Annotation of statistical models analyzed in this study

For the weight loss outcomes (6-month and 2-year), the following linear model is fitted to the pooled sample if no significant interactions between SNP and treatment groups.

\[ WL_i = \beta_0 + \beta_{W0}W_{0i} + \beta_SS_i + \beta_LS LS_i + \beta_{ME} ME_i + \beta_A A_i + \beta_M M_i + \beta_{AA} AA_i + \beta_H H_i + \beta_{AP} AP_i + \beta_{AI} AI_i + \epsilon_i \]

\( WL_i \): the weight loss outcome for the \( i \)th subject

\( \beta_0 \): Intercept

\( W_{0i} \): Weight at baseline for subject \( i \)

\( S_i \): Number of effective alleles \((0,1,2)\) of the SNP under test in subject \( i \)

\( LS_i, ME_i \): Indicators for subject \( i \) belonging to the Lifestyle and Metformin groups respectively

\( A_i \): Subject \( i \)'s age at baseline

\( M_i \): Indicator for subject \( i \) being a man

\( AA_i, H_i, AP_i, AI_i \): Indicators for subject \( i \) being an African American, Hispanic, Asian or Pacific Islander, American Indian, respectively

\( \beta_{W0}, \beta_S, \beta_{LS}, \beta_{ME}, \beta_A, \beta_M, \beta_{AA}, \beta_H, \beta_{AP}, \beta_{AI} \): Regression coefficients for the corresponding covariate

\( \epsilon_i \): Independent random errors following a mean-zero normal distribution with constant variance.

In the presence of significant interactions between SNP and treatment groups, the following linear regression model is fitted within each treatment group

\[ WL_i = \beta_0 + \beta_{W0}W_{0i} + \beta_SS_i + \beta_A A_i + \beta_MM_i + \beta_{AA} AA_i + \beta_H H_i + \beta_{AP} AP_i + \beta_{AI} AI_i + \epsilon_i \]

In this case, three sets of treatment-specific coefficient estimates will be output. For the weight regain outcome, subjects could have more than one regain rate measure at different time points during the followup after 6 month. The following two linear mixed models are fitted for each of the 16 SNPs in either the pooled sample or the treatment-specific samples.

\[ WL_{ij} = \beta_0 + \beta_{W0}W_{0ij} + \beta_SS_{ij} + \beta_A A_{ij} + \beta_M M_{ij} + \beta_{AA} AA_{ij} + \beta_H H_{ij} + \beta_{AP} AP_{ij} + \beta_{AI} AI_{ij} + \epsilon_{ij} \]

\[ WL_{ij} = \beta_0 + \beta_{W0}W_{0ij} + \beta_SS_{ij} + \beta_A A_{ij} + \beta_M M_{ij} + \beta_{AA} AA_{ij} + \beta_H H_{ij} + \beta_{AP} AP_{ij} + \beta_{AI} AI_{ij} + \epsilon_{ij} \]

for the \( j \)th weight regain measure in subject \( i \). Notice the error terms within the same subject \( \epsilon_{ij} \) are no longer independent, instead an auto-regressive covariance structure is assumed where the correlation coefficient between \( \epsilon_{ij} \) decreases exponentially. That is, if the correlation coefficient between \( \epsilon_{i1} \) and \( \epsilon_{i2} \) is \( \rho \), the correlation coefficient between \( \epsilon_{i1} \) and \( \epsilon_{i3} \) would be \( \rho^2 \).
**Supplementary Data**

**Genetic risk scores (GRS) and weight-regain from 6 months through study end**

We constructed three GRS comprising: i) all measured SNPs coded with the effect alleles as those associated with baseline BMI in the DPP; ii) SNPs associated with weight-regain in the overall DPP cohort (as described above); iii) all SNPs showing statistically significant gene x lifestyle interactions, where the SNP effect estimate on weight-regain differed in magnitude between the lifestyle and placebo arms of the trial. As Supplemental Figure 1 illustrates, weight regain rates were comparable between the lifestyle and placebo arms for participants with a low GRS (Supplemental Figures 1A-C), but differed substantially in those with a high GRS, indicating that persons with a heavy genetic burden struggle to maintain reduced weight when engaging in programs of intensive lifestyle modification.

The first GRS model showed no overall association with rate of weight-regain ($P=0.13$). The second GRS yielded similar effects across three arms ($P_{interaction}=0.70$), with one unit (allele) increase conveying 0.22, 0.37 and 0.31 kg/yr/allele faster weight-regain rates in the lifestyle ($P=0.04$), metformin ($P=0.01$) and placebo ($P=0.11$) groups respectively (panel B). On average, the second GRS was associated with 0.28kg/yr/allele faster ($P=0.0006$) rate of weight-regain. The third GRS effects (panel C) differed by treatment ($P_{interaction}=0.005$), with -0.35, -0.08, and 0.40 kg/yr/allele weight-regain rates in the lifestyle ($P=0.01$), metformin ($P=0.64$), and placebo ($P=0.09$) groups, respectively.

