# Triangulating evidence of the cause-effect relationship between sclerostin inhibition and cardiovascular outcomes

## Tables

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| **Outcome** | **Method** | **Fixed** | | | | | | | **Random** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **r2** | **w (kb)** | **Beta** | **95% CI** | **SE** | **Pval** | **Instruments** | **r2** | **w (kb)** | **Beta** | **95% CI** | **SE** | **Pval** | **Instruments** |
| bmd | Top SNP | 0.00 | 250000 | 0.93 | 0.84, 1.02 | 0.05 | 4.8e-92 | 1 | 0.00 | 250000 | 1.12 | 1.02, 1.23 | 0.06 | 3.9e-92 | 1 |
| bmd | Pruning | 0.10 | 250000 | 1.03 | 0.95, 1.12 | 0.04 | 1.7e-132 | 2 | 0.10 | 250000 | 1.12 | 1.02, 1.23 | 0.06 | 3.9e-92 | 1 |
| bmd |  | 0.30 | 250000 | 1.00 | 0.93, 1.08 | 0.04 | 6.2e-144 | 3 | 0.30 | 250000 | 1.05 | 0.96, 1.15 | 0.05 | 5.2e-101 | 2 |
| bmd |  | 0.50 | 250000 | 1.00 | 0.93, 1.08 | 0.04 | 6.2e-144 | 3 | 0.50 | 250000 | 1.05 | 0.96, 1.15 | 0.05 | 5.2e-101 | 2 |
| bmd |  | 0.70 | 250000 | 0.57 | 0.1, 1.04 | 0.24 | 1.7e-02 | 5 | 0.70 | 250000 | 1.05 | 0.96, 1.15 | 0.05 | 5.2e-101 | 2 |
| bmd | PCA | 99.29 | 3 | 0.84 | 0.76, 0.92 | 0.04 | 6.9e-82 | 75 | 99.58 | 1 | 0.93 | 0.78, 1.08 | 0.07 | 1.2e-32 | 22 |
| bmd |  | 99.92 | 5 | 0.94 | 0.87, 1.02 | 0.04 | 2.1e-121 | 75 | 99.97 | 2 | 1.06 | 0.96, 1.16 | 0.05 | 3.6e-92 | 22 |

| **Outcome** | **Method** | **Fixed** | | | | | | | **Random** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **r2** | **w (kb)** | **OR** | **95% CI** | **SE** | **Pval** | **Instruments** | **r2** | **w (kb)** | **OR** | **95% CI** | **SE** | **Pval** | **Instruments** |
| hf | Top SNP | 0.00 | 250000 | 0.18 | 0.09, 0.37 | 0.36 | 2.5e-06 | 1 | 0.00 | 250000 | 0.12 | 0.05, 0.28 | 0.43 | 7.7e-07 | 1 |
| hf | Pruning | 0.10 | 250000 | 0.15 | 0.08, 0.29 | 0.33 | 8.1e-09 | 2 | 0.10 | 250000 | 0.12 | 0.05, 0.28 | 0.43 | 7.7e-07 | 1 |
| hf |  | 0.30 | 250000 | 0.17 | 0.09, 0.32 | 0.32 | 3.4e-08 | 3 | 0.30 | 250000 | 0.16 | 0.07, 0.34 | 0.39 | 2.4e-06 | 2 |
| hf |  | 0.50 | 250000 | 0.17 | 0.09, 0.32 | 0.32 | 3.4e-08 | 3 | 0.50 | 250000 | 0.16 | 0.07, 0.34 | 0.39 | 2.4e-06 | 2 |
| hf |  | 0.70 | 250000 | 0.38 | 0.15, 0.97 | 0.48 | 4.3e-02 | 5 | 0.70 | 250000 | 0.16 | 0.07, 0.34 | 0.39 | 2.4e-06 | 2 |
