Supplemental Table 1: WLS participant response and attrition for survey waves 1993, 2004, and 2011. The number of participants from each survey wave included in the 'MI by 72 Years of Age' analysis, as well as the number of participants who died before each survey wave is included.

Participant Attrition	**1993 Survey Wave**	**2004 Survey Wave**	**2011 Survey Wave**
Total participant response to WLS (n =)	8493	7265	5968
Included in 'MI by 72 Years of Age' analysis (n =)	6013	5757	5939
Non-respondents who died before survey wave (n =)	587	1287	1587
Attrition from WLS for other reasons (n=)	1237	1765	2762

Supplemental Information 1: Explanation of WLS variables used to create the two dependent variables for the current study.

This study examined potential MI associated factors using environmental, health, social, behavioral, and genetic data available through the Wisconsin Longitudinal Study (WLS). In order to create our dependent MI variables, we compiled data from the 2004 and 2011 WLS surveys including National Death Index (NDI) data collected by the WLS. The first dependent variable created by this study, 'MI by 72 Years of Age', was coded as "Yes" if a participant answered 'yes' to the question, "Did you have a heart attack or myocardial infarction?" during the 2004 telephone interview, or answered 'yes' to the question, "Did participant ever have a heart attack or myocardial infarction?" during the 2011 in-person or telephone interview, or if the participant ever died of an acute MI according to the National Death Index (ICD-9 or ICD-10 codes; collected by the WLS through 2006 at the time of this study), thereby including anyone who ever reported having a MI to the WLS. The 'MI by 72 Years of Age' dependent variable was coded "No" if the participant answered 'no' to the question, "Has a doctor ever told participant they had a heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems?" during the 2011 survey round, or 'no' to the question, "Did participant ever have a heart attack or myocardial infarction?" during the same survey period. This resulted in MI data for 6,198 graduates, with 776 participants coded as "Yes" and 5,422 coded as "No" for the given MI variable. Additionally, this dependent variable was linked to a dataset which included independent variables collected from all WLS survey years, 1957-2011.

The second dependent variable, 'MI Between 65-72 Years of Age', included ONLY those participants who answered 'no' to the question, "Has a doctor ever told you that you had a heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems?" or answered 'no' to the question, "Did you have a heart attack or myocardial infarction?" during the 2004 telephone interview, and thereby only included those who had not had a MI yet by 2004. The variable was coded as "Yes" if the participant answered 'yes' to the question, "Did participant ever have a heart attack or myocardial infarction?" during the 2011 in-person or telephone interview, or if the participant died of an acute MI after 2004 according to the National Death Index (ICD-9 or ICD-10 codes; collected by the WLS through 2006 at the time of this study). This MI variable was coded "No" if the participant answered 'no' to the question, "Has a doctor ever told participant they had a heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems?" during the 2011 survey round, or 'no' to the question, "Did participant ever have a heart attack or myocardial infarction?" during the same survey period. This resulted in MI data for 5,321 graduates, with 213 participants coded as "Yes" and 5,108 coded as "No" for the given (dependent) MI variable. In addition, this dependent variable was linked to a dataset which included only independent variables collected during the 2004 survey year or earlier.

Supplemental Information 2: List of dependent variables, all independent environmental, health, social, and behavioral variables, and additional ApoE genetic variables with current study descriptions and associated WLS coding.

