**Additional Files**

Additional Tables (1-6)

Additional Figure (1)

**Additional Table 1.** **Mediating Roles of the Bone-Vascular Axis in Increased Insulin Resistance Attributable to Selected Pollutants Based on the Results of Single-Mediator Models.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Pollutants** | **MA (Days)** | **Outcome** | **Mediator** | **Mediation Effect†** | **Proportion Mediated**  **(%)** |
| PM2.5 | 2 | Insulin | sRANKL/OPG ratio | 0.090 (0.017, 0.185) | 33 |
| PNC100-560 | 3 | Insulin | sRANKL/OPG ratio | 0.071 (0.006, 0.155) | 39 |
| PSC5-100 | 3 | Insulin | sRANKL/OPG ratio | 0.129 (0.025, 0.268) | 47 |
| PNC100-560 | 3 | Insulin | BMP-2 | 0.004 (0.000, 0.009) | 3 |
| PSC5-100 | 5 | Insulin | BMP-2 | 0.007 (0.000, 0.015) | 3 |
| CO | 5 | Insulin | BMP-2 | 0.007 (0.002, 0.013) | 5 |
| PM2.5 | 1 | Insulin | IL-10 | 0.024 (0.003, 0.050) | 10 |
| PM2.5 | 2 | Insulin | IL-10 | 0.021 (0.004, 0.044) | 9 |
| CO | 2 | Insulin | IL-10 | 0.024 (0.004, 0.053) | 8 |
| CO | 5 | Insulin | IL-10 | 0.021 (0.004, 0.046) | 8 |
| CO | 7 | Insulin | IL-10 | 0.027 (0.005, 0.056) | 14 |
| PM2.5 | 1 | Insulin | IL-22 | 0.024 (0.003, 0.053) | 10 |
| PM2.5 | 2 | Insulin | IL-22 | 0.023 (0.003, 0.050) | 10 |
| CO | 5 | Insulin | IL-22 | 0.033 (0.006, 0.068) | 12 |
| CO | 7 | Insulin | IL-22 | 0.029 (0.003, 0.062) | 14 |
| PM2.5 | 3 | IR | OPG | -0.042 (-0.071, -0.019) | 44 |
| PM2.5 | 5 | IR | OPG | -0.042 (-0.071, -0.018) | 43 |
| PM2.5 | 7 | IR | OPG | -0.044 (-0.073, -0.019) | 53 |
| CO | 2 | IR | OPG | -0.023 (-0.051, -0.001) | 21 |
| CO | 3 | IR | OPG | -0.047 (-0.081, -0.020) | 34 |
| CO | 5 | IR | OPG | -0.052 (-0.089, -0.022) | 29 |
| CO | 7 | IR | OPG | -0.058 (-0.098, -0.023) | 39 |
| PM2.5 | 2 | IR | MCP-1 | -0.023 (-0.055, -0.001) | 19 |
| PM2.5 | 3 | IR | MCP-1 | -0.042 (-0.082, -0.009) | 42 |
| PM2.5 | 5 | IR | MCP-1 | -0.039 (-0.079, -0.003) | 34 |
| PM2.5 | 7 | IR | MCP-1 | -0.037 (-0.074, -0.006) | 38 |
| CO | 2 | IR | MCP-1 | -0.038 (-0.084, -0.006) | 29 |
| CO | 3 | IR | MCP-1 | -0.039 (-0.082, -0.008) | 32 |
| CO | 5 | IR | MCP-1 | -0.045 (-0.096, -0.001) | 24 |
| CO | 7 | IR | MCP-1 | -0.047 (-0.098, -0.004) | 29 |
| PM2.5 | 3 | IR | RANTES | -0.023 (-0.048, -0.005) | 26 |
| PM2.5 | 5 | IR | RANTES | -0.027 (-0.053, -0.006) | 27 |
| PM2.5 | 7 | IR | RANTES | -0.025 (-0.05, -0.006) | 30 |
| CO | 5 | IR | RANTES | -0.025 (-0.053, -0.005) | 15 |
| CO | 7 | IR | RANTES | -0.027 (-0.056, -0.006) | 19 |
| PM2.5 | 2 | Adiponectin | OPG | 0.063 (0.025, 0.110) | 42 |
| PM2.5 | 3 | Adiponectin | OPG | 0.076 (0.039, 0.122) | 40 |
| PM2.5 | 5 | Adiponectin | OPG | 0.082 (0.043, 0.128) | 51 |
| PM2.5 | 7 | Adiponectin | OPG | 0.081 (0.042, 0.127) | 51 |
| CO | 5 | Adiponectin | OPG | 0.111 (0.060, 0.172) | 66 |
| CO | 7 | Adiponectin | OPG | 0.117 (0.062, 0.182) | 60 |
| PM2.5 | 2 | Adiponectin | IL-2 | 0.028 (0.003, 0.063) | 16 |
| PM2.5 | 3 | Adiponectin | IL-2 | 0.022 (0.002, 0.051) | 10 |
| PM2.5 | 5 | Adiponectin | IL-2 | 0.021 (0.002, 0.048) | 11 |
| PM2.5 | 7 | Adiponectin | IL-2 | 0.021 (0.001, 0.049) | 11 |
| PNC5-100 | 3 | Adiponectin | IL-2 | -0.032 (-0.075, -0.003) | 18 |
