Supplement 1: Exclusionary characteristics

Subjects could be included if they were 18-65 years old, reported smoking an average of > 10 cigarettes that each yielded > 0.5 mg nicotine per day, and displayed end-expired air CO > 10 ppm. Exclusion criteria included: coronary heart disease; myocardial infarction; cardiac rhythm disorder; chest pains (unless history, exam, and EKG clearly indicated a non-cardiac source); cardiac disorder (including but not limited to valvular heart disease, heart murmur, heart failure); hypertension (systolic >140 mm Hg, diastolic >100 mm Hg for individuals with diagnosed hypertension, and > 160/100 for those with no previous diagnosis); hypotension (systolic <90 mm Hg, diastolic <60 mm Hg); history of skin allergy; active skin condition (psoriasis) within the last five years; skin disorder except minor skin conditions (including but not limited to facial acne, minor localized infections, and superficial minor wounds.); liver or kidney disorder (except kidney stones, gallstones); gastrointestinal problems or disease other than gastroesophageal reflux or heartburn; ulcers; lung disorder (including but not limited to COPD, emphysema, and asthma); brain abnormality (including but not limited to, stroke, brain tumor, seizure disorder); history of fainting; problems giving blood samples; difficulty passing urine; diabetes treated with insulin, non-insulin treated diabetes (unless glucose was < 180mg/dcl and HbA1c was < 7%); current cancer or treatment for cancer in the past 6 months (except basal or squamous cell skin cancer); other major medical condition; current psychiatric disease (with the exception of depression, anxiety disorders, OCD and ADHD); alcohol or drug abuse; use of an investigational drug within the last 30 days, psychiatric medications (including antidepressants, anti-psychotics or any other medications known to affect smoking cessation (e.g., clonidine); use of smokeless tobacco (chewing tobacco, snuff), cigars, pipes, nicotine replacement therapy, or other smoking cessation treatment within the last 2 weeks; pregnancy or nursing mothers.

Supplement 2: Genotyping

DNA was extracted from blood samples using QIAamp Blood DNA Maxi Kits (Valencia, CA). DNA was quantitated using OD260 and picogreen (Invitogen, Carlsbad, CA), and genotyped using Affymetrix 6.0 arrays. Briefly, 250 ng of individual DNA was digested using *Sty* I or *Nsp* I, ligated to corresponding oligonucleotide adaptors and amplified using a GeneAmp PCR System 9700 (Applied Biosystems, Foster City CA). Conditions were 3 min at 94°C, 30 cycles of 30 sec at 94°C, 45 sec at 60°C, 15 sec at 68°C and a final 7 min 68°C extension. PCR products were purified using magnetic beads (Agencort Ampure, Beckman Coulter, Beverly, MA) and a filtration system (MultiScreen Deep Well Solvinert Low Binding Hydrophilic PTFE; Millipore, Billerica, MA). 135 μg of purified PCR products were digested for 35 min at 37°C with 30 units of DNase I to produce 30-200 bp fragments, as verified by agarose gel electrophoresis. Fragments were end-labeled using terminal deoxynucleotidyl transferase and biotinylated dideoxynucleotides and hybridized to Affymetrix 6.0 arrays which were stained, washed and scanned as described [35-38].

Supplement 3: assignment of v 1.0 quit success genotype scores

Genotypes and v1.0 scores were assigned for each participant by investigators blinded to clinical phenotype. We assessed alleles at the 12,058 SNPs for which at least one of three previously-reported smoking cessation success clinical trial samples had identified nominally-highly-significant ($P < 0.01$) differences between successful *vs* unsuccessful quitters, based on strength and replicability of the associations 18. We eliminated SNPs for which HapMap minor allele frequencies were 0 and SNPs for which opposite phase of association was demonstrated in two samples. Average p values for SNPs that displayed nominally-significant associations in multiple samples were determined, a factor [F1 = 0.01 – *P*(average)] was determined for each SNP. F1 factors for all such SNPs were scaled such that a subject homozygous for all of these abstinence-associated SNPs would thus score 900. SNPs that were

