-0.08,0.18) |  |
|  | NA | 131 | - | - |  |
| Hypertension | No | 228 | -1.68 (0.07) | Reference | 0.86 |
|  | Yes | 1067 | -1.67 (0.04) | 0.01 (-0.14,0.16) |  |
|  | NA | 129 | - | - |  |
| Family glaucoma history | No | 487 | -1.73 (0.07) | Reference | 0.27 |
|  | Yes | 713 | -1.64 (0.04) | 0.09 (-0.07,0.25) |  |
|  | NA | 224 | - | - |  |
| Alcohol use | No | 569 | -1.63 (0.03) | Reference | 0.14 |
|  | Yes | 661 | -1.71 (0.04) | -0.08 (-0.18,0.03) |  |
|  | NA | 194 | - | - |  |
| Tobacco use | No | 538 | -1.66 (0.04) | Reference | 0.73 |
|  | Yes | 694 | -1.68 (0.04) | -0.02 (-0.12,0.09) |  |
|  | NA | 192 | - | - |  |
| Previous glaucoma surgery | No | 895 | -1.70 (0.03) | Reference | 0.50 |
|  | Yes | 383 | -1.64 (0.08) | 0.06 (-0.11,0.23) |  |
|  | NA | 146 | - | - |  |


| LMX1B | GC | 27 | $-1.39(0.31)$ | Reference | . |
| :--- | :--- | :--- | :--- | ---: | ---: |
|  | GG | 1127 | $-1.68(0.04)$ | $-0.29(-0.90,0.32)$ | 0.36 |
|  | missing | 270 | - | - | . |
| TRIM66 | TC | 146 | $-1.77(0.19)$ | Reference | . |
|  | TT | 1004 | $-1.65(0.03)$ | $0.11(-0.26,0.48)$ | 0.55 |
|  | missing | 274 | - | - |  |

RNFL=retinal nerve fiber layer; CI=confidence interval; $\mathrm{BMI}=$ body mass index

Table 5: Univariable analysis of clinical risk factors of increasing RNFL progression rate

|  | \# of eyes | Regression Coefficient for <br> rate of RNFL change (95\% CI) | P-value |
| :--- | :--- | ---: | ---: |
| CCT (per $10 \mu \mathrm{~m} /$ increase) | 1228 | $-0.00(-0.02,0.01)$ | 0.766 |
| CDR (per 0.1 increase) | 863 | $0.12(0.08,0.16)$ | $<.001$ |
| IOP (per 1 mmHg increase) | 1148 | $-0.00(-0.02,0.01)$ | 0.622 |
| MD (per 1 dB increase) | 1004 | $-0.04(-0.05,-0.03)$ | $<.001$ |
| PSD (per 1 dB increase) | 1001 | $0.09(0.06,0.11)$ | $<.001$ |
| RNFL (per $10 \mu \mathrm{~m} /$ increase $)$ | 1424 | $-0.54(-0.60,-0.47)$ | $<.001$ |
| VA (per 0.1 logMAR increase) | 727 | $0.03(0.01,0.06)$ | 0.007 |

OR=odds ratio; $\mathrm{CI}=$ confidence interval; CCT=central corneal thickness; CDR=cup-to-disc ratio; IOP=intraocular pressure; MD=mean deviation; PSD=pattern standard deviation; RNFL=retinal nerve fiber layer thickness; VA=visual acuity

Table 6: Univariable analysis for qualitative phenotypes risk factors of increasing RNFL progression rate