**Mediation analyses**

Secondary analyses were performed to determine whether changes in selected behaviors mediated associations between genotypes and obesity traits. SNPs significantly affecting each of these three traits were selected. Each SNP-outcome combination was tested for potential mediators. Candidate mediators were diet adherence, leisure time physical activity (LTPA), percent calories from protein, snack frequency, sweet and dessert frequency, fruit frequency and vegetable frequency. While testing each candidate mediator, two models were fit separately with the only difference being whether or not the candidate mediator was included as a covariate in the model. The same linear or mixed model (depending on outcome) was employed. From each pair of models, the difference in the two SNP regression coefficients and the standard errors of these differences were calculated. In these analyses, a statistically significant non-zero difference represents a discrepancy between the marginal SNP effect estimate and the SNP effect estimate that is conditional on the putative mediator, thus validating the intermediate function of the mediator from genotype to the outcome.

Although a number of nominally statistically significant associations were observed between SNPs and candidate energy balance behaviors (data not shown), there was no reliable evidence that any of these factors mediated the SNP effects on weight variables after correcting for multiple statistical comparisons (data not shown).
**SUPPLEMENTARY DATA**

**Pennington Biomedical Research Center**  
(Baton Rouge, LA)  
George A. Bray, MD*  
Iris W. Culbert, BSN, RN, CCRC**  
Catherine M. Champagne, PhD, RD  
Barbara Eberhardt, RD, LDN  
Frank Greenway, MD  
Fonda G. Guillory, LPN  
April A. Herbert, RD  
Michael L. Jeiffis, LPN  
Betty M. Kennedy, MPA  
Jennifer C. Lovejoy, PhD  
Laura H. Morris, BS  
Lee E. Melancon, BA, BS  
Donna Ryan, MD  
Deborah A. Sanford, LPN  
Kenneth G. Smith, BS, MT  
Lisa L. Smith, BS  
Julia A. St.Amant, RTR  
Richard T. Tulley, PhD  
Paula C. Vicknair, MS, RD  
Donald Williamson, PhD  
Jeffery J. Zachwieja, PhD

**University of Chicago**  
(Chicago, IL)  
Kenneth S. Polonsky, MD*  
Janet Tobian, MD, PhD*  
David Ehrmann, MD*  
Margaret J. Matulik, RN, BSN**  
Bart Clark, MD  
Kirsten Czech, MS  
Catherine DeSandre, BA  
Ruthanne Hilbrich, RD  
Wylie McNabb, EdD  
Ann R. Semenske, MS, RD

**Jefferson Medical College**  
(Philadelphia, PA)  
Jose F. Caro, MD*  
Pamela G. Watson, RN, ScD*  
Barry J. Goldstein, MD, PhD*  
Kellie A. Smith, RN, MSN**  
Jewel Mendoza, RN, BSN**  
Renee Liberoni, MPH  
Constance Pepe, MS, RD  
John Spandorfer, MD

**University of Miami**  
(Miami, FL)  
Richard P. Donahue, PhD*  
Ronald B. Goldberg, MD*  
Ronald Prineas, MD, PhD*  
Patricia Rowe, MPA**  
Jeanette Calles, MSED  
Paul Cassanova-Romero, MD  
Hermes J. Flores, MD  
Anna Giannella, RD, MS  
Lascelles Kirby, MS

**The University of Texas Health Science Center**  
(San Antonio, TX)  
Steven M. Haffner, MD, MPH*  
Maria G. Montez, RN, MSHP, CDE**  
Carlos Lorenzo, MD, PhD  
Arlene Martinez, RN, BSN, CDE

**University of Colorado**  
(Denver, CO)  
Richard F. Hamman, MD, DrPH*  
Patricia V. Nash, MS**  
Lisa Testaverde, MS**  
Denise R. Anderson, RN, BSN  
Larry B. Ballonoff, MD  
Alexis Bouffard, MA  
B. Ned Calonge, MD, MPH  
Lynne Delve  
Martha Farago, RN  
James O. Hill, PhD  
Shelley R. Hoyer, BS  
Bonnie T. Jortberg, MS, RD, CDE  
Dione Lenz, RN, BSN  
Marsha Miller, MS, RD  
David W. Price, MD  
Judith G. Regensteiner, PhD  
Helen Seagle, MS, RD  
Carissa M. Smith, BS  
Sheila C. Steinke, MS  
Brent VanDorsten, PhD

**Joslin Diabetes Center**  
(Boston, MA)  
Edward S. Horton, MD*  
Kathleen E. Lawton, RN**  
Ronald A. Arky, MD  
Marybeth Bryant  
Jacqueline P. Burke, BSN  
Enrique Caballero, MD  
Karen M. Callaphan, BA  
Om P. Ganda, MD  
Therese Franklin  
Sharon D. Jackson, MS, RD, CDE  
Alan M. Jacobsen, MD  
Lyn M. Kula, RD  
Margaret Kocal, RN, CDE  
Maureen A. Malloy, BS  
Maryanne Nicosia, MS, RD  
Cathryn F. Oldmixon, RN  
Jocelyn Pan, BS, MPH  
Marizel Quitingon  
Stacy Rubtchinsky, BS

SUPPLEMENTARY DATA

Ellen W. Seely, MD
Dana Schweizer, BSN
Donald Simonson, MD
Fannie Smith, MD
Caren G. Solomon, MD, MPH
James Warram, MD

VA Puget Sound Health Care System and
University of Washington (Seattle, WA)
Steven E. Kahn, MB, ChB*
Brenda K. Montgomery, RN, BSN, CDE**
Wilfred Fujimoto, MD
Robert H. Knopp, MD
Edward W. Lipkin, MD
Michelle Marr, BA
Dace Trence, MD

