

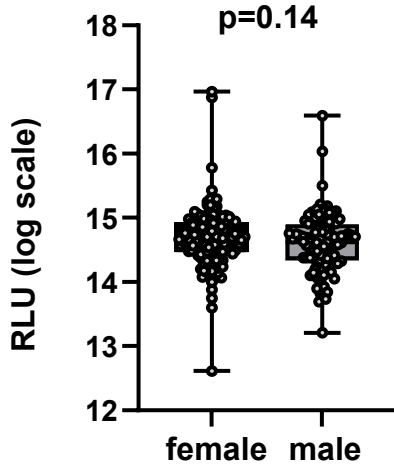
Plasma Levels of Anti-Phosphocholine IgM Antibodies are Negatively Correlated with Bone Mineral Density in Humans.

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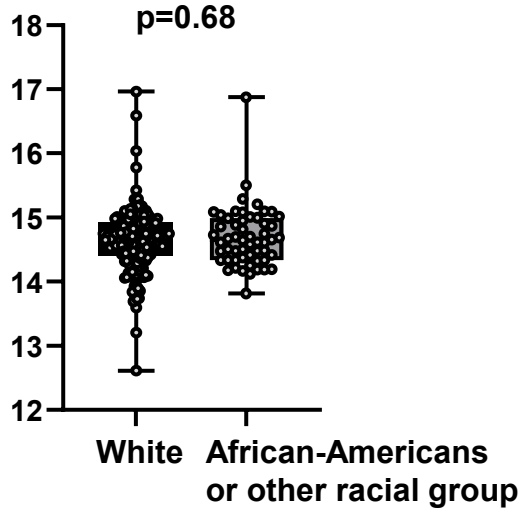
Supplementary Figure S1