|  |  | \# of eyes | Rate of RNFL progression (um/y) Mean (SE) | Difference (95\% CI) | value |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Disc shape | Round | 243 | -1.54 (0.05) | Reference | 0.004 |
|  | Oval | 237 | -1.80 (0.05) | -0.26 (-0.41, -0.11) |  |
|  | Missing | 944 | -1.67 (0.05) | -0.13 (-0.28,0.01) |  |
| Disc Size | Abnormal | 3 | -1.46 (0.20) | Reference | 0.742 |
|  | Normal | 479 | -1.67 (0.03) | -0.21 (-0.61,0.19) |  |
|  | Missing | 942 | -1.67 (0.05) | -0.22 (-0.63,0.19) |  |
| Shape of cup | Conical | 156 | -1.66 (0.05) | Reference | 0.695 |
|  | Cylindrical | 256 | -1.71 (0.05) | -0.05 (-0.20,0.10) |  |
|  | Bean Pot | 62 | -1.56 (0.11) | 0.10 (-0.15,0.34) |  |
|  | Missing | 950 | -1.67 (0.05) | -0.01 (-0.15,0.14) |  |
| Cup Depth | Shallow | 54 | -1.59 (0.09) | Reference | 0.692 |
|  | Moderate | 315 | -1.70 (0.04) | -0.11 (-0.29,0.08) |  |
|  | deep | 110 | -1.64 (0.07) | -0.05 (-0.27,0.16) |  |
|  | Missing | 945 | -1.67 (0.05) | -0.08 (-0.28,0.11) |  |
| Rim plane position constant through 360 | No | 69 | -1.70 (0.07) | Reference | 0.900 |
|  | Yes | 410 | -1.66 (0.04) | 0.04 (-0.12,0.20) |  |
|  | Missing | 945 | -1.67 (0.05) | 0.03 (-0.14,0.20) |  |
| Beta PPA | No | 157 | -1.52 (0.06) | Reference | 0.014 |
|  | Yes | 325 | -1.74 (0.04) | -0.22 (-0.36, -0.08) |  |
|  | Missing | 942 | -1.67 (0.05) | -0.15 (-0.31, -0.00) |  |
| Tilted disc | No | 441 | -1.65 (0.04) | Reference | 0.502 |
|  | Yes | 41 | -1.80 (0.11) | -0.14 (-0.37,0.09) |  |
|  | Missing | 942 | -1.67 (0.05) | -0.02 (-0.14,0.10) |  |
| Disc hemorrhage | No | 475 | -1.66 (0.03) | Reference | 0.799 |
|  | Yes | 7 | -2.03 (0.56) | -0.37 (-1.48,0.74) |  |
|  | Missing | 942 | -1.67 (0.05) | -0.01 (-0.13,0.11) |  |
| Arteriole narrowing | No | 473 | -1.67 (0.03) | Reference | 0.339 |
|  | Yes | 9 | -1.43 (0.14) | 0.25 (-0.05,0.54) |  |
|  | Missing | 942 | -1.67 (0.05) | -0.00 (-0.12,0.12) |  |


| Venule narrowing | No | 475 | -1.66 (0.03) | Reference | 0.875 |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  | Yes | 7 | -1.80 (0.26) | -0.14 (-0.65, 0.38) |  |
|  | Missing | 942 | -1.67 (0.05) | -0.01 (-0.13,0.11) |  |
| Baring of the lamina cribrosa | No | 128 | -1.79 (0.06) | Reference | 0.090 |
|  | Yes | 354 | -1.62 (0.04) | 0.17 (0.02,0.32) |  |
|  | Missing | 942 | -1.67 (0.05) | 0.12 (-0.04,0.28) |  |
| Baring of the circumlinear vessels | No | 340 | -1.68 (0.04) | Reference | 0.838 |
|  | Yes | 141 | -1.63 (0.07) | 0.05 (-0.12,0.22) |  |
|  | Missing | 943 | -1.67 (0.05) | 0.01 (-0.12,0.13) |  |
| Vessels overpass | No | 471 | -1.68 (0.03) | Reference | 0.828 |
|  | Yes | 7 | -1.41 (0.43) | 0.27 (-0.57, 1.11) |  |
|  | Missing | 946 | -1.67 (0.05) | 0.01 (-0.11,0.12) |  |
| Bayonetting | No | 319 | -1.69 (0.04) | Reference | 0.711 |
|  | Moderate | 134 | -1.61 (0.06) | 0.08 (-0.07,0.23) |  |
|  | Severe | 26 | -1.77 (0.20) | -0.08 (-0.49,0.33) |  |
|  | Missing | 945 | -1.67 (0.05) | 0.02 (-0.11,0.14) |  |
| Nasalization of the vessels | No | 308 | -1.75 (0.04) | Reference | 0.012 |
|  | Yes | 174 | -1.52 (0.06) | 0.24 (0.09,0.39) |  |
|  | Missing | 942 | -1.67 (0.05) | 0.08 (-0.05,0.21) |  |
| Cilio-retinal vessels | No | 381 | -1.68 (0.04) | Reference | 0.854 |
|  | Yes | 101 | -1.63 (0.07) | 0.04 (-0.11,0.20) |  |
|  | Missing | 942 | -1.67 (0.05) | 0.00 (-0.12,0.13) |  |
| Gray crescent | No | 445 | -1.65 (0.04) | Reference | 0.515 |
|  | Yes | 37 | -1.81 (0.13) | -0.16 (-0.42, 0.11) |  |
|  | Missing | 942 | -1.67 (0.05) | -0.02 (-0.14,0.10) |  |
| Conus pigmentosus | No | 434 | -1.69 (0.03) | Reference | 0.202 |
|  | Yes | 48 | -1.48 (0.11) | 0.21 (-0.01,0.43) |  |
|  | Missing | 942 | -1.67 (0.05) | 0.01 (-0.11,0.14) |  |
| Notching of neural rim | No | 449 | -1.69 (0.03) | Reference | 0.257 |
|  | Yes | 30 | -1.41 (0.16) | 0.28 (-0.04,0.59) |  |
|  | Missing | 945 | -1.67 (0.05) | 0.02 (-0.10,0.14) |  |
| Pallor of the neural rim | No | 475 | -1.67 (0.03) | Reference | 0.943 |
|  | Yes | 7 | -1.60 (0.21) | 0.07 (-0.35,0.49) |  |
|  | Missing | 942 | -1.67 (0.05) | -0.00 (-0.13,0.12) |  |