University of Tennessee (Memphis, TN)
Abbas E. Kitabchi, PhD, MD, FACP*
Mary E. Murphy, RN, MS, CDE, MBA**
William B. Applegate, MD, MPH
Michael Bryer-Ash, MD
Sandra L. Frieson, RN
Raed Imseis, MD
Helen Lambeth, RN, BSN
Lynne C. Lichtermann, RN, BSN
Hooman Oktaei, MD
Lily M.K. Rutledge, RN, BSN
Amy R. Sherman, RD, LD
Clara M. Smith, RD, MHP, LDN
Judith E. Soberman, MD
Beverly Williams-Cleaves, MD

Northwestern University’s Feinberg School of Medicine (Chicago, IL)
Boyd E. Metzger, MD*
Mariana K. Johnson, MS, RN**
Catherine Behrend
Michelle Cook, MS
Marian Fitzgibbon, PhD
Mimi M. Giles, MS, RD
Deloris Heard, MA
Cheryl K.H. Johnson, MS, RN
Diane Larsen, BS
Anne Lowe, BS
Megan Lyman, BS
David McPherson, MD
Mark E. Molitch, MD
Thomas Pitts, MD
Renee Reinhart, RN, MS
Susan Roston, RN, RD
Pamela A. Schinleber, RN, MS

Massachusetts General Hospital (Boston, MA)
David M. Nathan, MD*
Charles McKittrick, BSN**
Heather Turgeon, BSN**
Kathy Abbott
Ellen Anderson, MS, RD
Laurie Bissett, MS, RD
Enrico Caglieri, MD
Jose C. Florez, MD, PhD*
Linda Delahanty, MS, RD
Valerie Goldman, MS, RD
Alexandra Poulos

University of California-San Diego (San Diego, CA)
Jerrold M. Olefsky, MD*
Mary Lou Carrion-Petersen, RN, BSN**
Elizabeth Barrett-Connor, MD
Steven V. Edelman, MD
Robert R. Henry, MD
Javiva Horne, RD
Simona Szerdi Janesch, BA
Diana Leos, RN, BSN
Sundar Mudaliar, MD
William Polonsky, PhD
Jean Smith, RN
Karen Vejvoda, RN, BSN, CDE, CCRC

St. Luke’s-Roosevelt Hospital (New York, NY)
F. Xavier Pi-Sunyer, MD*
Jane E. Lee, MS**
David B. Allison, PhD
Nancy J. Aronoff, MS, RD
Jill P. Crandall, MD
Sandra T. Foo, MD
Carmen Pal, MD
Kathy Parkes, RN
Mary Beth Pena, RN
Ellen S. Rooney, BA
Gretchen E.H. Van Wye, MA
Kristine A. Viscovich, ANP

Indiana University (Indianapolis, IN)
David G. Marrero, PhD*
Melvin J. Prince, MD*
Susie M. Kelly, RN, CDE**
Yolanda F. Dotson, BS
Edwin S. Fineberg, MD
John C. Guare, PhD
Angela M. Hadden
James M. Ignaut, MA
Marcia L. Jackson
Marion S. Kirkman, MD
Kieren J. Mather, MD
Beverly D. Porter, MSN
Paris J. Roach, MD
Nancy D. Rowland, BS, MS
Madelyn L. Wheeler, RD

SUPPLEMENTARY DATA

Gaye Koenning, MS, RD**
M. Kaye Kramer, BSN, MPH**
Susan Barr, BS
Miriam Boraz
Lisa Clifford, BS
Rebecca Culyba, BS
Marlene Frazier
Ryan Gilligan, BS
Susan Harrer, MLT
Louann Harris, RN
Susan Jeffries, RN, MSN
Andrea Kriska, PhD
Qurashia Manjoo, MD
Monica Mullen, MHP, RD
Alicia Noel, BS
Amy Otto, PhD
Linda Semler, MS, RD
Cheryl F. Smith, PhD
Marie Smith, RN, BSN
Elizabeth Venditti, PhD
Valarie Weinzierl, BS
Katherine V. Williams, MD, MPH
Tara Wilson, BA

University of Hawaii (Honolulu, HI)
Richard F. Arakaki, MD*
Renee W. Latimer, BSN, MPH**
Narleen K. Baker-Ladao, BS
Ralph Beddow, MD
Lorna Dias, AA
Jillian Inouye, RN, PhD
Marjorie K. Mau, MD
Kathy Mikami, BS, RD
Pharis Mohideen, MD
Sharon K. Odom, RD, MPH
Raynette U. Perry, AA

Southwest American Indian Centers (Phoenix, AZ; Shiprock, NM; Zuni, NM)
William C. Knowler, MD, DrPH**
Norman Cooeyate**
Mary A. Hoskin, RD, MS**
Carol A. Percy, RN, MS**
Kelly J. Acton, MD, MPH
Vickie L. Andre, RN, FNP
Rosalyn Barber
Shandin Begay, MPH
Peter H. Bennett, MB, FRCP
Mary Beth Benson, RN, BSN
Evelyn C. Bird, RD, MPH
Brenda A. Broussard, RD, MPH, MBA, CDE
Marcella Chavez, RN, AS
Tara DaCawyma
Matthew S. Doughty, MD
Roberta Duncan, RD