Variable Description, Survey Year	**WLS variable code**
Used to create Dependent Variables	
Year of Death	deatyr
Cause of Death	ndi02
Myocardial Infarction, 2004	*gx351re & gx352re
Myocardial Infarction, 2011	*hx351re & hx352re
Independent Variables	
Sex	sexrsp
Age (current)	brdxdy
IQ (Henmon-Nelson test score), 1957	gwiiq_bm
Number of Children, 1993	rd001kd
Number of Children, 2004	gd001kd
Number of Children, 2011	hd001kd
Deceased Child, 2004	gd102kd
Not Married, 1993	rc001re
Not Married, 2004	gc001re
Not Married, 2011	hc001re
Total Household Income, 2004	gp260hec
Total Household Income, 2011	hp260hec
Importance of Financial Situation, 1993	rb036re
Satisfied with Financial Situation, 2004	gp226re
Satisfied with Financial Situation, 2011	hp226re
Parent or Sibling Heart Attack before age 55, 2004	ixa06rec
Parent or Sibling Heart Attack after age 55, 2004	ixa07rec
High Cholesterol, 2004	ix146rer
High Cholesterol, 2011	jx146rer
Parent or Sibling High Cholesterol, 2004	ixa03rec
High Blood Pressure, 1993	mx101rer
High Blood Pressure, 2004	gx341re
High Blood Pressure, 2011	hx341re
Osteoporosis, 2004	ix150rer
Osteoporosis, 2011	jx150rer
Parent or Sibling Osteoporosis, 2004	ixa11rec
Stroke, 2004	gx356re
Stroke, 2011	hx356re
Parent or Sibling Stroke before age 65, 2004	ixa04rec
Parent or Sibling Stroke after age 65, 2004	ixa05rec
Diabetes, 1993	mx095rer
Diabetes, 2004	gx342re
Diabetes, 2011	hx342re
Parent or Sibling Diabetes, 2004	ixa08rec
Parent or Sibling Alzheimer's Disease, 2004	ixa09rec
Ever Smoked Cigarettes, 1993	mx012rer
Ever Smoked Cigarettes, 2004	ix012rer

Variable Description, Survey Year	WLS variable code
Ever Smoked Cigarettes, 2011	jx012rer
Years Smoked, 1993	*mx012rer & mx014rer
Years Smoked, 2004	*ix012rer & ix014rer
Years Smoked, 2011	*jx012rer & jx014rer
Packs/Day Smoked, 1993	*mx012rer & mx015rer
Packs/Day Smoked, 2004	*ix012rer & ix015rer
Packs/Day Smoked, 2011	*jx012rer & jx015rer
Pack-Years Smoked, 1993	*mx012rer & mx014rer & mx015rer
Pack-Years Smoked, 2004	*ix012rer & ix014rer & ix015rer
Pack-Years Smoked, 2011	*jx012rer & jx014rer & jx015rer
Ever Smoked Pipe, Cigars, or used Snuff or Chewing Tobacco Regularly, 2004	ixt01rer
Body Mass Index, 1993	mx011rec
Body Mass Index, 2004	ix011rec
Body Mass Index, 2011	jx011rec
Age Weighed Most, 2004	ixw02rer
Age Weighed Most, 2011	jxw02rer
Overweight, Underweight, or Right Weight, 2004	ixw05rer
Overweight, Underweight, or Right Weight, 2011	jxw05rer
Using Exercise to Lose or Maintain Weight, 2004	ixw08rer
Using Exercise to Lose or Maintain Weight, 2011	jxw08rer
Most Ever Weighed, 2004	ixw01rer
Most Ever Weighed, 2011	jxw01rer
Hours/Month Light Activity, Alone or with Others, 2004	ixe01rer
Hours/Month Vigorous Activity, Alone or with Others, 2004	ixe02rer
Hours/Month Light Activity Alone, 2004	iz165rer
Hours/Month Light Activity Alone, 2011	jz165rer
Hours/Month Light Activity with Others, 2004	iz168rer
Hours/Month Light Activity with Others 2011	jz168rer
Light Activity Alone 10 Years Ago, 2004	iz166rer
Light Activity Alone 5 Years Ago, 2011	jz166rer
Light Activity with Others 10 Years Ago, 2004	iz169rer
Light Activity with Others 5 Years Ago, 2011	jz169rer
Light Activity Alone when 35, 2004	iz167rer
Light Activity with Others when 35, 2004	iz170rer
Hours/Month Vigorous Activity Alone, 2004	iz171rer
Hours/Month Vigorous Activity Alone, 2011	jz171rer
Hours/Month Vigorous Activity with Others, 2004	iz174rer
Hours/Month Vigorous Activity with Others, 2011	jz174rer
Vigorous Activity Alone 10 Years Ago, 2004	iz172rer
Vigorous Activity Alone 5 Years Ago, 2011	jz172rer
Vigorous Activity with Others 10 Years Ago, 2004	iz175rer
Vigorous Activity with Others 5 Years Ago, 2011	jz175rer
Vigorous Activity Alone when 35, 2004	iz173rer
Vigorous Activity with Others when 35, 2004	iz176rer
Hours/Week Watch T.V., 2004	iz108rer
Hours/Week Watch T.V., 2011	jz108rer

