

## Online Data Supplement

### Reduced Bone Density and Vertebral Fractures in Smokers: Men and COPD Patients at Increased Risk

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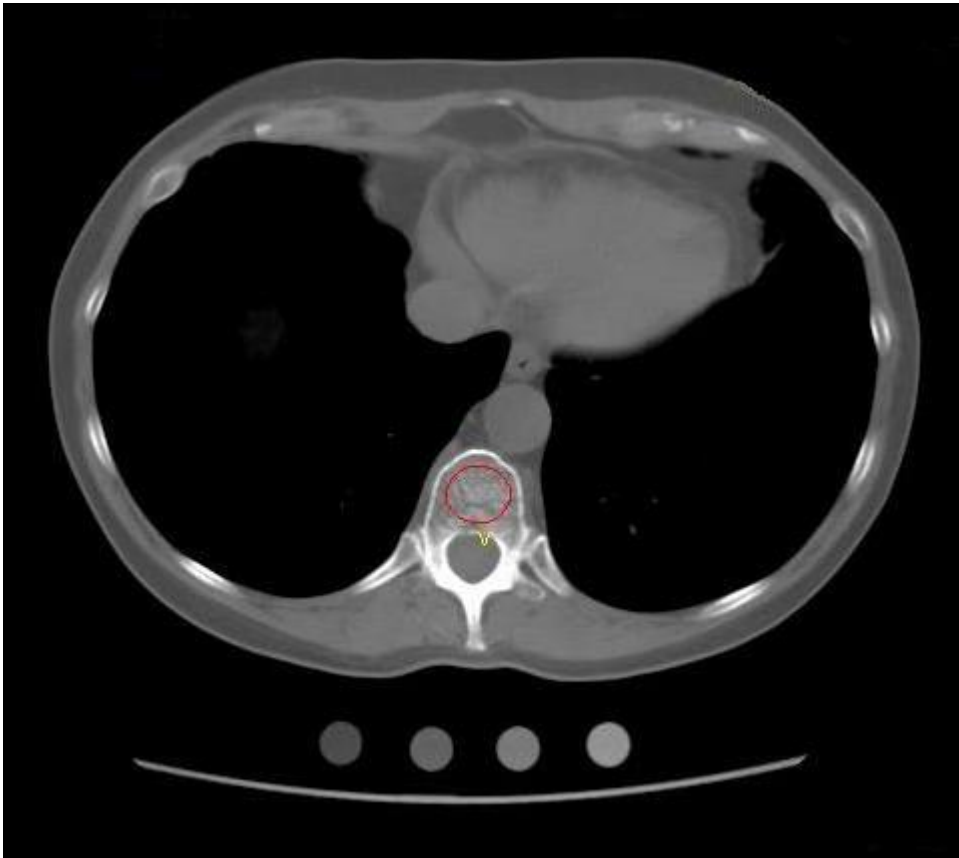
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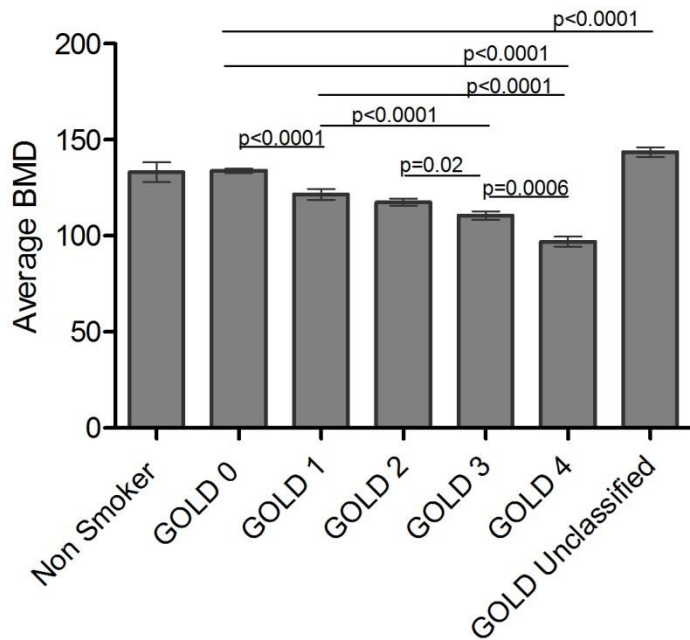
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**Figure E1:** Axial CT image