Cyndy Edgerton, RD
Jacqueline M. Ghahte
Justin Glass, MD
Martia Glass, MD
Dorothy Gohdes, MD
Wendy Grant, MD
Robert L. Hanson, MD, MPH
Ellie Horse
Louise E. Ingraham, MS, RD, LN
Merry Jackson
Priscilla Jay
Royleen S. Kaskalla
David Kessler, MD
Kathleen M. Kobus, RNC-ANP
Jonathan Krakoff, MD
Catherine Manus, LPN
Sara Michaels, MD
Tina Morgan
Yolanda Nashboo (deceased)
Julie A. Nelson, RD
Steven Poirier, MD
Evette Polcynski, MD
Mike Reidy, MD
Jeanine Roumain, MD, MPH
Debra Rowse, MD
Sandra Sangster
Janet Sewenenewa
Darryl Tonemah, PhD
Charlton Wilson, MD
Michelle Yazzie

George Washington University Biostatistics Center (DPP Coordinating Center Rockville, MD)
Raymond Bain, PhD*
Sarah Fowler, PhD*
Tina Brenneman**
Solome Abebe
Jackie Callaghan
Sharon L. Edelstein, ScM
Yuping Gao
Kristina L. Grimes
Nisha Grover
Lori Haffner, MS
Steve Jones
Tara L. Jones
Richard Katz, MD
John M. Lachin, ScD
Pamela Mucik
Robert Orlosky
James Rochon, PhD
Alla Sapozhnkova
Hanna Sherif, MS

SUPPLEMENTARY DATA

Charlotte Stimpson
Marinella Temprosa, MS
Fredricka Walker-Murray
Central Biochemistry Laboratory (Seattle, WA)
Santica Marcovina, PhD, ScD*
Greg Styrelwicz, PhD**
F. Alan Aldrich

Carotid Ultrasound
Dan O’Leary, MD*

CT Scan Reading Center
Elizabeth Stamm, MD*

Epidemiological Cardiology Research Center- Epicare (Winston-Salem, NC)
Pentti Rautaharju, MD, PhD*
Ronald J. Prineas, MD, PhD**
Teresa Alexander
Charles Campbell, MS
Sharon Hall
Yabing Li, MD
Margaret Mills
Nancy Pemberton, MS
Farida Rautaharju, PhD
Zhuming Zhang, MD

Nutrition Coding Center (Columbia, SC)
Elizabeth Mayer-Davis, PhD*
Robert R. Moran, PhD**

Quality of Well-Being Center (La Jolla, CA)
Ted Ganiats, MD*
Kristin David, MHP*
Andrew J. Sarkin, PhD*

NIH/NIDDK (Bethesda, MD)
R. Eastman, MD
Judith Fradkin, MD
Sanford Garfield, PhD

Centers for Disease Control & Prevention (Atlanta, GA)
Edward Gregg, PhD
Ping Zhang, PhD

University of Michigan (Ann Arbor, MI)
William Herman, MD, MPH

+Genetics Working Group
Jose C. Florez, MD, PhD1,2
David Altshuler, MD, PhD1,2
Paul I.W. de Bakker, PhD2
Paul W. Franks, PhD, MPhil, MS6,7
Robert L. Hanson, MD, MPH3
Kathleen Jablonski, PhD6
William C. Knowler, MD, DrPH3
Jarred B. McAteer, AB1,2
Toni I. Pollin, PhD4
Alan R. Shuldiner, MD4

1=Massachusetts General Hospital
2=Broad Institute
3=NIDDK
4=University of Maryland
5=Coordinating Center
6=Lund University, Sweden
7=Harvard School of Public Health