Variable Description, Survey Year	WLS variable code
How often Watched T.V. 10 Years Ago, 2004	iz109rer
How often Watched T.V. when 35, 2004	iz110rer
How often Watched T.V. 5 Years Ago, 2011	jz109rer
Person in Family to Share Feelings and Concerns, 1993	mv053rer
Person in Family to Share Feelings and Concerns, 2004	iv053rer
Person in Family to Share Feelings and Concerns, 2011	jv053rer
Friend Outside Family to Share Feelings and Concerns, 1993	mv054rer
Friend Outside Family to Share Feelings and Concerns, 2004	iv054rer
Friend Outside Family to Share Feelings and Concerns, 2011	jv054rer
Trouble Sleeping in Past 6 Months, 1993	mx019rer
Trouble Sleeping in Past 6 Months, 2004	ix019rer
Days/Week Sleep Restlessly, 1993	mu020rer
Days/Week Sleep Restlessly, 2004	iu020rer
Days/Week Sleep Restlessly, 2011	ju020rer
Hours of Sleep on a Weekday, 2011	jxsl11re
Worry a Lot, 1993	mh029rer
Worry a Lot, 2004	ih029rer
Worry a Lot, 2011	jh029rer
Feel Confident and Positive about Yourself, 1993	mn049rer
Feel Confident and Positive about Yourself, 2004	in049rer
Feel Confident and Positive about Yourself, 2011	jn049rer
Created Lifestyle to Your Liking, 1993	mn017rer
Created Lifestyle to Your Liking, 2004	in017rer
Created Lifestyle to Your Liking, 2011	jn017rer
Days/Week Feel Fearful, 1993	mu019rer
Days/Week Feel Fearful, 2004	iu019rer
Days/Week Feel Fearful, 2011	ju019rer
Days/Week Feel Relaxed, 2004	iu047rer
Days/Week Feel Relaxed, 2011	ju047rer
Are Relaxed and Handle Stress Well, 1993	rh020re
Summary Score Speilberger Anger Index, 2004	iuc34rec
Summary Score Speilberger Anger Index, 2011	jua34rec
Summary Score Hostility Index, 2004	iu026rec
Summary Score Speilberger Anxiety Index, 2004	iua33rec
Summary Score Speilberger Anxiety Index, 2011	jua33rec
Summary Score Psychological Well-Being, 1993	rn014rei
Summary Score Distress/Depression, 1993	mu001rec
Summary Score Distress/Depression, 2004	iu001rec
Summary Score Distress/Depression, 2011	ju001rec
Days/Week Feel Depressed, 1993	mu013rer
Days/Week Feel Depressed, 2004	iu013rer
Days/Week Feel Depressed, 2011	ju013rer
Ever Drank Alcohol, 1993	ru025re
Ever Drank Alcohol, 2004	gu025re
Ever Drank Alcohol, 2011	hu025re
Days/Month Drink Alcohol, 1993	*ru025re & ru026re
Days/Month Drink Alcohol, 2004	*gu025re & gu026re
Days/Month Drink Alcohol, 2011	*hu025re & hu026re
Drinks/Day on Days Drank Alcohol, 1993	*ru025re & ru027re
Drinks/Day on Days Drank Alcohol, 2004	*gu025re & gu027re