OR=odds ratio; $\mathrm{Cl}=$ confidence interval

Table 7: Univariable analysis of demographic risk factors of being a moderate or fast functional progressor

|  | levels | N | \# of fast progressors (\%) | OR (95\% CI) | $P$ value |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Age (years) | <=60 | 304 | 26 (8.55\%) | Ref | 0.517 |
|  | (60,70] | 415 | 48 (11.57\%) | 1.41 (0.77,2.59) |  |
|  | >70 | 609 | 62 (10.18\%) | 1.19 (0.66,2.13) |  |
|  | Missing | 96 | 32 (33.33\%) | - |  |
| Age (per 10 year increase) |  |  |  | 0.97 (0.81,1.17) | 0.782 |
| Sex | Male | 648 | 95 (14.66\%) | Ref | 0.008 |
|  | Female | 772 | 73 (9.46\%) | 0.59 (0.40,0.87) |  |
|  | Missing | 4 | 0 (0.00\%) | - |  |
| BMI ( $\mathrm{kg} / \mathrm{m}^{2}$ ) | < 25 | 262 | 33 (12.60\%) | Ref | 0.668 |
|  | 25-30 | 466 | 45 (9.66\%) | 0.77 (0.44,1.37) |  |
|  | >=30 | 563 | 58 (10.30\%) | 0.83 (0.49,1.42) |  |
|  | Missing | 133 | 32 (24.06\%) | - |  |
| BMI (per $1 \mathrm{~kg} / \mathrm{m}^{2}$ change) |  |  |  | 0.99 (0.95,1.03) | 0.464 |
| Diabetes | No | 735 | 75 (10.20\%) | Ref | 0.674 |
|  | Yes | 558 | 62 (11.11\%) | 1.09 (0.72,1.66) |  |
|  | Missing | 131 | 31 (23.66\%) | - |  |
| Hypertension | No | 228 | 17 (7.46\%) | Ref | 0.146 |
|  | Yes | 1067 | 120 (11.25\%) | 1.57 (0.85,2.87) |  |
|  | Missing | 129 | 31 (24.03\%) | - |  |
| Family glaucoma history | No | 487 | 54 (11.09\%) | Ref | 0.588 |
|  | Yes | 713 | 70 (9.82\%) | 0.89 (0.57,1.37) |  |
|  | Missing | 224 | 44 (19.64\%) | - |  |
| Alcohol use | No | 569 | 54 (9.49\%) | Ref | 0.278 |
|  | Yes | 661 | 50 (7.56\%) | 0.78 (0.49,1.23) |  |
|  | Missing | 194 | 64 (32.99\%) | - |  |
| Tobacco use | No | 538 | 46 (8.55\%) | Ref | 0.801 |
|  | Yes | 694 | 57 (8.21\%) | 0.94 (0.59,1.50) |  |
|  | Missing | 192 | 65 (33.85\%) | - |  |
| Previous glaucoma surgery | No | 895 | 75 (8.38\%) | Ref | 0.004 |
|  | Yes | 383 | 56 (14.62\%) | 1.90 (1.23,2.92) |  |
|  | Missing | 146 | 37 (25.34\%) | - |  |
| LMX1B | GC | 27 | 8 (29.63\%) | Ref | 0.011 |


|  | GG | 1127 | $123(10.91 \%)$ | $0.28(0.10,0.75)$ |  |
| :--- | :--- | :--- | :--- | ---: | ---: |
|  | Missing | 270 | $37(13.70 \%)$ | - |  |
| TRIM66 | TC | 146 | $28(19.18 \%)$ | Ref | 0.015 |
|  | TT | 1004 | $102(10.16 \%)$ | $0.50(0.28,0.88)$ |  |
|  | Missing | 274 | $38(13.87 \%)$ | - |  |