Using the calcium calibration rods (circular densities at base of scan image) that is imbedded in the CT scanner pad under the subject and its density data stored within the chest CT image, with dedicated software (Image Analysis, Lexington, KY), volumetric bone density (mg/cc) is determined for each selected vertebra where a region of interest has been defined. This method reduces the effect of falsely increased BMD values from measuring the additional density of adjacent tissues including bony osteophytes associated with degenerative spine disease and differences in fat and lean mass.



**Figure E2:** Mean BMD is significantly decreased in COPD subjects compared to smokers without COPD

Smokers were classified using post-bronchodilator spirometry based on a modified GOLD classification for COPD (eTable 1). Average vBMD was calculated for each group. GOLD unclassified smokers had FEV<sub>1</sub> or FVC less than 80% of their predicted values based on age and gender but a normal FEV<sub>1</sub>/FVC ratio and therefore are smokers without COPD. GOLD groups 1 – 4 show step-wise decreases in vBMD that are significant at each level except between GOLD 1 and GOLD 2 groups. Both GOLD unclassified and GOLD 0 smokers have significantly higher vBMD than the COPD subjects. GOLD U subjects have significantly higher vBMD than GOLD 0 subjects (p<0.0001).

**Table E1:** Modified Global Initiative for Chronic Obstructive Lung Disease (GOLD) Classification as used in the COPDGene Study, defines severity of obstruction using post-bronchodilator spirometry and includes all chronic smokers.

Stage	Description	Spirometric Characteristics
GOLD 0	Chronic Smoker without spirometric obstruction based on population values – not related to symptoms (not part of the current 2011 GOLD classification system)	FEV <sub>1</sub> ≥ 80% predicted FEV <sub>1</sub> /FVC > 0.7
GOLD 1	Mild COPD	FEV <sub>1</sub> /FVC < 0.7 FEV <sub>1</sub> ≥ 80% predicted
GOLD 2	Moderate COPD	FEV <sub>1</sub> /FVC < 0.7 FEV <sub>1</sub> < 80% predicted, but > 50% predicted
GOLD 3	Severe COPD	FEV <sub>1</sub> /FVC < 0.7 FEV <sub>1</sub> < 50% but > 30% predicted
GOLD 4	Very Severe COPD	FEV <sub>1</sub> /FVC < 0.7 FEV <sub>1</sub> < 30% predicted
GOLD Unclassified	Chronic smoker – Preserved Ratio with Impaired Spirometry	FEV <sub>1</sub> /FVC > 0.7 FEV <sub>1</sub> or FVC < 80% predicted



**Table E2: Baseline Characteristics of QCT BMD Cohort Compared to Remaining COPDGene Subjects**

	<b>Bone Density Cohort</b>	<b>Cohort without Bone Density Measures</b>	<b>P value</b>
N	3321	6979	
Age (SD)	59.4 (9.0)	59.7 (9.0)	NS
Gender, % male	52%	54%	NS
Race, % African-American	31.3%	34.1%	p=0.005
School completed (% with some college or more)	60.9%	61.0%	NS
BMI (SD)	28.8 (6.2)	28.8 (6.3)	NS
Current Smoker, %	51.6%	53.0%	NS
Pack-years (SD)	43.7 (24.4)	44.5 (25.2)	NS
Six minute walk distance (feet)	1406 (388)	1328 (402)	p<0.0001
Resting O2 Saturation	95.8 (3.3)	96.3 (2.7)	p<0.0001
Chronic Oral Steroid Use, %	2.3%	2.6%	NS
Inhaled Steroid Use, %	23.4%	23.3%	NS
Treated with steroids in past year for exacerbation, N (%)	514 (16.4%)	1507 (17.0%)	NS
GOLD Status, N (%)			p<0.0001
Non Smokers	63 (1.9%)	45 (0.7%)	
Smoker Controls	1442 (43.6%)	2946 (42.5%)	
GOLD 1	240 (7.3%)	554 (8.0%)	
GOLD 2	598 (18.1%)	1324 (19.1%)	
GOLD 3	377 (11.4%)	785 (11.3%)	
GOLD 4	189 (5.7%)	417 (6.0%)	
GOLD Unclassified	397 (12.0%)	860 (12.4%)	
Physician Diagnosed Osteoporosis, %	8.7%	8.9%	NS
Prior Diagnosis of Hip Fracture, %	2.1%	1.7%	NS
SF-36 PCS	43.9 (11.1)	44.3 (11.0)	NS
SF-36 MCS	49.0 (12.0)	49.2 (11.7)	NS
SGRQ total score	27.6 (23.4)	26.9 (22.7)	NS