Variable Description , Survey Year	WLS variable code
Drinks/Day on Days Drank Alcohol, 2011	*hu025re & hu027re
Alcoholic Drinks/Month, 1993	*ru025re & ru028re
Alcoholic Drinks/Month, 2004	*gu025re & gu028re
Alcoholic Drinks/Month, 2011	*hu025re & hu028re
Days/Month Drank 5+ Alcoholic Drinks/Day, 1993	*ru025re & ru029re
Days/Month Drank 5+ Alcoholic Drinks/Day, 2004	*gu025re & gu029re
Days/Month Drank 5+ Alcoholic Drinks/Day, 2011	*hu025re & hu029re
Family Worries Distract from Work, 1993	my004rer
Family Worries Distract from Work, 2004	iy004rer
Summary Score Family Stress at Work, 1993	my001rei
Job Worries Distract You at Home, 2004	ig309rer
How Often You Found Work Stressful, 2004	gg201jj
How Often You Found Work Stressful, 2011	hg201jj
Dangerous Conditions at Work, 1993	rg054jjc
Dangerous Conditions at Work, 2004	gg054jjc
Dangerous Conditions at Work, 2011	hg054jjc
Frequency Working under Pressure of Time, 1993	rg048jjc
Frequency Working under Pressure of Time, 2004	gg048jjc
Frequency Working under Pressure of Time, 2011	hg048jjc
Authority to Hire and Fire Others at Work, 1993	rg028jjf
Authority to Hire and Fire Others at Work, 2004	gg028jjf
Authority to Hire and Fire Others at Work, 2011	hg028jjf
Frequency Work Required Physical Effort, 1993	rg046jjc
Frequency Work Required Physical Effort, 2004	gg046jjc
Frequency Work Required Physical Effort, 2011	hg046jjc
Hours/Week Working on Computer, 2004	gg204jj
Hours/Week Working on Computer, 2011	hg204jj
Total Years of College, 1975	edyrcm
Total Years of College, 1993	rb002rec
Your Situation Compared to Others in America, 2004	ig301rer
Your Situation Compared to Others in Your Community, 2004	ig302rer
Close Friend Ever Died, 2004	id001cre
Close Friend Ever Died, 2011	jd001cre
Parent Drug Abuse Caused Problems for Family, 2004	id002cre
Sibling Ever Physically Abused You, 2004	id003cre
Experienced Life-Threatening Disaster, 2004	id004cre
Experienced Life-Threatening Disaster, 2011	jd004cre
Child or Grandchild Served in Combat, 2011	jd050cre
You Served in War or Combat, 2004	id005cre
Witnessed Severe Injury or Death, 2004	id006cre
Witnessed Severe Injury or Death, 2011	jd006cre
Ever Gone Deeply into Debt, 2004	id007cre
Ever Gone Deeply into Debt, 2011	jd007cre
Child Ever Gone Deeply into Debt, 2011	jd070cre
Ever had Serious Legal Difficulties, 2004	id008cre
Ever had Serious Legal Difficulties, 2011	jd008cre
Ever been in Jail or Prison, 2004	id009cre
Ever been in Jail or Prison, 2011	jd009cre
Spouse Ever Physically Abused You, 2004	id010cre
Spouse Ever Physically Abused You, 2011	jd010cre