| CO | 5 | Adiponectin | IL-2 | 0.030 (0.003, 0.069) | 13 |
| CO | 7 | Adiponectin | IL-2 | 0.026 (0.001, 0.001) | 10 |
| PM2.5 | 2 | Adiponectin | CXCL-8 | 0.034 (0.008, 0.071) | 22 |
| PM2.5 | 3 | Adiponectin | CXCL-8 | 0.032 (0.007, 0.066) | 18 |
| PM2.5 | 5 | Adiponectin | CXCL-8 | 0.028 (0.006, 0.059) | 16 |
| PM2.5 | 7 | Adiponectin | CXCL-8 | 0.023 (0.002, 0.051) | 13 |
| PSC100-560 | 2 | Adiponectin | CXCL-8 | 0.020 (0.001, 0.049) | 14 |
| CO | 5 | Adiponectin | CXCL-8 | 0.041 (0.009, 0.084) | 24 |
| CO | 7 | Adiponectin | CXCL-8 | 0.034 (0.004, 0.075) | 26 |
| PM2.5 | 2 | Adiponectin | IL-10 | 0.022 (0.002, 0.049) | 13 |
| PM2.5 | 3 | Adiponectin | IL-10 | 0.012 (0.000, 0.031) | 7 |
| PM2.5 | 5 | Adiponectin | IL-10 | 0.018 (0.001, 0.04) | 10 |
| PM2.5 | 7 | Adiponectin | IL-10 | 0.026 (0.001, 0.056) | 14 |
| PNC5-100 | 7 | Adiponectin | IL-10 | -0.027 (-0.065, -0.001) | 13 |
| CO | 5 | Adiponectin | IL-10 | 0.021 (0.001, 0.049) | 12 |
| CO | 7 | Adiponectin | IL-10 | 0.028 (0.002, 0.062) | 13 |
| PM2.5 | 2 | Adiponectin | MCP-1 | 0.080 (0.031, 0.143) | 42 |
| PM2.5 | 3 | Adiponectin | MCP-1 | 0.079 (0.031, 0.138) | 38 |
| PM2.5 | 5 | Adiponectin | MCP-1 | 0.084 (0.034, 0.142) | 43 |
| PM2.5 | 7 | Adiponectin | MCP-1 | 0.074 (0.030, 0.127) | 39 |
| PSC100-560 | 5 | Adiponectin | MCP-1 | 0.051 (0.010, 0.106) | 27 |
| CO | 5 | Adiponectin | MCP-1 | 0.114 (0.049, 0.194) | 58 |
| CO | 7 | Adiponectin | MCP-1 | 0.106 (0.043, 0.182) | 45 |
| PM2.5 | 2 | Adiponectin | sCD163 | 0.026 (0.004, 0.058) | 16 |
| PM2.5 | 3 | Adiponectin | sCD163 | 0.020 (0.003, 0.046) | 11 |
| PM2.5 | 5 | Adiponectin | sCD163 | 0.025 (0.004, 0.051) | 15 |
| PM2.5 | 7 | Adiponectin | sCD163 | 0.024 (0.004, 0.049) | 15 |
| PSC100-560 | 1 | Adiponectin | sCD163 | 0.019 (0.001, 0.047) | 20 |
| CO | 5 | Adiponectin | sCD163 | 0.031 (0.006, 0.065) | 19 |
| CO | 7 | Adiponectin | sCD163 | 0.032 (0.006, 0.066) | 16 |
| PM2.5 | 2 | Adiponectin | IL-1RA | 0.029 (0.002, 0.067) | 18 |
| PM2.5 | 3 | Adiponectin | IL-1RA | 0.022 (0.001, 0.055) | 12 |
| PM2.5 | 5 | Adiponectin | IL-1RA | 0.026 (0.001, 0.058) | 15 |
| PM2.5 | 7 | Adiponectin | IL-1RA | 0.026 (0.001, 0.059) | 15 |
| CO | 5 | Adiponectin | IL-1RA | 0.033 (0.003, 0.076) | 19 |
| CO | 7 | Adiponectin | SIL1RA | 0.034 (0.002, 0.078) | 16 |
| PSC5-100 | 1 | Resistin | OPG | -0.04 (-0.095, -0.002) | 29 |
| PNC100-560 | 2 | Resistin | BMP-4 | -0.04 (-0.087, -0.005) | 27 |
| PNC5-100 | 7 | CNTF | sRANKL/OPG ratio | 0.261 (0.034, 0.523) | 60 |
| PM2.5 | 2 | CNTF | BMP-4 | -0.050 (-0.095, -0.010) | 42 |
| PM2.5 | 5 | CNTF | BMP-4 | -0.067 (-0.104, -0.036) | 44 |
| PM2.5 | 7 | CNTF | BMP-4 | -0.067 (-0.105, -0.036) | 54 |
| PM2.5 | 5 | CO | BMP-4 | -0.077 (-0.124, -0.037) | 47 |
| PM2.5 | 7 | CO | BMP-4 | -0.083 (-0.130, -0.042) | 63 |
| PM2.5 | 2 | CNTF | RANTES | -0.020 (-0.046, -0.002) | 17 |
| PM2.5 | 5 | CNTF | RANTES | -0.024 (-0.052, -0.001) | 17 |
| PM2.5 | 7 | CNTF | RANTES | -0.022 (-0.048, -0.002) | 17 |
| CO | 5 | CNTF | RANTES | -0.028 (-0.060, -0.005) | 25 |
| CO | 7 | CNTF | RANTES | -0.028 (-0.060, -0.004) | 22 |