Anti-PC IgM

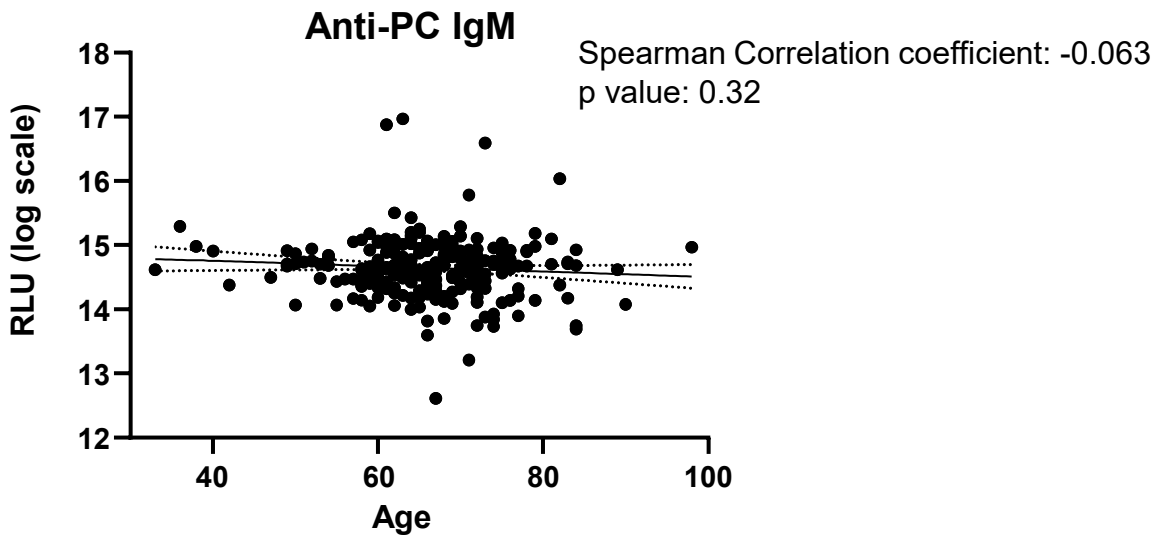
A



B



C

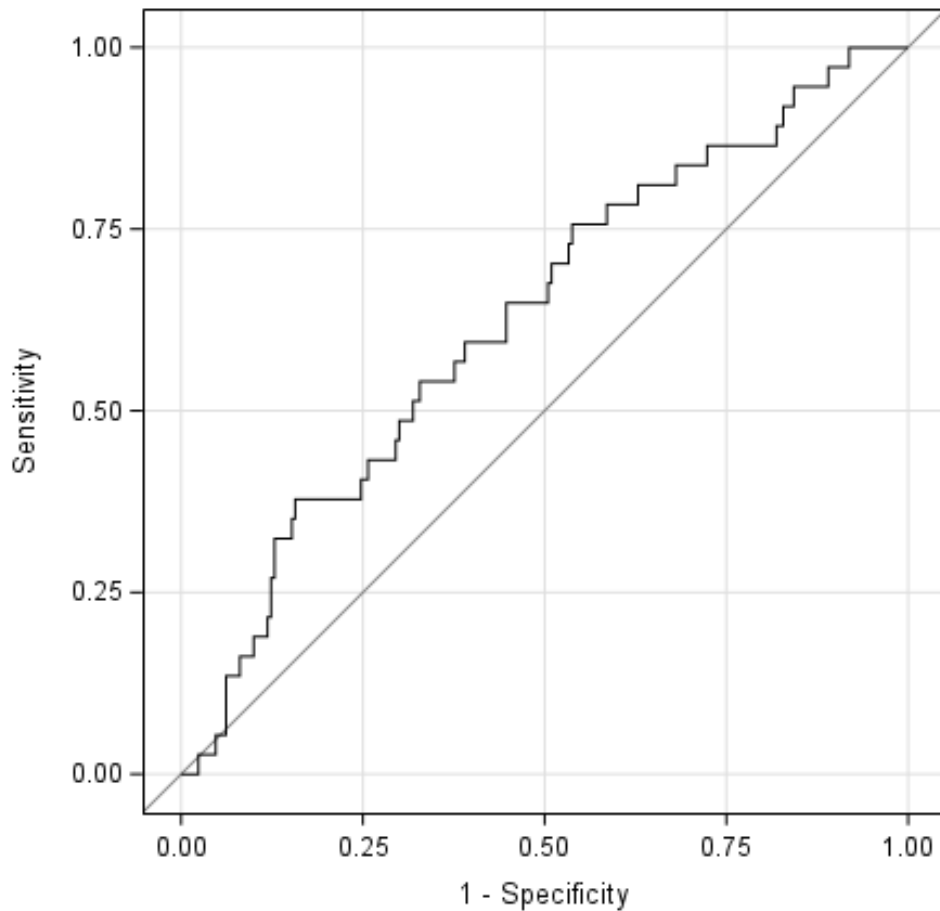


Supplementary Figure S1: A) Anti- PC IgM levels (log transformed) in females and males, and White vs African Americans or other racial groups. Data analyzed by Wilcoxon Rank Sum test. B) Spearman correlation coefficient assessing the linear association between anti-PC IgM antibodies and age. A logarithmic transformation was applied to the IgM anti-PC measures prior to analysis.

Supplementary Figure S2

ROC Curve

Area under the curve=0.6274



Supplementary Figure S2: Receiver-operating characteristic curve of the age, sex and race adjusted anti-PC IgM levels. The area under the curve provides a measure of predictive power for the diagnosis of low bone mass.

Supplementary Table S1. Summary of Laboratory Measures.

| Variable | N | Mean (SD) | Median (IQR) | Normal range |
|------------------------------------|----------|-------------------------|--------------------------|---------------------|
| Calcium (mg/dL) | 246 | 9.3 (0.3) | 9.2 (0.5) | 8.3-10.3 |
| Ionized Calcium (mmol/L) | 82 | 1.17 (0.05) | 1.16 (0.07) | 1.13-1.32 |
| PTH (pg/ml) | 91 | 46.3 (18.6) | 41.6 (26.4) | 12-88 |
| 25-OH-Vitamin D (ng/ml) | 191 | 39.3 (16.8) | 36.9 (19.8) | 30-100 |
| Phosphate (mg/dL) | 101 | 3.6 (0.6) | 3.6 (0.7) | 2.5-4.9 |
| Creatinine (mg/dL) | 247 | 0.97 (0.26) | 0.90 (0.30) | 0.6-1.3 |
| Albumin (g/dL) | 244 | 3.9 (0.3) | 4.0 (0.4) | 3.4-5.0 |
| EGFR (ml/min/1.73 m ²) | 246 | 57.7 (5.5) | 60.1 (0.0) | >60 |
| C-reactive protein (mg/L) | 240 | 4.9 (7.9) | 2.3 (4.7) | 0-6.0 |
| IgG (mg/dL) | 243 | 1068.7 (289.3) | 1032.5 (359.6) | 610.3-1616.0 |
| IgM (mg/dL) | 243 | 92.6 (60.1) | 77.9 (51.7) | 35-242 |
| IgM Anti-PC Adjusted RLU | 247 | 2634330.56 (2217721.07) | 23332357.11 (1209001.39) | |