Variable Description , Survey Year	WLS variable code
Child Ever been Divorced, 2004	id011cre
Child Ever been Divorced, 2011	jd011cre
Child Ever had Life-Threatening Illness or Accident, 2004	id012cre
Child Ever had Life-Threatening Illness or Accident, 2011	jd012cre
Grandchild Ever had Life-Threatening Illness or Accident, 2011	jd120cre
Adult Child Ever Moved Back Home, 2004	id013cre
Adult Child Ever Moved Back Home, 2011	jd013cre
Ever had Increased Responsibility for Grandchildren, 2004	id014cre
Ever had Increased Responsibility for Grandchildren, 201	jd014cre
Aging Parent or In-law Ever Moved into Your Home, 2004	id015cre
Aging Parent or In-law Ever Moved into Your Home, 2011	jd015cre
Ever Placed Spouse, Parent, or In-law into Nursing Home, 2004	id016cre
Ever Placed Spouse, Parent, or In-law into Nursing Home, 2011	jd016cre
Ever Seriously Thought about Taking Your Own Life, 2004	id017cre
Ever Seriously Thought about Taking Your Own Life, 2011	jd017cre
When Stressed Turn to Work, 2004	id101rer
When Stressed Turn to Work, 2011	jd101rer
When Stressed Concentrate Your Efforts, 2004	id102rer
When Stressed Concentrate Your Efforts, 2011	jd102rer
When Stressed Pretend it's Not Real, 2004	id103rer
When Stressed Pretend it's Not Real, 2011	jd103rer
When Stressed Give up Trying to Deal, 2004	id104rer
When Stressed Give up Trying to Deal, 2011	jd104rer
When Stressed Say Things to let Negative Feelings Go, 2004	id107rer
When Stressed Say Things to let Negative Feelings Go, 2011	jd107rer
When Stressed Try to Make Situation Positive, 2004	id108rer
When Stressed Try to Make Situation Positive, 2011	jd108rer
When Stressed Criticize Yourself, 2004	id109rer
When Stressed Criticize Yourself, 2011	jd109rer
When Stressed Try to Think About it Less, 2004	id113rer
When Stressed Try to Think About it Less, 2011	jd113rer
When Stressed Express Negative Feelings, 2004	id115rer
When Stressed Express Negative Feelings, 2011	jd115rer
When Stressed Learn to Live with It, 2004	id116rer
When Stressed Learn to Live with It, 2011	jd116rer
When Stressed Think Hard about Steps to Take, 2004	id117rer
When Stressed Think Hard about Steps to Take, 2011	jd117rer
When Stressed Blame Yourself, 2004	id118rer
When Stressed Blame Yourself, 2011	jd118rer
Summary Score Extraversion, 1993	mh001rei
Summary Score Extraversion, 2004	ih001rei
Summary Score Extraversion, 2011	jh001rei
Summary Score Openness, 1993	mh032rei
Summary Score Openness, 2004	ih032rei
Summary Score Openness, 2011	jh032rei
Summary Score Neuroticism, 1993	mh025rei
Summary Score Neuroticism, 2004	ih025rei
Summary Score Neuroticism, 2011	jh025rei
Summary Score Conscientiousness, 1993	mh017rei
Summary Score Conscientiousness, 2004	ih017rei