OR=odds ratio; $\mathrm{Cl}=$ confidence interval; $\mathrm{BMI}=$ body mass index

Table 8: Univariable analysis for ocular risk factors for being a moderate or fast functional progressor

|  | \# of <br> eyes | \# of fast functional <br> progressors (\%) | OR (95\%CI) | P value |
| :--- | :--- | :--- | ---: | ---: |
| CCT (per $10 \mu \mathrm{~m} /$ increase) | 1228 | $139(11.32 \%)$ | $1.01(0.96,1.07)$ | 0.636 |
| CDR (per 0.1 increase) | 607 | $27(4.45 \%)$ | $0.91(0.72,1.15)$ | 0.428 |
| IOP (per 1 mmHg increase) | 936 | $68(7.26 \%)$ | $1.05(1.03,1.08)$ | $<.001$ |
| MD (per 1 dB increase) | 1424 | $168(11.80 \%)$ | $1.01(0.98,1.04)$ | 0.469 |
| PSD (per 1 dB increase) | 1417 | $168(11.86 \%)$ | $1.03(0.98,1.08)$ | 0.195 |
| RNFL (per $10 \mu \mathrm{~m} /$ increase) | 628 | $31(4.94 \%)$ | $1.00(0.74,1.36)$ | 0.990 |
| VA (per 0.1 logMAR increase) | 532 | $20(3.76 \%)$ | $1.05(0.92,1.19)$ | 0.462 |

OR=odds ratio; CI=confidence interval; CCT=central corneal thickness; CDR=cup-to-disc ratio IOP=intraocular pressure; $\mathrm{MD}=$ mean deviation; $\mathrm{PSD}=$ pattern standard deviation; RNFL=retinal nerve fiber layer thickness; VA=visual acuity

Table 9: Univariable analysis for qualitative phenotype risk factors for being a moderate or fast functional progressor

|  | Level | \# of eyes | \# of moderate or fast progressors (\%) | OR (95\% CL) | $\begin{gathered} P \\ \text { value } \end{gathered}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Disc shape | Round | 140 | 5 (3.57\%) | Reference | 0.486 |
|  | Oval | 156 | 8 (5.13\%) | 1.50 (0.48,4.65) |  |
|  | Missing | 1128 | 155 (13.74\%) | - |  |
| Disc Size | Recorded | 297 | 13 (4.38\%) | - |  |
|  | Missing | 1127 | 155 (13.75\%) | - |  |
| Shape of cup | Conical | 101 | 6 (5.94\%) | Reference | 0.717 |
|  | Cylindrical | 152 | 6 (3.95\%) | 0.69 (0.22,2.16) |  |
|  | Bean Pot | 34 | 1 (2.94\%) | 0.48 (0.06,4.17) |  |
|  | Missing | 1137 | 155 (13.63\%) | - |  |
| Cup Depth | Shallow | 21 | 2 (9.52\%) | Reference | 0.460 |
|  | Moderate | 195 | 8 (4.10\%) | $0.39(0.08,1.85)$ |  |
|  | deep | 77 | 3 (3.90\%) | 0.37 (0.06,2.21) |  |
|  | Missing | 1131 | 155 (13.70\%) | - |  |
| Rim plane position constant through 360 | No | 53 | 2 (3.77\%) | Reference | 0.768 |
|  | Yes | 240 | 11 (4.58\%) | 1.26 (0.27,6.00) |  |
|  | Missing | 1131 | 155 (13.70\%) | - |  |
| Beta PPA | No | 80 | 6 (7.50\%) | Reference | 0.113 |
|  | Yes | 216 | 7 (3.24\%) | 0.41 (0.14,1.23) |  |
|  | Missing | 1128 | 155 (13.74\%) | - |  |
| Tilted disc | No | 264 | 9 (3.41\%) | Reference | 0.031 |
|  | Yes | 32 | 4 (12.50\%) | $\begin{array}{r} 4.01 \\ (1.14,14.13) \end{array}$ |  |
|  | Missing | 1128 | 155 (13.74\%) | - |  |
| Disc hemorrhage | No | 295 | 13 (4.41\%) | - |  |
|  | Yes | 2 | 0 (0.00\%) | - |  |
|  | Missing | 1127 | 155 (13.75\%) | - |  |
| Arteriole narrowing | No | 295 | 12 (4.07\%) | Reference | 0.030 |
|  | Yes | 2 | 1 (50.00\%) | $\begin{array}{r} 23.12 \\ (1.36,392.27) \end{array}$ |  |
|  | Missing | 1127 | 155 (13.75\%) | - |  |