†We assessed possible mediators of the associations between air pollution and health outcomes; the statistical significance (*p*-value <0.05) of the mediation effects was determined by examining whether the 95% confidence interval (CI) contains 0. Moving average (MA) concentrations of air pollutants over the last 24 hours prior to each participant’s clinic visit are presented as 1 MA day, 1 to 2 days as 2 MA days, 1 to 3 days as 3 MA days and up to 7 MA days. Abbreviations: OPG, osteoprotegerin; sRANKL, soluble receptor activator of nuclear factor-κB ligand; BMP, bone morphogenetic protein; sIRα, soluble insulin receptor ectodomain; IL, interleukin; sCD163, soluble CD163; HGF, hepatocyte growth factor; CNTF, ciliary neurotrophic factor; CCL, C-C chemokine ligand; CXCL-8, C-X-C chemokine motif ligand-8; sIL1RA, soluble IL-1 receptor antagonist; PM2.5, particulate matter in diameter <2.5 μm; CO, carbon monoxide; PNCX, number concentration of particulate in given size ranges (nm); PSCX, surface area concentration of particulate in given size ranges (nm).

**Additional Table 2.** **Mediating Roles of the Bone-Vascular Axis in elevated Immune-Inflammatory Responses Attributable to Selected Pollutants Based on the Results of Single-Mediator Models.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Pollutants** | **MA (Days)** | **Outcome** | **Mediator** | **Mediation Effect†** | **Proportion Mediated**  **(%)** |
| PM2.5 | 2 | CCL-2 | OPG | 0.128 (0.055, 0.209) | 40 |
| PM2.5 | 3 | CCL-2 | OPG | 0.159 (0.096, 0.230) | 40 |
| PM2.5 | 5 | CCL-2 | OPG | 0.159 (0.103, 0.222) | 41 |
| PM2.5 | 7 | CCL-2 | OPG | 0.161 (0.102, 0.228) | 47 |
| CO | 3 | CCL-2 | OPG | 0.182 (0.098, 0.275) | 42 |
| CO | 5 | CCL-2 | OPG | 0.2130 (0.137, 0.300) | 41 |
| CO | 7 | CCL-2 | OPG | 0.227 (0.146, 0.319) | 47 |
| PNC100-560 | 7 | CCL-2 | OPG | 0.567 (0.230, 0.934) | 43 |
| PNC100-560 | 7 | CCL-2 | BMP-4 | 0.200 (0.008, 0.459) | 19 |
| CO | 2 | CCL-2 | BMP-4 | 0.055 (0.002, 0.123) | 14 |
| PM2.5 | 5 | sCD163 | OPG | 0.089 (0.053, 0.132) | 49 |
| PM2.5 | 3 | sCD163 | BMP-4 | 0.030 (0.002, 0.067) | 20 |
| PNC100-560 | 7 | sCD163 | BMP-4 | 0.146 (0.013, 0.325) | 19 |
| PM2.5 | 3 | IL-10 | BMP-2 | 0.015 (0.003, 0.032) | 17 |
| PM2.5 | 5 | IL-10 | BMP-2 | 0.010 (0.001, 0.024) | 9 |
| CO | 5 | IL-10 | BMP-2 | 0.017 (0.003, 0.038) | 13 |
| CO | 7 | IL-10 | BMP-2 | 0.016 (0.002, 0.036) | 8 |
| PM2.5 | 3 | IL-22 | BMP-2 | 0.027 (0.008, 0.052) | 22 |
| PM2.5 | 5 | IL-22 | BMP-2 | 0.020 (0.003, 0.041) | 19 |
| CO | 3 | IL-22 | BMP-2 | 0.029 (0.005, 0.059) | 18 |
| CO | 5 | IL-22 | BMP-2 | 0.033 (0.008, 0.063) | 21 |
| PM2.5 | 5 | CCL-5 | OPG | 0.134 (0.087, 0.187) | 52 |
| PNC100-560 | 3 | CCL-5 | OPG | 0.219 (0.008, 0.442) | 26 |
| PNC100-560 | 5 | CCL-5 | OPG | 0.338 (0.115, 0.579) | 30 |
| PNC100-560 | 7 | CCL-5 | OPG | 0.451 (0.183, 0.744) | 35 |
| PM2.5 | 2 | CCL-5 | BMP-4 | 0.042 (0.007, 0.089) | 22 |
| PM2.5 | 3 | CCL-5 | BMP-4 | 0.050 (0.017, 0.094) | 23 |
| PM2.5 | 5 | CCL-5 | BMP-4 | 0.049 (0.016, 0.09) | 18 |
| PM2.5 | 7 | CCL-5 | BMP-4 | 0.052 (0.019, 0.094) | 24 |
| CO | 5 | CCL-5 | BMP-4 | 0.059 (0.020, 0.110) | 20 |
| CO | 7 | CCL-5 | BMP-4 | 0.064 (0.023, 0.117) | 24 |