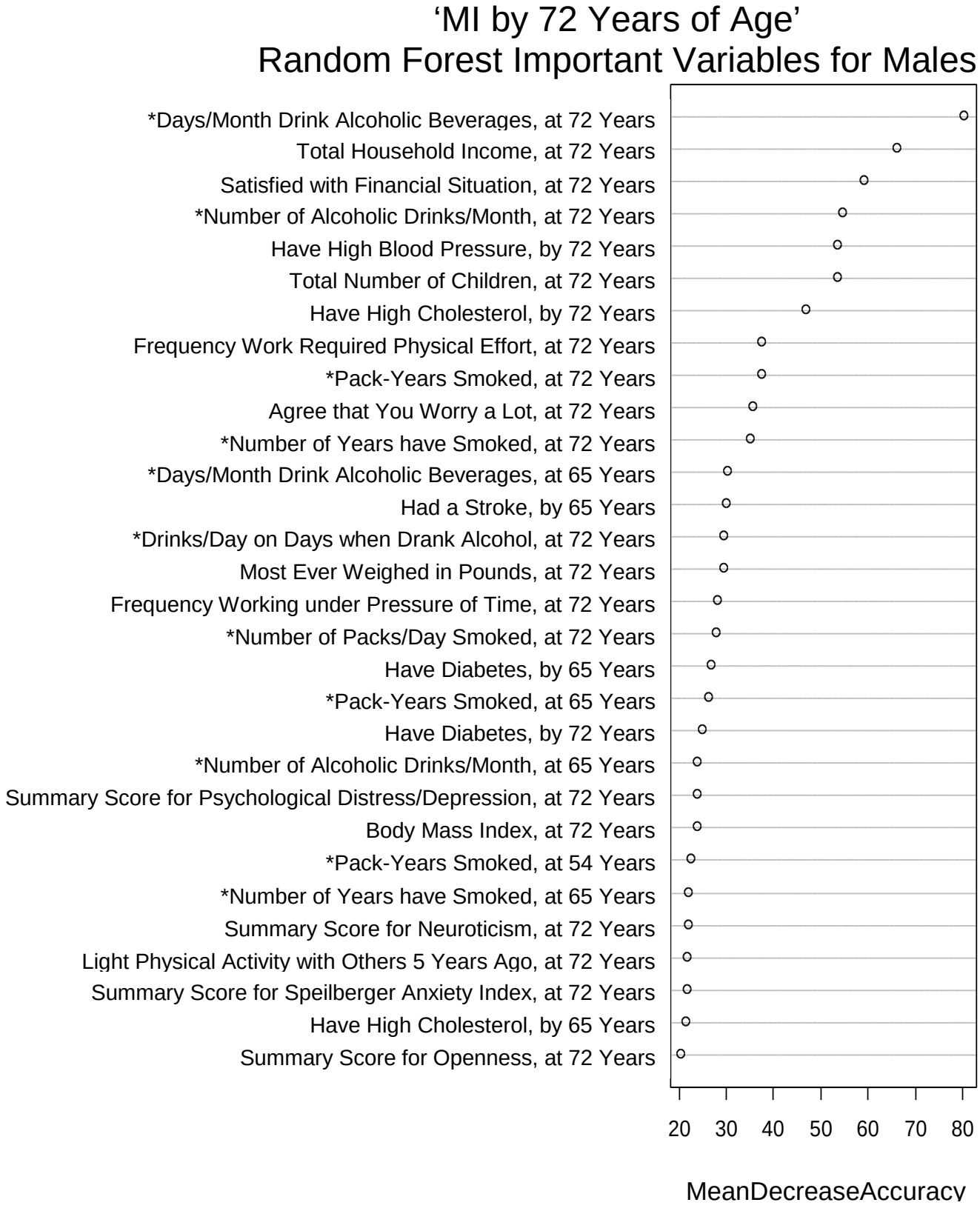
Variable Description, Survey Year	**WLS variable code**
Summary Score Conscientiousness, 2011	jh017rei
Summary Score Agreeableness, 1993	mh009rei
Summary Score Agreeableness, 2004	ih009rei
Summary Score Agreeableness, 2011	jh009rei
Female-Specific Variables	
Age First Menstruated, 2004	in190rer
Menstruated in Last 12 Months, 1993	mn119rer
Age Last Menstruated, 1993	mn120rer
Age Last Menstruated, 2004	in120rer
Gone through Menopause, 1993	mn121rer
Taken Hormones for Menopausal Symptoms, 1993	mn125rer
Taken Hormones for Menopausal Symptoms, 2004	in125rer
Stopped Menstruating before Taking Hormones for Menopausal Symptoms, 2004	in209rer
Age taking First Hormone for Menopausal Symptoms, 1993	mn147rec
First Hormone for Menopausal Symptoms, 1993	mn150rec
Still taking First Hormone for Menopausal Symptoms, 1993	mn149rec
Age Stopped First Hormone for Menopausal Symptoms, 1993	mn148rec
Ever Stopped taking Hormones for Menopausal Symptoms, 2004	in222rer
Age Stopped taking Hormones for Menopausal Symptoms, 2004	in223rer
Age Stopped taking Estrogen and Progesterone for Menopausal Symptoms, 2004	in134rer
Age Stopped taking Testosterone for Menopausal Symptoms, 2004	in207rer
Menopausal Symptoms when Stopped taking Hormones, 2004	in235rer
Ever had Surgery to Remove Uterus and/or Ovaries, 1993	mn122rer
Ever had Surgery to Remove Uterus and/or Ovaries, 2004	in122rer
Age had Surgery to Remove Uterus and/or Ovaries, 1993	mn124rer
Ever had Surgery to Remove Uterus, 2004	in123cre
Age had Surgery to Remove Uterus, 2004	in124are
Ever had Surgery to Remove One of Your Ovaries, 2004	in123bre
Age had Surgery to Remove One of Your Ovaries, 2004	in124cre
Ever had Surgery to Remove Both of Your Ovaries, 2004	in123are
Age had Surgery to Remove Both of Your Ovaries, 2004	in124bre
Genetic (SNP) Related Variables	
Genotype is Allele ApoE4 +/-	*rs429358 & rs7412
Genotype is Allele ApoE2 +/-	*rs429358 & rs7412
Genotype for ApoE is E4/E4	*rs429358 & rs7412
Genotype for ApoE is E2/E2	*rs429358 & rs7412
Participant Genotype for ApoE	*rs429358 & rs7412