* denotes Principal Investigator
** denotes Program Coordinator

### Supplementary Table 1. Participant characteristics (max N=3,819)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Lifestyle</th>
<th>Metformin</th>
<th>Placebo</th>
<th>Troglitazone</th>
<th>P-value</th>
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<tbody>
<tr>
<td>N</td>
<td>1079</td>
<td>1073</td>
<td>1082</td>
<td>585</td>
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<tr>
<td>Male</td>
<td>32%</td>
<td>34%</td>
<td>31%</td>
<td>34%</td>
<td>0.404</td>
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<tr>
<td>Baseline age (years)</td>
<td>51 (11)</td>
<td>51 (10)</td>
<td>50 (10)</td>
<td>50 (10)</td>
<td>0.469</td>
</tr>
<tr>
<td>Baseline weight (kg)</td>
<td>94 (21)</td>
<td>94 (20)</td>
<td>94 (20)</td>
<td>93 (19)</td>
<td>0.774</td>
</tr>
<tr>
<td>Baseline BMI (kg/m²)</td>
<td>34 (7)</td>
<td>34 (7)</td>
<td>34 (7)</td>
<td>34 (6)</td>
<td>0.311</td>
</tr>
<tr>
<td>Baseline waist circumference (cm)</td>
<td>105 (15)</td>
<td>105 (14)</td>
<td>105 (14)</td>
<td>104 (14)</td>
<td>0.605</td>
</tr>
<tr>
<td>Baseline SAT L4 (cm²)</td>
<td>308 (125)</td>
<td>301 (129)</td>
<td>314 (127)</td>
<td></td>
<td>0.449</td>
</tr>
<tr>
<td>Baseline SAT L5 (cm²)</td>
<td>443 (152)</td>
<td>433 (154)</td>
<td>449 (151)</td>
<td></td>
<td>0.408</td>
</tr>
<tr>
<td>Baseline VAT L4 (cm²)</td>
<td>200 (85)</td>
<td>195 (83)</td>
<td>199 (90 )</td>
<td></td>
<td>0.701</td>
</tr>
<tr>
<td>Baseline VAT L5 (cm²)</td>
<td>163 (65)</td>
<td>158 (65)</td>
<td>159 (65)</td>
<td></td>
<td>0.500</td>
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<tr>
<td>Baseline LTPA (MET hrs/wk)</td>
<td>16 (22)</td>
<td>16 (26)</td>
<td>17 (29)</td>
<td>15 (16)</td>
<td>0.390</td>
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<tr>
<td>Baseline energy Intake (kJ)</td>
<td>2137 (1071)</td>
<td>2144 (986)</td>
<td>2098 (1052)</td>
<td>2118 (989)</td>
<td>0.739</td>
</tr>
<tr>
<td>Short-term weight loss (kg) (0-6 m)</td>
<td>6.7 (5.6)</td>
<td>2.3 (4.0)</td>
<td>0.3 (4.0)</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Long-term weight loss (kg) (0-24 m)</td>
<td>5.4 (7.6)</td>
<td>2.1 (5.7)</td>
<td>0.0 (5.5)</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Weight regain (kg) (6m to study end)</td>
<td>3.0 (8.2)</td>
<td>2.4 (7.7)</td>
<td>0.8 (7.3)</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data are percentage or Mean (SD), stratified by treatment assignment. P-values from ANOVA F-tests and Chi-Square test of independence. LTPA: leisure-time physical activity. The sample size (N=3,819) is the maximum number used in baseline analyses and includes participants who were subsequently randomized to troglitazone treatment (in which only baseline data is available), in addition to those randomized to lifestyle, metformin, or placebo. Sample sizes for: short-term weight loss (n=3085); long-term weight loss (n=3015); weight regain (n=1411); baseline measures of VAT and SAT (n=869). We include individuals subsequently randomized to troglitazone in the baseline analyses to maximize statistical power. However, these individuals are not included in the prospective analyses as they represent a relatively small subgroup of the DPP population, which is likely underpowered for treatment stratified analyses.
# Supplementary Data

## Supplementary Table 2. SNP identities and frequencies

<table>
<thead>
<tr>
<th>Nearest gene</th>
<th>SNP</th>
<th>Minor(major) allele</th>
<th>Frequency of effect allele</th>
<th>Genotype Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MC4R</strong></td>
<td>rs17782313</td>
<td>C(T)</td>
<td>n=1646 (23%)</td>
<td>TT (n= 2109, 60%)  CT (n= 1224, 35%) CC (n= 211, 6%)</td>
</tr>
<tr>
<td><strong>FTO</strong></td>
<td>rs9939609</td>
<td>A(T)</td>
<td>n= 2809 (41%)</td>
<td>TT (n= 1235, 36%)  AT (n= 1623, 47%) AA (n= 593, 17%)</td>
</tr>
<tr>
<td><strong>MTCH2</strong></td>
<td>rs10838738</td>
<td>G(A)</td>
<td>n= 2088 (31%)</td>
<td>AA (n= 1679, 49%)  GA (n= 1372, 40%) GG (n= 358, 11%)</td>
</tr>
<tr>
<td><strong>NEGR1</strong></td>
<td>rs2815752</td>
<td>G(A)</td>
<td>n= 2437 (36%)</td>
<td>AA (n= 1440, 42%)  GA (n= 1529, 45%) GG (n= 454, 13%)</td>
</tr>
<tr>
<td><strong>TMEM18</strong></td>
<td>rs6548238</td>
<td>T(C)</td>
<td>n= 1024 (15%)</td>
<td>CC (n= 2484, 72%)  TC (n= 866, 25%) TT (n= 79, 2%)</td>
</tr>
<tr>
<td><strong>SH2B1</strong></td>
<td>rs7498665</td>
<td>C(T)</td>
<td>n= 2524 (37%)</td>
<td>TT(n= 1371, 40%)  CT (n= 1554, 46%) CC (n= 485, 14%)</td>
</tr>
<tr>
<td><strong>SEC16B</strong></td>
<td>rs10913469</td>
<td>C(T)</td>
<td>n= 1395 (21%)</td>
<td>TT(n= 2058, 63%)  CT (n= 1041, 32%) CC (n= 177, 5%)</td>
</tr>
<tr>
<td><strong>BDNF</strong></td>
<td>rs6265</td>
<td>T(C)</td>
<td>n= 1090 (16%)</td>
<td>CC (n= 2442, 71%)  TC (n= 890, 26%) TT (n= 100, 3%)</td>
</tr>
<tr>
<td><strong>FAIM2</strong></td>
<td>rs7138803</td>
<td>A(G)</td>
<td>n= 2144 (32%)</td>
<td>GG (n= 1634, 48%)  AG (n= 1384, 41%) AA (n= 380, 11%)</td>
</tr>
<tr>
<td><strong>KTCD15</strong></td>
<td>rs29941</td>
<td>A(G)</td>
<td>n= 2135 (31%)</td>
<td>GG (n= 1653, 48%)  AG (n= 1401, 41%) AA (n= 367, 11%)</td>
</tr>
<tr>
<td><strong>PPARG</strong></td>
<td>rs1801282</td>
<td>Ala(Pro)</td>
<td>n= 585 (9%)</td>
<td>PP (n= 2787, 83%)  PA (n= 553, 16%) AA (n= 16, 0%)</td>
</tr>
<tr>
<td><strong>LYPLAL1</strong></td>
<td>rs2605100</td>
<td>A(G)</td>
<td>n= 1709 (24%)</td>
<td>GG (n= 2016, 58%)  AG (n= 1267, 36%) AA (n= 221, 6%)</td>
</tr>
<tr>
<td><strong>ETV5</strong></td>
<td>rs7647305</td>
<td>T(C)</td>
<td>n= 1573 (23%)</td>
<td>CC (n= 2091, 61%)  TC (n= 1133, 33%) TT (n= 220, 6%)</td>
</tr>
<tr>
<td><strong>GNPDA2</strong></td>
<td>rs10938397</td>
<td>G(A)</td>
<td>n= 2614 (38%)</td>
<td>AA (n= 1360, 40%)  GA (n= 1546, 45%) GG (n= 534, 16%)</td>
</tr>
<tr>
<td><strong>TFAP2B</strong></td>
<td>rs987237</td>
<td>G(A)</td>
<td>n= 1460 (21%)</td>
<td>AA (n= 2206, 63%) GA(n= 1084, 31%) GG (n= 188, 5%)</td>
</tr>
<tr>
<td><strong>MSRA</strong></td>
<td>rs7826222</td>
<td>G(C)</td>
<td>n= 1209 (17%)</td>
<td>CC (n= 2423, 69%)  GC (n= 953, 27%) GG(G= 128, 4%)</td>
</tr>
</tbody>
</table>
### Supplementary Table 3. Comparison of risk increasing alleles in the published literature and the DPP for selected SNPs