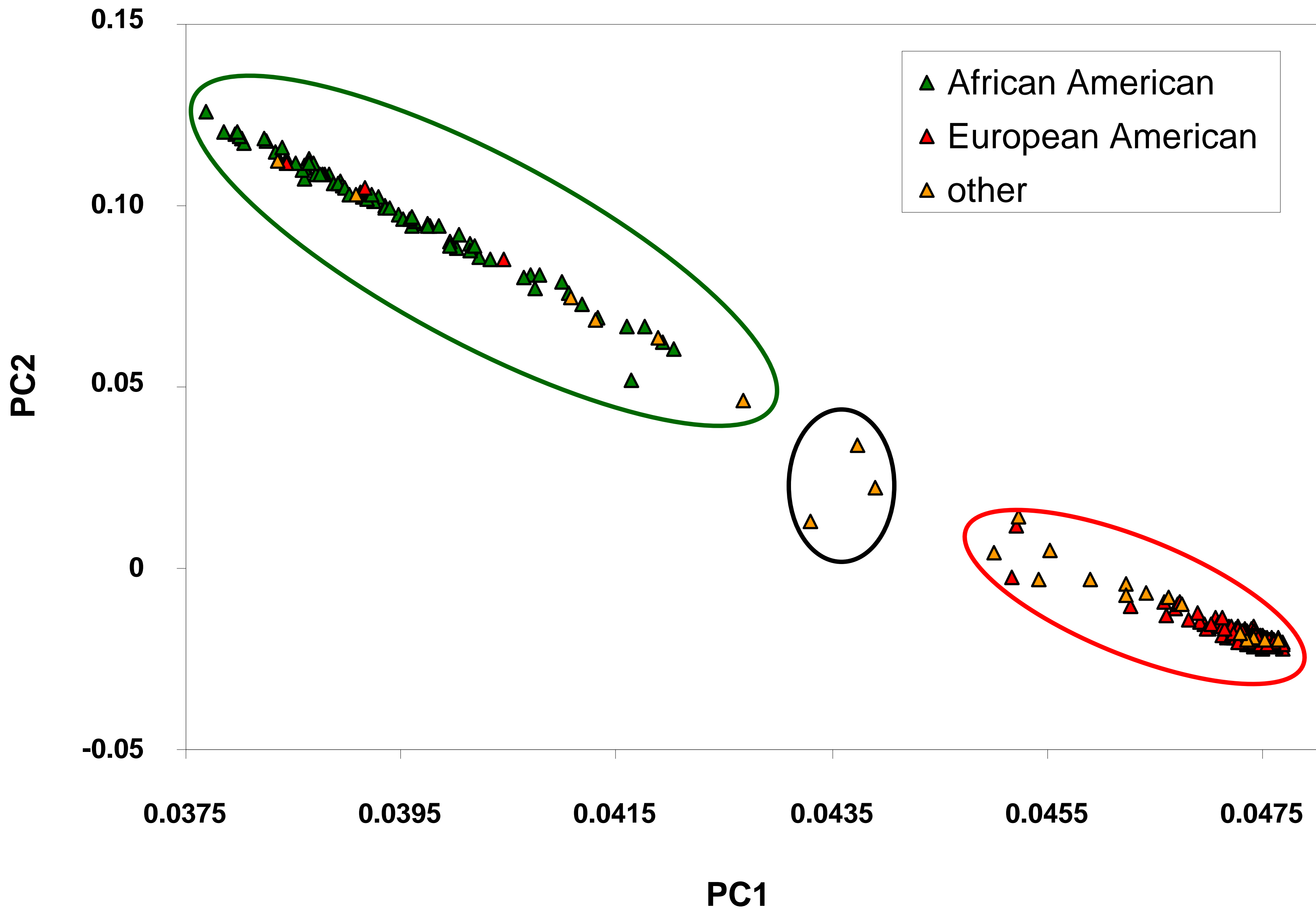
associated with abstinence in only one of the three prior samples were scaled to a total of 100. For each subject, an individual abstinence score was determined by 1) multiplying the factor for each SNP by the count of abstinence alleles for that SNP, and then 2) summing those values for the set of all SNPs. Each individual could thus achieve a quit-success genotype score of 1000. In preplanned analyses, we compared individuals with upper- to lower half quit success scores, seeking to a) minimize effects of unknown distributions and other properties of these scores and b) parallel the analyses used for FTND scores and changes in CO levels.

Supplementary Figures:

Fig. S1. Principal component analysis based on 1 million SNP genotypes separate the participants in this trial according to their ethnic background (PC1 and PC2 together account for over 95% of meaningful variance). Individuals were assigned to the groups based on predominant ethnicity in the PC1/PC2 cluster (African American cluster circled green, European American cluster circled red). 3 individuals with ambiguous cluster assignment were excluded from the analysis (circled black). The legend indicates "self reported" ethnicity.

Fig. S2. Smoking abstinence as a function of nicotine patch dose (NRT dose), dependence (FTND) and quit success genotype score. Upper panel depicts percent 10-week continuous abstinence after the quit date; lower panel depicts percent 4-week continuous abstinence from week 7 to week 10 after the quit date.

Fig. S3. Six-month point (7-day) abstinence at 6 months after the quit date, as a function of nicotine patch dose (NRT dose), dependence (FTND) and quit success genotype score.