OR=odds ratio; $\mathrm{Cl}=$ confidence interval

Table 10: Univariable analysis for demographic risk factors of increasing MD rate of change

|  | Levels | N | Rate of RNFL change Mean (SE) | Difference (95\% CI) | value |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Age (years) | <=60 | 304 | -0.38 (0.01) | Reference | 0.18 |
|  | $(60,70]$ | 415 | -0.41 (0.01) | -0.03 (-0.07,0.00) |  |
|  | >70 | 609 | -0.40 (0.01) | -0.02 (-0.05,0.01) |  |
|  | Missing | 96 | - | - |  |
| Age at enrollment (per 10-year increase) |  |  |  | $\begin{array}{r} \hline-0.00(-0.01 \\ 0.01) \end{array}$ | 0.92 |
| sex | Male | 648 | -0.41 (0.01) | Reference | 0.13 |
|  | Female | 772 | -0.39 (0.01) | 0.02 (-0.01,0.04) |  |
|  | Missing | 4 | - | - |  |
| BMI (kg/m ${ }^{2}$ ) | $<25$ | 262 | -0.42 (0.01) | Reference | 0.13 |
|  | 25-30 | 466 | -0.40 (0.01) | 0.02 (-0.01,0.05) |  |
|  | >=30 | 563 | -0.39 (0.01) | 0.03 (0.00,0.07) |  |
|  | Missing | 133 | - | - |  |
| BMI (per kg/m² increase) |  |  |  | $\begin{array}{r} 0.0027 \\ (0.0006,0.0048) \end{array}$ | 0.01 |
| Diabetes | No | 735 | -0.40 (0.01) | Reference | . |
|  | Yes | 558 | -0.40 (0.01) | 0.00 (-0.02,0.02) | 0.81 |
|  | Missing | 131 | - | - | . |
| Hypertension | No | 228 | -0.39 (0.01) | Reference |  |
|  | Yes | 1067 | -0.40 (0.01) | -0.00 (-0.03,0.02) | 0.71 |
|  | Missing | 129 | - | - |  |
| Family glaucoma history | No | 487 | -0.40 (0.01) | Reference | . |
|  | Yes | 713 | -0.40 (0.01) | -0.00 (-0.02,0.02) | 0.98 |
|  | Missing | 224 | - | - | . |
| Alcohol use | No | 569 | -0.39 (0.01) | Reference | . |
|  | Yes | 661 | -0.39 (0.01) | 0.00 (-0.02,0.02) | 0.77 |
|  | Missing | 194 | - | - | . |
| Tobacco use | No | 538 | -0.39 (0.01) | Reference | . |
|  | Yes | 694 | -0.39 (0.01) | -0.00 (-0.02,0.02) | 0.72 |
|  | Missing | 192 | - | - | . |
| Previous glaucoma surgery | No | 895 | -0.39 (0.01) | Reference | . |
|  | Yes | 383 | -0.41 (0.01) | -0.02 (-0.05,0.01) | 0.22 |
|  | Missing | 146 | - | - | . |


| LMX1B | GC | 27 | $-0.47(0.03)$ | Reference | . |
| :--- | :--- | :--- | :--- | ---: | ---: |
|  | GG | 1127 | $-0.40(0.01)$ | $0.06(-0.00,0.13)$ | 0.07 |
|  | Missing | 270 | - | - | . |
| TRIM66 | TC | 146 | $-0.43(0.02)$ | Reference | . |
|  | TT | 1004 | $-0.40(0.01)$ | $0.03(-0.00,0.07)$ | 0.06 |
|  | Missing | 274 | - | - | - |