†We assessed possible mediators of the associations between air pollution and health outcomes; the statistical significance (*p*-value <0.05) of the mediation effects was determined by examining whether the 95% confidence interval (CI) contains 0. Moving average (MA) concentrations of air pollutants over the last 24 hours prior to each participant’s clinic visit are presented as 1 MA day, 1 to 2 days as 2 MA days, 1 to 3 days as 3 MA days and up to 7 MA days. Abbreviations: OPG, osteoprotegerin; BMP, bone morphogenetic protein; IL, interleukin; sCD163, soluble CD163; CCL, C-C chemokine ligand; PM2.5, particulate matter in diameter <2.5 μm; PNCX, number concentration of particulate in given size ranges (nm); CO, carbon monoxide.

**Additional Table 3.** **Mediating Roles of Immune-Inflammatory Indicators in Selected Pollutants-Associated Activation of the Bone-Vascular Axis Based on the Results of Single-Mediator Models.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Pollutants** | **MA (Days)** | **Outcome** | **Mediator** | **Mediation Effect†** | **Proportion Mediated**  **(%)** |
| PM2.5 | 2 | OPG | IL-2 | 0.027 (0.005, 0.058) | 14 |
| PM2.5 | 3 | OPG | IL-2 | 0.022 (0.004, 0.047) | 8 |
| PM2.5 | 5 | OPG | IL-2 | 0.020 (0.003, 0.042) | 6 |
| PM2.5 | 7 | OPG | IL-2 | 0.019 (0.002, 0.043) | 6 |
| PNC5-100 | 1 | OPG | IL-2 | -0.087 (-0.204, -0.001) | 11 |
| CO | 3 | OPG | IL-2 | 0.029 (0.004, 0.062) | 9 |
| CO | 5 | OPG | IL-2 | 0.027 (0.004, 0.058) | 7 |
| CO | 7 | OPG | IL-2 | 0.024 (0.001, 0.055) | 5 |
| PM2.5 | 2 | OPG | CXCL-8 | 0.038 (0.009, 0.075) | 17 |
| PM2.5 | 3 | OPG | CXCL-8 | 0.034 (0.009, 0.066) | 12 |
| PM2.5 | 5 | OPG | CXCL-8 | 0.033 (0.009, 0.063) | 11 |
| PM2.5 | 7 | OPG | CXCL-8 | 0.027 (0.003, 0.057) | 19 |
| CO | 3 | OPG | CXCL-8 | 0.037 (0.005, 0.078) | 13 |
| CO | 5 | OPG | CXCL-8 | 0.047 (0.013, 0.089) | 12 |
| CO | 7 | OPG | CXCL-8 | 0.041 (0.007, 0.084) | 10 |
| PM2.5 | 2 | OPG | IL-10 | 0.025 (0.009, 0.046) | 12 |
| PM2.5 | 3 | OPG | IL-10 | 0.025 (0.009, 0.046) | 5 |
| PM2.5 | 5 | OPG | IL-10 | 0.021 (0.008, 0.037) | 7 |
| PM2.5 | 7 | OPG | IL-10 | 0.031 (0.015, 0.052) | 10 |
| CO | 5 | OPG | IL-10 | 0.024 (0.007, 0.045) | 6 |
| CO | 7 | OPG | IL-10 | 0.032 (0.013, 0.056) | 8 |
| PNC5-100 | 5 | OPG | IL-10 | -0.338 (-0.661, -0.085) | 15 |
| PM2.5 | 2 | OPG | IL-22 | 0.028 (0.004, 0.056) | 13 |
| PM2.5 | 3 | OPG | IL-22 | 0.027 (0.005, 0.053) | 10 |
| PM2.5 | 5 | OPG | IL-22 | 0.029 (0.007, 0.054) | 9 |
| PM2.5 | 7 | OPG | IL-22 | 0.024 (0.003, 0.048) | 8 |
| CO | 5 | OPG | IL-22 | 0.039 (0.008, 0.074) | 10 |
| CO | 7 | OPG | IL-22 | 0.034 (0.005, 0.068) | 8 |
| PM2.5 | 2 | OPG | CCL-2 | 0.146 (0.075, 0.225) | 49 |
| PM2.5 | 3 | OPG | CCL-2 | 0.147 (0.087, 0.215) | 45 |
| PM2.5 | 5 | OPG | CCL-2 | 0.152 (0.101, 0.209) | 43 |
| PM2.5 | 7 | OPG | CCL-2 | 0.136 (0.085, 0.193) | 40 |
| CO | 5 | OPG | CCL-2 | 0.135 (0.054, 0.222) | 39 |
| CO | 7 | OPG | CCL-2 | 0.198 (0.123, 0.281) | 43 |
| PM2.5 | 3 | OPG | CCL-5 | 0.078 (0.025, 0.136) | 33 |
| PM2.5 | 5 | OPG | CCL-5 | 0.099 (0.055, 0.149) | 35 |
| PM2.5 | 7 | OPG | CCL-5 | 0.090 (0.045, 0.140) | 32 |
| CO | 3 | OPG | CCL-5 | 0.037 (-0.027, 0.104) | 17 |
| CO | 5 | OPG | CCL-5 | 0.097 (0.038, 0.161) | 29 |
| CO | 7 | OPG | CCL-5 | 0.101 (0.042, 0.166) | 26 |
| PNC5-100 | 5 | OPG | CCL-5 | -1.233 (-2.267, -0.266) | 40 |
| PM2.5 | 2 | OPG | sCD163 | 0.040 (0.010, 0.077) | 18 |
| PM2.5 | 3 | OPG | sCD163 | 0.031 (0.008, 0.060) | 12 |
| PM2.5 | 5 | OPG | sCD163 | 0.038 (0.017, 0.064) | 13 |
| PM2.5 | 7 | OPG | sCD163 | 0.036 (0.016, 0.062) | 13 |
| CO | 5 | OPG | sCD163 | 0.045 (0.018, 0.079) | 12 |
| CO | 7 | OPG | sCD163 | 0.047 (0.020, 0.081) | 12 |
| PM2.5 | 2 | OPG | SIL1RA | 0.077 (0.026, 0.134) | 33 |
| PM2.5 | 3 | OPG | SIL1RA | 0.059 (0.015, 0.109) | 22 |
| PM2.5 | 5 | OPG | SIL1RA | 0.067 (0.030, 0.109) | 22 |
| PM2.5 | 7 | OPG | SIL1RA | 0.068 (0.031, 0.112) | 23 |
| CO | 2 | OPG | SIL1RA | 0.061 (0.005, 0.124) | 22 |
| CO | 5 | OPG | SIL1RA | 0.079 (0.028, 0.139) | 21 |
| CO | 7 | OPG | SIL1RA | 0.085 (0.034, 0.145) | 21 |
| CO | 3 | sRANKL/OPG ratio | IL-22 | 0.059 (0.012, 0.112) | 22 |
| CO | 3 | sRANKL/OPG ratio | sIL1RA | 0.068 (0.005, 0.143) | 27 |
| PM2.5 | 3 | BMP-2 | IL-10 | 0.003 (0.00004, 0.007) | 16 |
| CO | 5 | BMP-2 | IL-10 | 0.006 (0.002, 0.011) | 22 |
| PM2.5 | 3 | BMP-2 | IL-10 | 0.004 (0.001, 0.008) | 18 |
| CO | 5 | BMP-2 | IL-10 | 0.005 (0.001, 0.011) | 21 |
| CO | 5 | BMP-2 | IL-10 | 0.005 (0.001, 0.011) | 19 |
| PM2.5 | 3 | BMP-4 | CCL-5 | -0.063 (-0.121, -0.018) | 26 |
| PM2.5 | 5 | BMP-4 | CCL-5 | -0.076 (-0.131, -0.032) | 26 |
| PM2.5 | 7 | BMP-4 | CCL-5 | -0.069 (-0.121, -0.028) | 24 |
| CO | 2 | BMP-4 | CCL-5 | -0.029 (-0.088, 0.022) | 13 |
| CO | 5 | BMP-4 | CCL-5 | -0.079 (-0.145, -0.027) | 25 |
| CO | 7 | BMP-4 | CCL-5 | -0.080 (-0.147, -0.028) | 24 |