African American
European American
other
PC2
PC1
0.15
0.10
0.05
0
-0.05
0.0375
0.0395
0.0415
0.0435
0.0455
0.0475

Continuous abstinence (through week 10)

Low Quit-Success Genotype Score

High Quit-Success Genotype Score

Low dependence

High dependence

Percent abstinent

45 40 35 30 25 20 15 10 5 0

21 mg 42 mg 21 mg 42 mg

Nicotine patch dose

Low Dependence

High Dependence

Percent abstinent

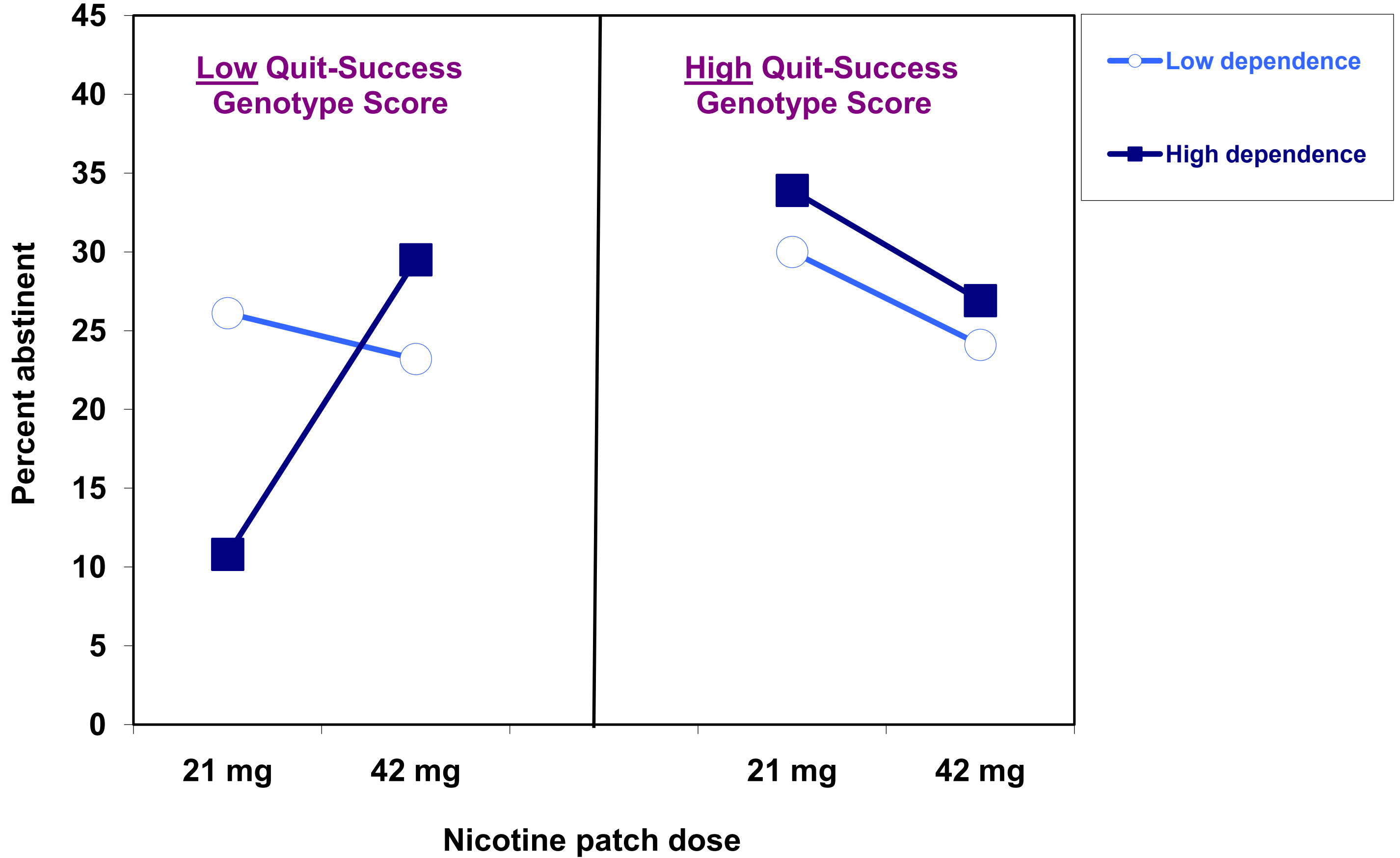
45 40 35 30 25 20 15 10 5 0

Low Quit-Success Genotype Score

High Quit-Success Genotype Score

21 mg 42 mg 21 mg 42 mg

Nicotine patch dose


Point (7-day) abstinence at 6-month follow-up
Low Quit-Success Genotype Score
High Quit-Success Genotype Score
Low dependence
High dependence
Percent abstinent
45
40
35
30
25
20
15
10
5
0
21 mg
42 mg
21 mg
42 mg
Nicotine patch dose