MD=mean deviation; OR=odds ratio; $\mathrm{Cl}=$ confidence interval; $\mathrm{BMI}=$ body mass index

Table 11: Univariable analysis for ocular risk factors of increasing MD progression rate

|  | \# of <br> eyes | Regression Coefficient for <br> rate of MD change (95\% CI) | P-value* |
| :--- | :--- | ---: | ---: |
| CCT (per $10 \mu \mathrm{~m} /$ increase) | 1228 | $-0.002(-0.005,0.001)$ | 0.160 |
| CDR (per 0.1 increase) | 607 | $0.008(0.004,0.012)$ | $<.001$ |
| IOP (per 1 mmHg increase) | 936 | $-0.001(-0.003,0.001)$ | 0.418 |
| MD (per 1 dB increase) | 1424 | $-0.006(-0.008,-0.003)$ | $<.001$ |
| PSD (per 1 dB increase) | 1417 | $0.000(-0.002,0.003)$ | 0.772 |
| RNFL (per $10 \mu \mathrm{~m} /$ /increase $)$ | 628 | $-0.015(-0.029,-0.002)$ | 0.025 |
| VA (per 0.1 logMAR increase) | 532 | $0.001(-0.001,0.003)$ | 0.451 |

OR=odds ratio; CI=confidence interval; CCT=central corneal thickness; CDR=cup-to-disc ratio; IOP=intraocular pressure; MD=mean deviation; $\mathrm{PSD}=$ pattern standard deviation; RNFL=retinal nerve fiber layer thickness; VA=visual acuity

Table 12: Univariable analysis for qualitative phenotype risk factors of increasing MD rate of change

|  |  | N | Rate of MD progression (dB/y) Mean (SE) | Difference (95\% CI) | $\begin{gathered} P \\ \text { value } \end{gathered}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Disc shape | Round | 140 | -0.40 (0.01) | Reference | 0.985 |
|  | Oval | 156 | -0.40 (0.01) | 0.00 (-0.01,0.02) |  |
|  | Missing | 1128 | -0.40 (0.01) | 0.00 (-0.02,0.02) |  |
| Disc Size | Abnormal | 3 | -0.41 (0.01) | Reference | 0.603 |
|  | Normal | 294 | -0.40 (0.00) | 0.01 (-0.01,0.03) |  |
|  | Missing | 1127 | -0.40 (0.01) | 0.01 (-0.01,0.04) |  |
| Shape of cup | Conical | 101 | -0.42 (0.01) | Reference | 0.078 |
|  | Cylindrical | 152 | -0.40 (0.01) | 0.02 (0.00,0.03) |  |
|  | Bean Pot | 34 | -0.39 (0.01) | 0.03 (0.00,0.06) |  |
|  | Missing | 1137 | -0.40 (0.01) | 0.01 (-0.00,0.03) |  |
| Cup Depth | Shallow | 21 | -0.42 (0.01) | Reference | 0.144 |
|  | Moderate | 195 | -0.41 (0.00) | 0.01 (-0.02,0.04) |  |
|  | deep | 77 | -0.39 (0.01) | 0.03 (-0.00,0.06) |  |
|  | Missing | 1131 | -0.40 (0.01) | 0.01 (-0.02,0.04) |  |
| Rim plane position constant through 360 | No | 53 | -0.41 (0.01) | Reference | 0.294 |
|  | Yes | 240 | -0.40 (0.00) | 0.01 (-0.00,0.02) |  |
|  | Missing | 1131 | -0.40 (0.01) | 0.01 (-0.01,0.03) |  |
| Beta PPA | No | 80 | -0.40 (0.01) | Reference | 0.996 |
|  | Yes | 216 | -0.40 (0.00) | 0.00 (-0.02,0.02) |  |
|  | Missing | 1128 | -0.40 (0.01) | 0.00 (-0.02,0.02) |  |
| Tilted disc | No | 264 | -0.40 (0.00) | Reference | 0.362 |
|  | Yes | 32 | -0.42 (0.01) | $\begin{array}{r} -0.02(- \\ 0.04,0.01) \end{array}$ |  |
|  | Missing | 1128 | -0.40 (0.01) | $\begin{array}{r} \hline-0.00(- \\ 0.02,0.01) \\ \hline \end{array}$ |  |
| Disc hemorrhage | No | 295 | -0.40 (0.00) | Reference | 0.891 |
|  | Yes | 2 | -0.39 (0.02) | 0.01 (-0.02,0.04) |  |
|  | Missing | 1127 | -0.40 (0.01) | $\begin{array}{r} \hline-0.00(- \\ 0.02,0.02) \\ \hline \end{array}$ |  |