IQR: interquartile range

RLU: relative light units

Supplementary Table S2. Spearman correlation coefficients between anti-PC IgM and total IgM

| | N | Spearman Correlation Coefficient | P-value |
|-----|----------|---|----------------|
| IgM | 243 | 0.58 | <0.0001 |

Supplementary Table S3. Spearman correlation coefficients between anti-PC IgM and DEXA T-scores

| Region | N | Spearman Correlation Coefficient | P-value |
|----------------------|----------|---|----------------|
| Lumbar L1-L4 | 221 | -0.1588 | 0.0181 |
| Femoral Neck | 239 | -0.1556 | 0.0161 |
| Femoral Trochanter | 239 | -0.1957 | 0.0024 |
| Total Femur | 239 | -0.1567 | 0.0153 |
| Forearm- Diaphysis | 247 | -0.1164 | 0.0678 |
| Forearm- Ultradistal | 247 | -0.0028 | 0.9648 |
| Forearm- Total | 247 | -0.0742 | 0.2450 |

Spearman correlation coefficients assessing the linear association between anti-PC IgM antibodies levels and DXA T-scores for each anatomical region. A logarithmic transformation was applied to the anti-PC IgM measures prior to analysis.

Supplementary Table S4. Spearman correlation coefficients between age, sex and race adjusted anti-PC IgM and DEXA T-scores

| Region | N | Spearman Correlation Coefficient | P-value |
|----------------------|----------|---|----------------|
| Lumbar L1-L4 | 221 | -0.1409 | 0.0363 |
| Femoral Neck | 239 | -0.1705 | 0.0083 |
| Femoral Trochanter | 239 | -0.2035 | 0.0016 |
| Total Femur | 239 | -0.1661 | 0.0101 |
| Forearm- Diaphysis | 247 | -0.1402 | 0.0276 |
| Forearm- Ultradistal | 247 | -0.0524 | 0.4127 |
| Forearm- Total | 247 | -0.1126 | 0.0772 |

Spearman correlation coefficients assessing the linear association between Age, Sex, and Race adjusted anti-PC IgM antibodies and DEXA T-scores for each anatomical region. A logarithmic transformation was applied to the anti-PC IgM measures prior to analysis. A linear regression on anti-PC IgM measures with covariates of Age, Sex, and Race was used to produce the residuals.

Supplementary Table S5. Spearman correlation coefficients between anti-PC IgM and DEXA Z-scores

| Region | N | Spearman Correlation Coefficient | P-value |
|----------------------|----------|---|----------------|
| Lumbar L1-L4 | 221 | -0.1591 | 0.0179 |
| Femoral Neck | 238 | -0.1789 | 0.0057 |
| Femoral Trochanter | 238 | -0.1828 | 0.0047 |
| Total Femur | 238 | -0.1623 | 0.0122 |
| Forearm- Diaphysis | 244 | -0.1357 | 0.0341 |
| Forearm- Ultradistal | 244 | -0.0291 | 0.6505 |
| Forearm- Total | 244 | -0.1077 | 0.0932 |

Spearman correlation coefficients assessing the linear association between anti-PC IgM antibodies levels and DXA Z-scores for each anatomical region. A logarithmic transformation was applied to the anti-PC IgM measures prior to analysis.

Supplementary Table S6. Spearman correlation coefficients between age, sex and race adjusted anti-PC IgM and DEXA Z-scores

| Region | N | Spearman Correlation Coefficient | P-value |
|----------------------|----------|---|----------------|
| Lumbar L1-L4 | 221 | -0.1580 | 0.0188 |
| Femoral Neck | 238 | -0.1849 | 0.0042 |
| Femoral Trochanter | 238 | -0.1970 | 0.0023 |
| Total Femur | 238 | -0.1727 | 0.0076 |
| Forearm- Diaphysis | 244 | -0.1509 | 0.0184 |
| Forearm- Ultradistal | 244 | -0.0547 | 0.3946 |
| Forearm- Total | 244 | -0.1364 | 0.0332 |

Spearman correlation coefficients assessing the linear association between Age, Sex, and Race adjusted anti-PC IgM antibodies and DEXA S-scores for each anatomical region. A logarithmic transformation was applied to the anti-PC IgM measures prior to analysis. A linear regression on anti-PC IgM measures with covariates of Age, Sex, and Race was used to produce the residuals.