†We assessed possible mediators of the associations between air pollution and health outcomes; the statistical significance (*p*-value <0.05) of the mediation effects was determined by examining whether the 95% confidence interval (CI) contains 0. Moving average (MA) concentrations of air pollutants over the last 24 hours prior to each participant’s clinic visit are presented as 1 MA day, 1 to 2 days as 2 MA days, 1 to 3 days as 3 MA days and up to 7 MA days. Abbreviations: OPG, osteoprotegerin; BMP, bone morphogenetic protein; IL, interleukin; sCD163, soluble CD163; CCL, C-C chemokine ligand; CXCL-8, C-X-C chemokine motif ligand-8; sIL1RA, soluble IL-1 receptor antagonist; PM2.5, particulate matter in diameter <2.5 μm; PNCX, number concentration of particulate in given size ranges (nm); CO, carbon monoxide.

**Additional Table 4.** **Results of Mediation Analyses with Multiple Mediators.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **MA (Days)** | **Outcome** | **Mediation Effect†** | **Proportion Mediated**  **(%)** |
| PM2.5 | 1 | Insulin | 0.023 (0.000, 0.055) | 8.2 |
| PM2.5 | 3 | sIRα | -0.052 (-0.085, -0.027) | 48.9 |
| PM2.5 | 5 | sIRα | -0.056 (-0.103, -0.020) | 56.5 |
| PM2.5 | 7 | sIRα | -0.059 (-0.094, -0.023) | 71.1 |
| PM2.5 | 3 | CCL-2 | 0.149 (0.087, 0.234) | 50.6 |
| PM2.5 | 5 | CCL-2 | 0.128 (0.074, 0.206) | 33.6 |
| PM2.5 | 7 | CCL-2 | 0.139 (0.082, 0.236) | 43.2 |
| PM2.5 | 3 | CCL-5 | 0.163 (0.107, 0.194) | 60.6 |
| PM2.5 | 5 | CCL-5 | 0.169 (0.093, 0.212) | 60.2 |
| PM2.5 | 7 | CCL-5 | 0.175 (0.105, 0.219) | 79.0 |
| PM2.5 | 3 | IL-22 | 0.079 (0.043, 0.105) | 72.2 |
| PM2.5 | 2 | OPG | 0.104 (0.060, 0.148) | 54.3 |
| PM2.5 | 3 | OPG | 0.057 (0.038, 0.067) | 21.3 |
| PM2.5 | 5 | OPG | 0.148 (0.075, 0.226) | 50.0 |