<table>
<thead>
<tr>
<th>Nearest gene</th>
<th>SNP</th>
<th>Baseline BMI</th>
<th>Published studies</th>
<th>Diabetes Prevention Program</th>
<th>Weight loss at 6m</th>
<th>Weight loss at 24 m</th>
<th>Weight regain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>X-sectional BMI effect allele (other)</td>
<td>All</td>
<td>L</td>
<td>M</td>
<td>P</td>
</tr>
<tr>
<td><strong>MC4R</strong></td>
<td>rs17782313</td>
<td>C(T)</td>
<td>T - - -</td>
<td>T - - -</td>
<td>T - - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FTO</strong></td>
<td>rs9939609</td>
<td>A(T)</td>
<td>A - A A G</td>
<td>T - - -</td>
<td>A - - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MTCH2</strong></td>
<td>rs10838738</td>
<td>G(A)</td>
<td>A - A - -</td>
<td>C - - -</td>
<td>C - - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NEGR1</strong></td>
<td>rs2815752</td>
<td>A(G)</td>
<td>A G G -</td>
<td>G T - -</td>
<td>G T - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TMEM18</strong></td>
<td>rs6548238</td>
<td>C(T)</td>
<td>C - - -</td>
<td>C - - -</td>
<td>C - - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SH2B1</strong></td>
<td>rs7498665</td>
<td>T(C)</td>
<td>T T - -</td>
<td>C - - -</td>
<td>C - - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SEC16B</strong></td>
<td>rs10913469</td>
<td>C(T)</td>
<td>C - - -</td>
<td>C - - -</td>
<td>C - - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BDNF</strong></td>
<td>rs6265</td>
<td>C(T)</td>
<td>C - - -</td>
<td>C - - -</td>
<td>C - - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FAIM2</strong></td>
<td>rs7138803</td>
<td>A(G)</td>
<td>A - A - -</td>
<td>A - A - -</td>
<td>A - A - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>KTCD15</strong></td>
<td>rs29941</td>
<td>G(A)</td>
<td>G A - -</td>
<td>A - - -</td>
<td>A - - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PPARG</strong></td>
<td>rs1801282</td>
<td>Ala(Pro)</td>
<td>Ala Pro - -</td>
<td>Pro Pro - -</td>
<td>Pro Pro - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LYPLAL1</strong></td>
<td>rs2605100</td>
<td>G(A)</td>
<td>G - G G A</td>
<td>G - - -</td>
<td>G - - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ETV5</strong></td>
<td>rs7647305</td>
<td>C(T)</td>
<td>C - - -</td>
<td>T - - -</td>
<td>T - - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>GNPDA2</strong></td>
<td>rs10938397</td>
<td>G(A)</td>
<td>A - G G -</td>
<td>G - G - -</td>
<td>G - G - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TFAP2B</strong></td>
<td>rs987237</td>
<td>G(A)</td>
<td>G A - -</td>
<td>G - - -</td>
<td>G - - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MSRA</strong></td>
<td>rs7826222</td>
<td>G(C)</td>
<td>G C - -</td>
<td>C - - -</td>
<td>C - - -</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


*BMI0-baseline BMI; 6m WL- 6 month weight loss; 2y WL – 2 years weight loss; WR – weight regain.
**Supplementary Table 4.** Summary of association data for each of 16 known obesity loci with baseline weight (kg) and BMI (kg/m²) (N=3,819)