Supplementary Table S7. Spearman correlation coefficients between anti-PC IgM and DEXA T-scores

| Region | Spearman Correlation Coefficient –participants with T score <-1 (p-value) | | Spearman Correlation Coefficient – participants with T score ≥1 (p-value) | |
|--------------------|---|-------------------------|---|------------------|
| | | | | |
| Lumbar L1-L4 | n=76 | -0.2576 (0.0247) | n=145 | -0.0282 (0.7361) |
| Femoral Neck | n=145 | -0.1071 (0.1999) | n=94 | 0.1060 (0.3094) |
| Femoral Trochanter | n=96 | -0.1851 (0.0711) | n=143 | -0.0434 (0.6065) |
| Total Femur | n=93 | -0.0743 (0.4793) | n=146 | 0.1100 (0.1862) |

Spearman correlation coefficients assessing the linear association between anti-PC IgM antibodies levels and DXA T-scores for each anatomical region in participants with T-score <-1 and T score ≥-1. A logarithmic transformation was applied to the anti-PC IgM measures prior to analysis.

Supplementary Table S8. Spearman correlation coefficients between age, sex and race adjusted anti-PC IgM and DEXA T-scores

| Region | Spearman Correlation Coefficient –participants with T score <-1 (p-value) | | Spearman Correlation Coefficient –participants with T score ≥1 (p-value) | |
|--------------------|---|-------------------------|--|------------------|
| | | | | |
| Lumbar L1-L4 | n=76 | -0.2761 (0.0158) | n=145 | -0.0102 (0.9035) |
| Femoral Neck | n=145 | -0.1370 (0.1002) | n=94 | 0.0933 (0.3713) |
| Femoral Trochanter | n=96 | -0.1882 (0.0663) | n=143 | -0.0356 (0.6730) |
| Total Femur | n=93 | -0.0952 (0.3641) | n=146 | 0.1000 (0.2297) |

Spearman correlation coefficients assessing the linear association between Age, Sex, and Race adjusted anti-PC IgM antibodies and DEXA T-scores for each anatomical region in participants with T-score <-1 and T score ≥-1. A logarithmic transformation was applied to the anti-PC IgM measures prior to analysis. A linear regression on anti-PC IgM measures with covariates of Age, Sex, and Race was used to produce the residuals.

Supplementary Table S9. Univariate Linear regression model

Anti-PC IgM and DEXA T-scores

| Region T-score | R ² | p-value |
|--------------------|----------------|---------------|
| Lumbar L1-L4 | 0.0075 | 0.1991 |
| Femoral Neck | 0.0124 | 0.0863 |
| Femoral Trochanter | 0.0193 | 0.0317 |
| Total Femur | 0.0142 | 0.062 |

Age, sex and race adjusted anti-PC IgM Anti-PC IgM and DEXA T-scores

| Region T-score | R ² | p-value |
|--------------------|----------------|---------------|
| Lumbar L1-L4 | 0.0087 | 0.1665 |
| Femoral Neck | 0.0162 | 0.0496 |
| Femoral Trochanter | 0.0241 | 0.0162 |
| Total Femur | 0.0180 | 0.0383 |

Anti-PC IgM and DEXA Z-scores

| Region Z-score | R ² | p-value |
|--------------------|----------------|---------------|
| Lumbar L1-L4 | 0.0073 | 0.2050 |
| Femoral Neck | 0.0165 | 0.0475 |
| Femoral Trochanter | 0.0172 | 0.0432 |
| Total Femur | 0.0162 | 0.0499 |

Age, sex and race adjusted anti-PC IgM Anti-PC IgM and DEXA Z-scores

| Region Z-score | R ² | p-value |
|--------------------|----------------|---------------|
| Lumbar L1-L4 | 0.0120 | 0.1046 |
| Femoral Neck | 0.0202 | 0.0283 |
| Femoral Trochanter | 0.0249 | 0.0148 |
| Total Femur | 0.0221 | 0.0218 |

Univariate Linear Regression models were fit on the log-transformed data to calculate the R² and p values.