| PM2.5 | 7 | OPG | 0.049 (0.032, 0.059) | 16.6 |
| PM2.5 | 3 | sRANKL/OPG ratio | 0.044 (0.011, 0.113) | 23.6 |
| PM2.5 | 3 | BMP-2 | 0.009 (0.006, 0.013) | 34.5 |
| PM2.5 | 7 | BMP-2 | 0.012 (0.008, 0.018) | 68.0 |
| PM2.5 | 2 | CNTF | -0.086 (-0.104, -0.052) | 36.1 |
| PM2.5 | 5 | CNTF | -0.103 (-0.132, -0.053) | 33.3 |
| CO | 5 | sIRα | -0.063 (-0.115, -0.023) | 34.4 |
| CO | 7 | sIRα | -0.056 (-0.118, -0.015) | 35.2 |
| CO | 5 | CCL-2 | 0.175 (0.114, 0.277) | 33.1 |
| CO | 7 | CCL-2 | 0.197 (0.112, 0.311) | 44.3 |
| CO | 5 | CCL-5 | 0.217 (0.113, 0.262) | 61.1 |
| CO | 7 | CCL-5 | 0.244 (0.150, 0.303) | 84.9 |
| CO | 5 | IL-22 | 0.109 (0.057, 0.146) | 90.6 |
| CO | 2 | OPG | 0.060 (0.024, 0.090) | 36.5 |
| CO | 5 | OPG | 0.054 (0.030, 0.070) | 17.9 |
| CO | 3 | BMP-2 | 0.009 (0.006, 0.013) | 35.8 |
| CO | 5 | BMP-2 | 0.011 (0.007, 0.015) | 30.8 |
| CO | 7 | BMP-2 | 0.013 (0.008, 0.020) | 44.0 |

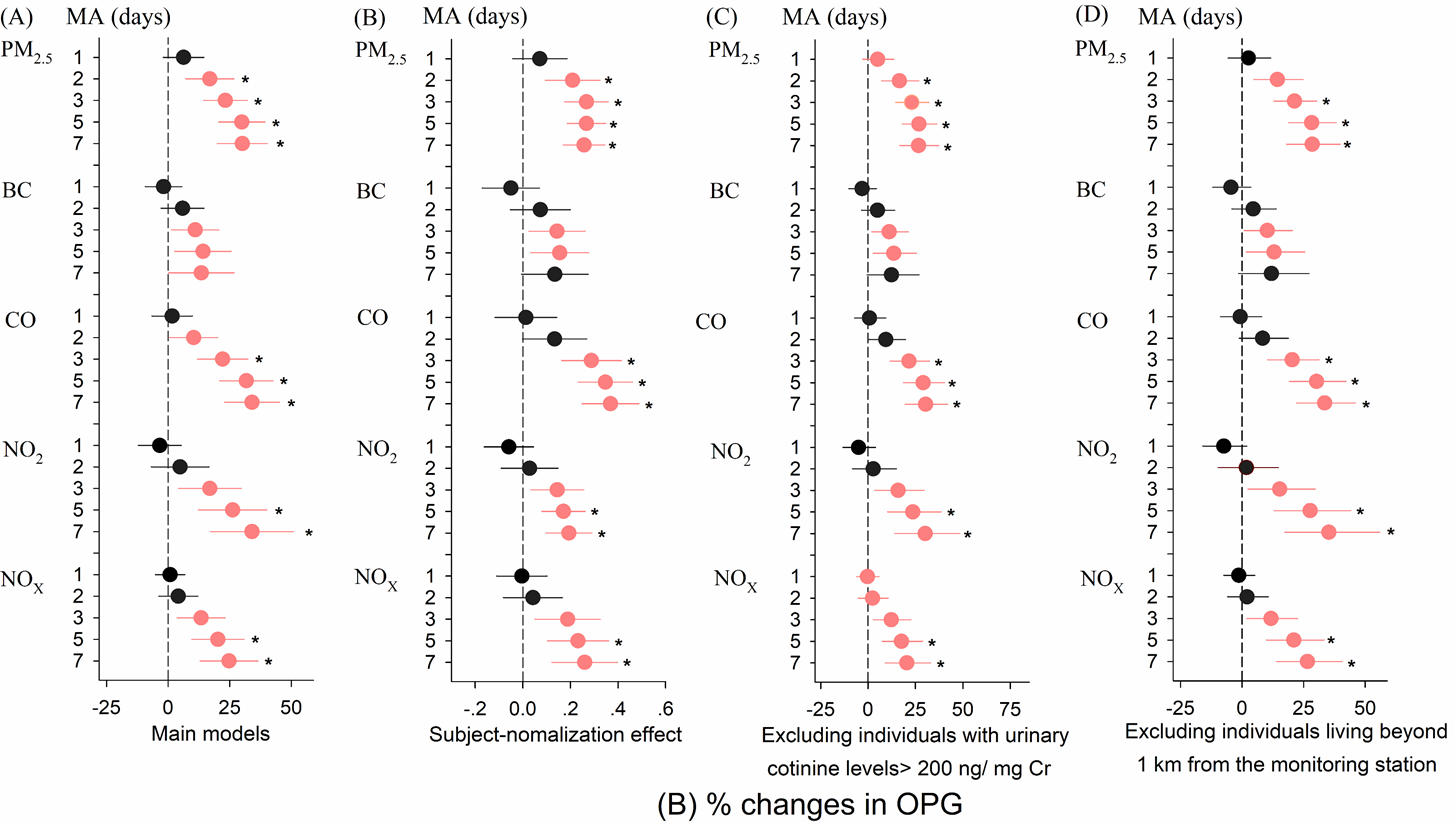
†We assessed possible mediators of the associations between air pollution and health outcomes; the statistical significance (*p*-value <0.05) of the mediation effects was determined by examining whether the 95% confidence interval contains 0. Moving average (MA) concentrations of air pollutants over the last 24 hours prior to each participant’s clinic visit are presented as 1 MA day, 1 to 2 days as 2 MA days, 1 to 3 days as 3 MA days and up to 7 MA days. Abbreviations: OPG, osteoprotegerin; sRANKL, soluble receptor activator of nuclear factor-κB ligand; BMP, bone morphogenetic protein; sIRα, soluble insulin receptor ectodomain; IL, interleukin; sCD163, soluble CD163; CNTF, ciliary neurotrophic factor; CCL, C-C chemokine ligand; CXCL-8, C-X-C chemokine motif ligand-8; PM2.5, particulate matter in diameter <2.5 μm; CO, carbon monoxide.