<table>
<thead>
<tr>
<th>Nearest gene</th>
<th>SNP</th>
<th>Effect allele</th>
<th>Weight (kg/allele)</th>
<th>BMI (kg/m²/allele)</th>
<th>Height (m/allele)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Coefficient(SE)</td>
<td>P-value</td>
<td>Coefficient(SE)</td>
</tr>
<tr>
<td><strong>MC4R</strong></td>
<td>rs17782313</td>
<td>C(T)</td>
<td>-0.63(0.52)</td>
<td>0.230</td>
<td>-0.14(0.18)</td>
</tr>
<tr>
<td><strong>FTO</strong></td>
<td>rs9939609</td>
<td>A(T)</td>
<td>0.91(0.46)</td>
<td>0.048</td>
<td>0.40(0.15)</td>
</tr>
<tr>
<td><strong>MTCH2</strong></td>
<td>rs10838738</td>
<td>G(A)</td>
<td>-0.32(0.50)</td>
<td>0.521</td>
<td>-0.23(0.17)</td>
</tr>
<tr>
<td><strong>NEGR1</strong></td>
<td>rs2815752</td>
<td>A(G)</td>
<td>-0.35(0.47)</td>
<td>0.462</td>
<td>0.04(0.16)</td>
</tr>
<tr>
<td><strong>TMEM18</strong></td>
<td>rs6548238</td>
<td>C(T)</td>
<td>0.60(0.63)</td>
<td>0.339</td>
<td>0.12(0.21)</td>
</tr>
<tr>
<td><strong>SH2B1</strong></td>
<td>rs7498665</td>
<td>T(C)</td>
<td>-0.04(0.47)</td>
<td>0.931</td>
<td>0.00(0.16)</td>
</tr>
<tr>
<td><strong>SEC16B</strong></td>
<td>rs10913469</td>
<td>C(T)</td>
<td>0.57(0.56)</td>
<td>0.303</td>
<td>0.26(0.19)</td>
</tr>
<tr>
<td><strong>BDNF</strong></td>
<td>rs6265</td>
<td>C(T)</td>
<td>-1.41(0.62)</td>
<td>0.024</td>
<td>-0.39(0.21)</td>
</tr>
<tr>
<td><strong>FAIM2</strong></td>
<td>rs7138803</td>
<td>A(G)</td>
<td>0.51(0.49)</td>
<td>0.299</td>
<td>0.28(0.16)</td>
</tr>
<tr>
<td><strong>KTCD15</strong></td>
<td>rs29941</td>
<td>G(A)</td>
<td>0.52(0.49)</td>
<td>0.291</td>
<td>0.27(0.17)</td>
</tr>
<tr>
<td><strong>PPARG</strong></td>
<td>rs1801282</td>
<td>Ala(Pro)</td>
<td>-1.82(0.84)</td>
<td>0.030</td>
<td>-0.50(0.28)</td>
</tr>
<tr>
<td><strong>LYPLAL1</strong></td>
<td>rs2605100</td>
<td>G(A)</td>
<td>-0.02(0.53)</td>
<td>0.970</td>
<td>0.01(0.18)</td>
</tr>
<tr>
<td><strong>ETV5</strong></td>
<td>rs7647305</td>
<td>C(T)</td>
<td>0.79(0.53)</td>
<td>0.136</td>
<td>0.28(0.18)</td>
</tr>
<tr>
<td><strong>GNPDA2</strong></td>
<td>rs10938397</td>
<td>G(A)</td>
<td>-1.60(0.46)</td>
<td>0.001</td>
<td>-0.47(0.15)</td>
</tr>
<tr>
<td><strong>TFAP2B</strong></td>
<td>rs987237</td>
<td>G(A)</td>
<td>0.16(0.55)</td>
<td>0.772</td>
<td>0.11(0.19)</td>
</tr>
<tr>
<td><strong>MSRA</strong></td>
<td>rs7826222</td>
<td>G(C)</td>
<td>-0.02(0.60)</td>
<td>0.971</td>
<td>0.15(0.15)</td>
</tr>
</tbody>
</table>

*Coefficients and P-values correspond to the additive allele effects adjusting for baseline age, sex and ethnicity.*
### Supplementary Table 5. Summary of association data for each of 16 known obesity loci and rate of weight regain from 6 months through trial end (kg/yr) in non-Hispanic White and by treatment arm