| Arteriole narrowing | No | 295 | -0.40 (0.00) | Reference | 0.431 |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  | Yes | 2 | -0.52 (0.04) | $\begin{array}{r} -0.12(-0.20,- \\ 0.05) \end{array}$ |  |
|  | Missing | 1127 | -0.40 (0.01) | $\begin{array}{r} -0.00(- \\ 0.02,0.02) \end{array}$ |  |
| Venule narrowing | No | 293 | -0.40 (0.00) | Reference | 0.457 |
|  | Yes | 4 | -0.34 (0.04) | 0.06 (-0.01,0.14) |  |
|  | Missing | 1127 | -0.40 (0.01) | 0.00 (-0.02,0.02) |  |
| Baring of the lamina cribrosa | No | 85 | -0.41 (0.01) | Reference | 0.169 |
|  | Yes | 212 | -0.40 (0.00) | 0.02 (-0.00,0.03) |  |
|  | Missing | 1127 | -0.40 (0.01) | 0.01 (-0.01,0.03) |  |
| Baring of the circumlinear vessels | No | 208 | -0.40 (0.00) | Reference | 0.822 |
|  | Yes | 88 | -0.40 (0.01) | 0.00 (-0.01,0.02) |  |
|  | Missing | 1128 | -0.40 (0.01) | 0.00 (-0.02,0.02) |  |
| Vessels overpass | No | 292 | -0.40 (0.00) | Reference | 0.957 |
|  | Yes | 0 | - | - |  |
|  | Missing | 1132 | -0.40 (0.01) | 0.00 (-0.02,0.02) |  |
| Bayonetting | No | 205 | -0.40 (0.00) | Reference | 0.436 |
|  | Moderate | 75 | -0.39 (0.01) | 0.01 (-0.00,0.03) |  |
|  | Severe | 13 | -0.42 (0.01) | $\begin{array}{r} -0.02(- \\ 0.05,0.01) \end{array}$ |  |
|  | Missing | 1131 | -0.40 (0.01) | 0.00 (-0.01,0.02) |  |
| Nasalization of the vessels | No | 195 | -0.41 (0.01) | Reference | 0.539 |
|  | Yes | 101 | -0.39 (0.01) | 0.01 (-0.01,0.03) |  |
|  | Missing | 1128 | -0.40 (0.01) | 0.00 (-0.01,0.02) |  |
| Cilio-retinal vessels | No | 243 | -0.40 (0.00) | Reference | 0.158 |
|  | Yes | 54 | -0.39 (0.01) | 0.02 (0.00,0.03) |  |
|  | Missing | 1127 | -0.40 (0.01) | 0.00 (-0.01,0.02) |  |
| Gray crescent | No | 272 | -0.40 (0.00) | Reference | 0.762 |
|  | Yes | 25 | -0.39 (0.01) | 0.01 (-0.01,0.03) |  |
|  | Missing | 1127 | -0.40 (0.01) | 0.00 (-0.02,0.02) |  |
| Conus pigmentosus | No | 269 | -0.40 (0.00) | Reference | 0.950 |
|  | Yes | 28 | -0.40 (0.01) | 0.00 (-0.01,0.02) |  |
|  | Missing | 1127 | -0.40 (0.01) | 0.00 (-0.02,0.02) |  |
| Notching of neural rim | No | 271 | -0.40 (0.00) | Reference | 0.624 |
|  | Yes | 22 | -0.39 (0.01) | 0.02 (-0.02,0.05) |  |
|  | Missing | 1131 | -0.40 (0.01) | 0.00 (-0.01,0.02) |  |


| Pallor of the neural rim | No | 291 | $-0.40(0.00)$ | Reference | 0.607 |
| :--- | :--- | :--- | :--- | ---: | ---: |
|  | Yes | 6 | $-0.38(0.02)$ | $0.02(-0.01,0.06)$ |  |
|  | Missing | 1127 | $-0.40(0.01)$ | $0.00(-0.02,0.02)$ |  |

MD=mean deviation; OR=odds ratio; $\mathrm{Cl}=$ confidence interval