**Additional Figure 1. Sensitivity Analyses**

(1)Main models; (2) Subject-nomalization effect(all selected biomarkers were normalized by first subtracting the mean value of the individual from the absolute value of the measurement, dividing the total by the standard deviation value of the individuals); (3) Main models excluding individuals with urinary cotinine levels above 200 ng/ mg Cr; (4) Main models excluding individuals living beyond 1 kilometer from the air monitoring station.

Error bars indicate 95% confidence intervals. Significant associations (*p*-value <0.05) are shown in red; Bonferroni corrections with significance (*p*-value<0.0025) are indicated by asterisks. Moving average concentrations of air pollutants over the last 24 hours prior to each participant’s clinic visit are presented as 1 MA day, 1 to 2 days as 2 MA days, 1 to 3 days as 3 MA days and up to 7 MA days. Abbreviations: MA, moving average;PM2.5, particulate matter in diameter <2.5 μm; BC, black carbon; CO, carbon monoxide; NO2, nitrogen dioxide; NOx, oxides of nitrogen; OPG, osteoprotegerin; BMP, bone morphogenetic protein; IL, interleukin.







 **Additional Table 5.** **Covariates Included in Final Models.**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcomes** |  |  |  |  |  | **Covariates** |  |  |  |  |  |
| **Age** | **Sex** | **BMI** | **WHR** | **DOW** | **Urinary cotinine** | **Urinary cortisol** | **Month of blood withdrawal** | **Temp** | **RH** | **Season** |
| OPG |  |  |  |  |  |  |  |  |  |  |  |
| sRANKL/OPG ratio |  |  |  |  |  |  |  |  |  |  |  |
| BMP-2 |  |  |  |  |  |  |  |  |  |  |  |
| BMP-4 |  |  |  |  |  |  |  |  |  |  |  |
| Insulin |  |  |  |  |  |  |  |  |  |  |  |
| sIRα |  |  |  |  |  |  |  |  |  |  |  |
| IL-2 |  |  |  |  |  |  |  |  |  |  |  |
| IL-10 |  |  |  |  |  |  |  |  |  |  |  |
| IL-22 |  |  |  |  |  |  |  |  |  |  |  |
| sCD163 |  |  |  |  |  |  |  |  |  |  |  |
| HGF |  |  |  |  |  |  |  |  |  |  |  |
| BTC |  |  |  |  |  |  |  |  |  |  |  |
| CNTF |  |  |  |  |  |  |  |  |  |  |  |
| CCL-2 |  |  |  |  |  |  |  |  |  |  |  |
| CCL-5 |  |  |  |  |  |  |  |  |  |  |  |
| CXCL-8 |  |  |  |  |  |  |  |  |  |  |  |
| sIL1RA |  |  |  |  |  |  |  |  |  |  |  |
| Adiponectin |  |  |  |  |  |  |  |  |  |  |  |
| Leptin |  |  |  |  |  |  |  |  |  |  |  |
| Resistin |  |  |  |  |  |  |  |  |  |  |  |

Abbreviations: BMI, body mass index; WHR, waist-hip ratio; DOW, day of the week; Temp, temperature; RH, relative humidity; OPG, osteoprotegerin; sRANKL, soluble receptor activator of nuclear factor-κB ligand; BMP, bone morphogenetic protein; sIRα, soluble insulin receptor ectodomain; IL, interleukin; sCD163, soluble CD163; HGF, hepatocyte growth factor; BTC, betacellulin; CNTF, ciliary neurotrophic factor; CCL, C-C chemokine ligand; CXCL-8, C-X-C chemokine motif ligand-8; sIL1RA, soluble IL-1 receptor antagonist.