**Table E3: Thoracic BMD, Osteoporosis and Vertebral Fractures across GOLD by Race and Gender\***

<i>Thoracic QCT BMD in Non-Hispanic White Subjects</i>							
n=2283	Non-smokers	Smoker Controls	GOLD U	GOLD 1	GOLD 2	GOLD 3	GOLD 4
Male	133.6 (34.7)	113.5 (33.9)	116.3 (38.0)	107.5 (32.0)	102.5 (37.6)	94.3 (37.8)	86.0 (31.5)
Female	128.5 (44.4)	129.5 (40)	126.3 (42.9)	114.9 (40)	110.3 (38.5)	109.1 (42)	96.7 (34.5)
<b>Significance</b>	NS	0.0001	0.07	NS	0.03	0.002	0.045
<i>Thoracic QCT BMD in African American Subjects *</i>							
n=1038		Smoker Controls	GOLD U	GOLD 1	GOLD 2	GOLD 3	GOLD 4
Male		151.9 (40)	154.8 (39)	158.9 (43)	142.4 (44.3)	143.4 (39)	121.5 (37)
Female		159.5 (48)	190.0 (49)	162.4 (54)	158.0 (50)	147.0 (41)	136.0 (52.5)
<b>Significance</b>		0.049	<0.0001	NS	0.04	NS	NS
<i>Low Bone Density<sup>†</sup> in Non-Hispanic White Subjects</i>							
n=2283	Non-smokers	Smoker Controls	GOLD U	GOLD 1	GOLD 2	GOLD 3	GOLD 4
Male	47.4%	71.5%	66.0%	75.5%	77.9%	87.4%	91.1%
Female	61.5%	56.8%	57.5%	65.1%	73.5%	72.2%	85.0%
<b>Significance</b>	0.04	<0.0001	NS	0.02	0.04	0.005	NS
<i>Low Bone Density<sup>†</sup> in African American Subjects*</i>							
n=1038		Smoker Controls	GOLD U	GOLD 1	GOLD 2	GOLD 3	GOLD 4
Male		33.0%	23.8%	20.7%	35.8%	39.6%	64.7%
Female		30.3%	9.3%	26.1%	34.7%	41.0%	53%
<b>Significance</b>		NS	0.0001	NS	NS	NS	NS
<i>Vertebral fractures<sup>‡</sup> in Non-Hispanic White Subjects*</i>							
n=664		Smoker Controls	GOLD U	GOLD 1	GOLD 2	GOLD 3	GOLD 4
Male		39.5 %	39.8 %	40.6 %	47.6 %	51.7 %	39.6 %
Female		25 %	23.2 %	29.1 %	33.8 %	40.9 %	35.3 %
<b>Significance</b>		p<0.0001	0.007	NS	0.003	NS	NS

<b>Vertebral fractures<sup>‡</sup> in African American Subjects*</b>							
n=228		Smoker Controls	GOLD U	GOLD 1	GOLD 2	GOLD 3	GOLD 4
Male		24.7 %	21.4 %	26.7 %	23.5 %	20.8 %	41.2%
Female		18.6 %	15.1 %	26.3 %	22.2 %	23.1 %	20%
<b>Significance</b>		NS	NS	NS	NS	NS	NS

\* The non-smoker group did not include sufficient African American nor fractures for analysis

† Percentage of subjects with T-score<sub>QCT</sub> ≤ -2.5

‡ Percentage of subjects with one or more fracture