| hf | PCA | 99.21 | 3 | 0.22 | 0.12, 0.42 | 0.32 | 4.9e-06 | 75 | 99.97 | 2 | 0.16 | 0.08, 0.36 | 0.40 | 6.6e-06 | 22 |
| hf |  | 99.93 | 5 | 0.20 | 0.11, 0.36 | 0.30 | 9.4e-08 | 75 | 99.97 | 2 | 0.16 | 0.08, 0.36 | 0.40 | 6.6e-06 | 22 |
| cad | Top SNP | 0.00 | 250000 | 1.30 | 1.02, 1.66 | 0.12 | 0.0338 | 1 | 0.00 | 250000 | 1.51 | 1.13, 2.01 | 0.15 | 0.0048 | 1 |
| cad | Pruning | 0.10 | 250000 | 1.27 | 1.01, 1.59 | 0.12 | 0.0413 | 2 | 0.10 | 250000 | 1.51 | 1.13, 2.01 | 0.15 | 0.0048 | 1 |
| cad |  | 0.30 | 250000 | 1.14 | 0.93, 1.41 | 0.11 | 0.2132 | 3 | 0.30 | 250000 | 1.16 | 0.9, 1.49 | 0.13 | 0.2670 | 2 |
| cad |  | 0.50 | 250000 | 1.14 | 0.93, 1.41 | 0.11 | 0.2132 | 3 | 0.50 | 250000 | 1.16 | 0.9, 1.49 | 0.13 | 0.2670 | 2 |
| cad |  | 0.70 | 250000 | 1.11 | 0.84, 1.47 | 0.14 | 0.4763 | 5 | 0.70 | 250000 | 1.16 | 0.9, 1.49 | 0.13 | 0.2670 | 2 |
| cad | PCA | 99.43 | 3 | 1.37 | 1.09, 1.72 | 0.12 | 0.0061 | 75 | 99.49 | 1 | 0.64 | 0.43, 0.94 | 0.20 | 0.0225 | 22 |
| cad |  | 99.93 | 5 | 1.21 | 0.99, 1.47 | 0.10 | 0.0668 | 75 | 99.97 | 2 | 1.16 | 0.9, 1.5 | 0.13 | 0.2430 | 22 |
| mi | Top SNP | 0.00 | 250000 | 1.28 | 0.9, 1.83 | 0.18 | 0.174 | 1 | 0.00 | 250000 | 1.46 | 0.95, 2.25 | 0.22 | 0.085 | 1 |
| mi | Pruning | 0.10 | 250000 | 1.36 | 0.97, 1.91 | 0.17 | 0.075 | 2 | 0.10 | 250000 | 1.46 | 0.95, 2.25 | 0.22 | 0.085 | 1 |
| mi |  | 0.30 | 250000 | 1.27 | 0.92, 1.74 | 0.16 | 0.141 | 3 | 0.30 | 250000 | 1.20 | 0.81, 1.76 | 0.20 | 0.365 | 2 |
| mi |  | 0.50 | 250000 | 1.27 | 0.92, 1.74 | 0.16 | 0.141 | 3 | 0.50 | 250000 | 1.20 | 0.81, 1.76 | 0.20 | 0.365 | 2 |
| mi |  | 0.70 | 250000 | 1.22 | 0.94, 1.58 | 0.13 | 0.136 | 5 | 0.70 | 250000 | 1.20 | 0.81, 1.76 | 0.20 | 0.365 | 2 |
| mi | PCA | 99.52 | 3 | 1.31 | 0.93, 1.83 | 0.17 | 0.120 | 75 | 99.57 | 1 | 0.77 | 0.43, 1.38 | 0.30 | 0.386 | 22 |
| mi |  | 99.94 | 5 | 1.30 | 0.96, 1.77 | 0.16 | 0.092 | 75 | 99.97 | 2 | 1.21 | 0.82, 1.78 | 0.20 | 0.346 | 22 |
| is | Top SNP | 0.00 | 250000 | 1.32 | 0.95, 1.85 | 0.17 | 0.099 | 1 | 0.00 | 250000 | 1.11 | 0.75, 1.65 | 0.20 | 0.60 | 1 |
| is | Pruning | 0.10 | 250000 | 1.18 | 0.87, 1.6 | 0.16 | 0.297 | 2 | 0.10 | 250000 | 1.11 | 0.75, 1.65 | 0.20 | 0.60 | 1 |
| is |  | 0.30 | 250000 | 1.23 | 0.91, 1.66 | 0.15 | 0.174 | 3 | 0.30 | 250000 | 1.26 | 0.88, 1.82 | 0.18 | 0.20 | 2 |