**Additional Table 6. Spearman Correlation Coefficients for** **Measured Biomarkers.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Biomarkers** | OPG | sRANKL | BMP-2 | BMP-4 | Insulin | sIRα | IL-2 | IL-10 | IL-22 | sCD163 | HGF | BTC | CNTF | CCL-2 | CCL-5 | CXCL-8 | sIL1RA | Adiponectin | Resistin | Leptin |
| OPG | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| sRANKL | 0.03 | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| BMP-2 | 0.04 | **0.38** | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| BMP-4 | **-0.14** | **0.50** | **0.34** | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Insulin | -0.01 | **0.16** | **0.25** | 0.07 | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| sIRα | **-0.36** | 0.01 | -0.07 | 0.01 | 0.05 | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| IL-2 | **0.24** | **0.16** | **0.21** | **0.20** | **0.12** | **-0.14** | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |
| IL-10 | **0.17** | **0.22** | **0.45** | **0.30** | **0.18** | -0.09 | **0.51** | 1 |  |  |  |  |  |  |  |  |  |  |  |  |
| IL-22 | **0.25** | **0.59** | **0.37** | **0.23** | **0.12** | **-0.11** | **0.37** | **0.57** | 1 |  |  |  |  |  |  |  |  |  |  |  |
| sCD163 | **0.36** | 0.02 | -0.02 | **-0.20** | -0.01 | -0.10 | **0.13** | -0.01 | 0.03 | 1 |  |  |  |  |  |  |  |  |  |  |
| HGF | **0.31** | **0.39** | **0.42** | **0.34** | **0.17** | **-0.18** | **0.28** | **0.33** | **0.27** | **0.15** | 1 |  |  |  |  |  |  |  |  |  |
| BTC | **0.37** | **0.47** | **0.17** | -0.01 | 0.07 | -0.05 | **0.37** | **0.30** | **0.63** | **0.31** | **0.14** | 1 |  |  |  |  |  |  |  |  |
| CNTF | -0.06 | **0.84** | **0.26** | **0.50** | **0.13** | 0.04 | **0.13** | **0.22** | **0.51** | -0.05 | **0.28** | **0.44** | 1 |  |  |  |  |  |  |  |
| CCL-2 | **0.45** | **0.15** | **0.17** | 0.04 | 0.09 | **-0.26** | **0.37** | **0.30** | **0.25** | **0.34** | **0.31** | **0.29** | 0.09 | 1 |  |  |  |  |  |  |
| CCL-5 | **0.49** | **-0.13** | **-0.13** | **-0.40** | -0.03 | **-0.13** | -0.06 | **-0.23** | -0.08 | **0.41** | 0.03 | **0.17** | **-0.26** | **0.21** | 1 |  |  |  |  |  |
| CXCL-8 | **0.30** | 0.02 | 0.10 | 0.05 | 0.03 | **-0.15** | **0.34** | **0.25** | **0.21** | **0.11** | 0.06 | **0.35** | 0.02 | **0.36** | **0.14** | 1 |  |  |  |  |
| sIL1RA | **0.39** | **0.37** | **0.20** | -0.02 | **0.15** | **-0.11** | **0.34** | **0.36** | **0.66** | **0.21** | **0.23** | **0.66** | **0.30** | **0.36** | **0.23** | **0.39** | 1 |  |  |  |
| Adiponectin | **0.38** | -0.08 | 0.06 | **-0.12** | -0.06 | **-0.14** | **0.20** | **0.13** | 0.07 | **0.14** | 0.03 | **0.20** | -0.09 | **0.23** | **0.13** | **0.27** | **0.17** | 1 |  |  |
| Resistin | **0.13** | **0.27** | **0.15** | **0.37** | 0.10 | **-0.17** | **0.20** | **0.25** | **0.16** | 0.08 | **0.41** | 0.09 | **0.37** | **0.22** | **-0.15** | **0.15** | **0.18** | -0.01 | 1 |  |
| Leptin | 0.06 | 0.09 | 0.10 | 0.03 | 0.01 | -0.04 | 0.07 | -0.02 | 0.01 | 0.05 | **0.21** | -0.03 | 0.07 | -0.05 | -0.11 | -0.09 | 0.09 | 0.02 | **0.20** | 1 |

Bolded correlation coefficients indicate *p*-value <0.05; bolded and underlined correlation coefficients represent Boniferrini correction (*p*-value <0.0025). Abbreviations: OPG, osteoprotegerin; sRANKL, soluble receptor activator of nuclear factor-κB ligand; BMP, bone morphogenetic protein; sIRα, soluble insulin receptor ectodomain; IL, interleukin; sCD163, soluble CD163; HGF, hepatocyte growth factor; BTC, betacellulin; CNTF, ciliary neurotrophic factor; CCL, C-C chemokine ligand; CXCL-8, C-X-C chemokine motif ligand-8; sIL1RA, soluble IL-1 receptor antagonist