<table>
<thead>
<tr>
<th>Nearest gene</th>
<th>SNP</th>
<th>Effect (other) allele</th>
<th>SNP * TX</th>
<th>TX ADJUSTED coefficient (SE)</th>
<th>P-VAL</th>
<th>LIFESTYLE coefficient (SE)</th>
<th>P-VAL</th>
<th>METFORMIN coefficient (SE)</th>
<th>P-VAL</th>
<th>PLACEBO coefficient (SE)</th>
<th>P-VAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>MC4R</td>
<td>rs17782313</td>
<td>C(T)</td>
<td>N</td>
<td>-0.48 (0.13)</td>
<td>&lt; 0.001</td>
<td>-0.59 (0.18)</td>
<td>&lt; 0.001</td>
<td>-0.15 (0.21)</td>
<td>0.458</td>
<td>-0.68 (0.37)</td>
<td>0.067</td>
</tr>
<tr>
<td>FTO</td>
<td>rs9939609</td>
<td>A(T)</td>
<td>Y</td>
<td>0.46 (0.15)</td>
<td>0.002</td>
<td>-0.76 (0.19)</td>
<td>&lt; 0.001</td>
<td>-0.06 (0.30)</td>
<td>0.837</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTCH2</td>
<td>rs10838738</td>
<td>G(A)</td>
<td>Y</td>
<td>-0.32 (0.17)</td>
<td>0.061</td>
<td>-0.04 (0.19)</td>
<td>0.827</td>
<td>0.55 (0.35)</td>
<td>0.114</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEGR1</td>
<td>rs2815752</td>
<td>A(G)</td>
<td>N</td>
<td>-0.38 (0.12)</td>
<td>0.001</td>
<td>-0.29 (0.16)</td>
<td>0.072</td>
<td>-0.50 (0.20)</td>
<td>0.013</td>
<td>-0.36 (0.32)</td>
<td>0.260</td>
</tr>
<tr>
<td>TMEM18</td>
<td>rs6548238</td>
<td>C(T)</td>
<td>Y</td>
<td>0.40 (0.21)</td>
<td>0.056</td>
<td>0.54 (0.27)</td>
<td>0.051</td>
<td>-1.13 (0.44)</td>
<td>0.011</td>
<td></td>
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</tr>
<tr>
<td>SH2B1</td>
<td>rs7498665</td>
<td>T(C)</td>
<td>N</td>
<td>0.17 (0.12)</td>
<td>0.150</td>
<td>0.01 (0.17)</td>
<td>0.937</td>
<td>0.19 (0.19)</td>
<td>0.308</td>
<td>0.59 (0.31)</td>
<td>0.054</td>
</tr>
<tr>
<td>SEC16B</td>
<td>rs10913469</td>
<td>C(T)</td>
<td>N</td>
<td>0.08 (0.15)</td>
<td>0.592</td>
<td>0.00 (0.22)</td>
<td>0.987</td>
<td>0.39 (0.23)</td>
<td>0.094</td>
<td>-0.11 (0.43)</td>
<td>0.796</td>
</tr>
<tr>
<td>BDNF</td>
<td>rs6265</td>
<td>C(T)</td>
<td>Y</td>
<td>0.21 (0.21)</td>
<td>0.312</td>
<td>0.80 (0.22)</td>
<td>&lt; 0.001</td>
<td>0.88 (0.41)</td>
<td>0.035</td>
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<td></td>
</tr>
<tr>
<td>FAIM2</td>
<td>rs7138803</td>
<td>A(G)</td>
<td>N</td>
<td>0.13 (0.12)</td>
<td>0.280</td>
<td>0.07 (0.17)</td>
<td>0.688</td>
<td>0.50 (0.20)</td>
<td>0.014</td>
<td>-0.11 (0.32)</td>
<td>0.729</td>
</tr>
<tr>
<td>KTCD15</td>
<td>rs29941</td>
<td>G(A)</td>
<td>Y</td>
<td>0.89 (0.17)</td>
<td>&lt; 0.001</td>
<td>-0.56 (0.20)</td>
<td>0.007</td>
<td>-0.71 (0.33)</td>
<td>0.031</td>
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<td></td>
</tr>
<tr>
<td>PPARG</td>
<td>rs1801282</td>
<td>Ala(Pro)</td>
<td>N</td>
<td>-0.79 (0.18)</td>
<td>&lt; 0.001</td>
<td>-0.91 (0.26)</td>
<td>&lt; 0.001</td>
<td>-0.84 (0.28)</td>
<td>0.003</td>
<td>-0.60 (0.50)</td>
<td>0.234</td>
</tr>
<tr>
<td>LYPLAL1</td>
<td>rs2605100</td>
<td>G(A)</td>
<td>N</td>
<td>-0.02 (0.13)</td>
<td>0.845</td>
<td>0.04 (0.18)</td>
<td>0.807</td>
<td>0.06 (0.21)</td>
<td>0.791</td>
<td>-0.43 (0.33)</td>
<td>0.200</td>
</tr>
<tr>
<td>ETV5</td>
<td>rs7647305</td>
<td>C(T)</td>
<td>N</td>
<td>-0.13 (0.13)</td>
<td>0.338</td>
<td>-0.50 (0.18)</td>
<td>0.005</td>
<td>0.77 (0.23)</td>
<td>&lt; 0.001</td>
<td>-0.09 (0.37)</td>
<td>0.805</td>
</tr>
<tr>
<td>GNPDA2</td>
<td>rs10938397</td>
<td>G(A)</td>
<td>N</td>
<td>0.01 (0.11)</td>
<td>0.899</td>
<td>-0.18 (0.16)</td>
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</tr>
<tr>
<td>TFAP2B</td>
<td>rs987237</td>
<td>G(A)</td>
<td>N</td>
<td>0.19 (0.15)</td>
<td>0.205</td>
<td>0.14 (0.22)</td>
<td>0.528</td>
<td>0.38 (0.22)</td>
<td>0.086</td>
<td>-0.11 (0.35)</td>
<td>0.759</td>
</tr>
<tr>
<td>MSRA</td>
<td>rs7826222</td>
<td>G(C)</td>
<td>N</td>
<td>-0.22 (0.16)</td>
<td>0.168</td>
<td>-0.31 (0.22)</td>
<td>0.154</td>
<td>-0.42 (0.25)</td>
<td>0.095</td>
<td>0.47 (0.40)</td>
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</tbody>
</table>
SUPPLEMENTARY DATA

Supplementary Figure 1. Mean rate of weight regain from 6 months through 4.5 years (kg/yr) by treatment arm and genetic risk score (GRS) quartiles. Panel A shows a GRS comprised of all 16 SNPs; Panel B shows data for a GRS composed of only those SNPs showing statistically significant main effects for weight regain in the DPP; Panel C shows data for a GRS composed of all SNPs showing statistically significant gene x lifestyle interactions in the DPP.