| is |  | 0.50 | 250000 | 1.23 | 0.91, 1.66 | 0.15 | 0.174 | 3 | 0.50 | 250000 | 1.26 | 0.88, 1.82 | 0.18 | 0.20 | 2 |
| is |  | 0.70 | 250000 | 1.15 | 0.91, 1.46 | 0.12 | 0.232 | 5 | 0.70 | 250000 | 1.26 | 0.88, 1.82 | 0.18 | 0.20 | 2 |
| is | PCA | 99.32 | 3 | 1.15 | 0.83, 1.59 | 0.16 | 0.403 | 75 | 99.97 | 2 | 1.25 | 0.87, 1.81 | 0.19 | 0.23 | 22 |
| is |  | 99.93 | 5 | 1.16 | 0.87, 1.54 | 0.15 | 0.324 | 75 | 99.97 | 2 | 1.25 | 0.87, 1.81 | 0.19 | 0.23 | 22 |
| hypertension | Top SNP | 0.00 | 250000 | 1.01 | 0.97, 1.06 | 0.02 | 0.54 | 1 | 0.00 | 250000 | 1.03 | 0.98, 1.09 | 0.03 | 0.24 | 1 |
| hypertension | Pruning | 0.10 | 250000 | 1.02 | 0.98, 1.06 | 0.02 | 0.31 | 2 | 0.10 | 250000 | 1.03 | 0.98, 1.09 | 0.03 | 0.24 | 1 |
| hypertension |  | 0.30 | 250000 | 1.03 | 0.99, 1.07 | 0.02 | 0.17 | 3 | 0.30 | 250000 | 1.03 | 0.98, 1.08 | 0.02 | 0.29 | 2 |
| hypertension |  | 0.50 | 250000 | 1.03 | 0.99, 1.07 | 0.02 | 0.17 | 3 | 0.50 | 250000 | 1.03 | 0.98, 1.08 | 0.02 | 0.29 | 2 |
| hypertension |  | 0.70 | 250000 | 1.01 | 0.98, 1.04 | 0.01 | 0.47 | 5 | 0.70 | 250000 | 1.03 | 0.98, 1.08 | 0.02 | 0.29 | 2 |
| hypertension | PCA | 99.32 | 3 | 1.01 | 0.97, 1.05 | 0.02 | 0.58 | 75 | 99.58 | 1 | 1.01 | 0.94, 1.09 | 0.04 | 0.71 | 22 |
| hypertension |  | 99.92 | 5 | 1.02 | 0.99, 1.06 | 0.02 | 0.25 | 75 | 99.97 | 2 | 1.03 | 0.98, 1.08 | 0.02 | 0.25 | 22 |
| t2dm | Top SNP | 0.00 | 250000 | 1.57 | 1.15, 2.13 | 0.16 | 0.0046 | 1 | 0.00 | 250000 | 1.82 | 1.26, 2.63 | 0.19 | 0.0014 | 1 |
| t2dm | Pruning | 0.10 | 250000 | 1.50 | 1.13, 1.99 | 0.15 | 0.0056 | 2 | 0.10 | 250000 | 1.82 | 1.26, 2.63 | 0.19 | 0.0014 | 1 |
| t2dm |  | 0.30 | 250000 | 1.42 | 1.09, 1.84 | 0.14 | 0.0101 | 3 | 0.30 | 250000 | 1.60 | 1.15, 2.22 | 0.17 | 0.0056 | 2 |
| t2dm |  | 0.50 | 250000 | 1.42 | 1.09, 1.84 | 0.14 | 0.0101 | 3 | 0.50 | 250000 | 1.60 | 1.15, 2.22 | 0.17 | 0.0056 | 2 |
| t2dm |  | 0.70 | 250000 | 1.26 | 1.04, 1.52 | 0.10 | 0.0188 | 5 | 0.70 | 250000 | 1.60 | 1.15, 2.22 | 0.17 | 0.0056 | 2 |
| t2dm | PCA | 99.30 | 3 | 1.52 | 1.14, 2.01 | 0.14 | 0.0040 | 75 | 99.54 | 1 | 1.17 | 0.69, 1.97 | 0.27 | 0.5763 | 22 |
| t2dm |  | 99.92 | 5 | 1.43 | 1.11, 1.84 | 0.13 | 0.0062 | 75 | 99.97 | 2 | 1.61 | 1.16, 2.24 | 0.17 | 0.0045 | 22 |

| **Method1** | **Method** | **SNP** | **EA** | **EAF** | **Beta** | **SE** | **PVal** | **N** | **i2** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Pruning | r2 = 1e-06 | rs7220711 | G | 0.33 | -0.04 | 0.01 | 1.1e-09 | 49,372 | 0.64 |
| Pruning | r2 = 0.1 | rs7220711 | G | 0.33 | -0.04 | 0.01 | 1.1e-09 | 49,372 | 0.64 |
| Pruning | r2 = 0.1 | rs71382995 | A | 0.08 | -0.05 | 0.01 | 3.1e-06 | 49,372 | 0.69 |
| Pruning | r2 = 0.3 | rs7220711 | G | 0.33 | -0.04 | 0.01 | 1.1e-09 | 49,372 | 0.64 |
| Pruning | r2 = 0.3 | rs66838809 | A | 0.09 | -0.07 | 0.01 | 7.8e-09 | 49,372 | 0.74 |
| Pruning | r2 = 0.3 | rs8073524 | G | 0.59 | -0.03 | 0.01 | 1.6e-06 | 49,372 | 0.00 |
| Pruning | r2 = 0.5 | rs7220711 | G | 0.33 | -0.04 | 0.01 | 1.1e-09 | 49,372 | 0.64 |
| Pruning | r2 = 0.5 | rs66838809 | A | 0.09 | -0.07 | 0.01 | 7.8e-09 | 49,372 | 0.74 |
| Pruning | r2 = 0.5 | rs8073524 | G | 0.59 | -0.03 | 0.01 | 1.6e-06 | 49,372 | 0.00 |
| Pruning | r2 = 0.7 | rs7220711 | G | 0.33 | -0.04 | 0.01 | 1.1e-09 | 49,372 | 0.64 |
| Pruning | r2 = 0.7 | rs66838809 | A | 0.09 | -0.07 | 0.01 | 7.8e-09 | 49,372 | 0.74 |
| Pruning | r2 = 0.7 | rs8073524 | G | 0.59 | -0.03 | 0.01 | 1.6e-06 | 49,372 | 0.00 |
| Pruning | r2 = 0.7 | rs80107551 | T | 0.09 | -0.06 | 0.01 | 9.5e-08 | 49,372 | 0.67 |
| Pruning | r2 = 0.7 | rs6503468 | T | 0.66 | 0.06 | 0.01 | 2.1e-08 | 14,009 | 0.39 |

| **Method1** | **Method** | **SNP** | **EA** | **EAF** | **Beta** | **SE** | **PVal** | **N** | **i2** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Pruning | r2 = 1e-06 | rs2342312 | G | 0.28 | -0.04 | 0.01 | 7.7e-07 | 49,372 | 0.03 |
| Pruning | r2 = 0.1 | rs2342312 | G | 0.28 | -0.04 | 0.01 | 7.7e-07 | 49,372 | 0.03 |
| Pruning | r2 = 0.3 | rs2342312 | G | 0.28 | -0.04 | 0.01 | 7.7e-07 | 49,372 | 0.03 |
| Pruning | r2 = 0.3 | rs8073524 | G | 0.59 | -0.03 | 0.01 | 1.6e-06 | 49,372 | 0.00 |
| Pruning | r2 = 0.5 | rs2342312 | G | 0.28 | -0.04 | 0.01 | 7.7e-07 | 49,372 | 0.03 |
| Pruning | r2 = 0.5 | rs8073524 | G | 0.59 | -0.03 | 0.01 | 1.6e-06 | 49,372 | 0.00 |
| Pruning | r2 = 0.7 | rs2342312 | G | 0.28 | -0.04 | 0.01 | 7.7e-07 | 49,372 | 0.03 |
| Pruning | r2 = 0.7 | rs8073524 | G | 0.59 | -0.03 | 0.01 | 1.6e-06 | 49,372 | 0.00 |