* Variable created by combining existing WLS variables.

Supplemental Information 3: Description of statistics showing sex as one of the top MI associated factors among WLS participants.

All analyses identified sex as one of the factors most associated with MI among WLS participants. Recursive partitioning showed that among those who ever had a MI by 72 years old, with all participants combined (males and females) the second highest factor associated with MI was sex, with prevalence among males in the WLS cohort at 13.1% and among females at 4.9% (OR=2.94, 95% CI= 2.38-3.63; tree not shown). Among those who experienced their MI between 65-72 years old, RP revealed that the top factor for MI was sex, with prevalence among males at 5.9% and among females at 2.5% (2.46, 1.84-3.29; tree not shown). In addition, RF selected sex as one of the 'important' MI associated factors for those who ever experienced a MI before 72 and as the most 'important' factor for those having a MI between 65-72 years (not shown). Finally, both LR and X^2 analyses identified sex as a significant factor for MI at any age (p-values <0.0001), with males in the WLS cohort more likely to have had a MI than females by 72 (2.75, 2.34-3.23) and between 65-72 (2.46, 1.84-3.29). Males and females were therefore analyzed separately throughout this study.

Supplemental Information 4: List of 'Important' MI associated factors by RF, for males who ever had a MI up to age 72 years in the WLS cohort.



* = Variable created by combining existing WLS variables

Supplemental Information 5: List of 'Important' MI associated factors by RF, for males who had a MI between 65-72 years of age in the WLS cohort.

* = Variable created by combining existing WLS variables

Supplemental Information 6: List of 'Important' MI associated factors by RF, for females who ever had a MI up to age 72 years in the WLS cohort.

* = Variable created by combining existing WLS variables

Supplemental Information 7: List of 'Important' MI associated factors by RF, for females who had a MI between 65-72 years of age in the WLS cohort.

* = Variable created by combining existing WLS variables

Supplemental Information 8: Additional discussion of recursive partitioning results for males who ever had a MI before age 72 in the WLS cohort.

Recursive partitioning (RP) analysis revealed that the most important interactive effects among factors associated with MI for males in the WLS who ever had a MI before age 72 were first having high cholesterol, then having diabetes, both by 65 years old, and the number of years smoked by 54 years old (see Figure 1). Beyond these interactions, for those with no high cholesterol or diabetes by 65 years, depression becomes an important factor associated with MI and then high cholesterol by 72 years and high blood pressure by 65 years old, and finally, how many alcoholic drinks were consumed each month at 72. For those with no high cholesterol by 65 years old, each of the additional factors listed above demonstrates at least a 3-fold increase in MI prevalence at each split (node) in the tree. For those who had no high cholesterol, no diabetes, and no (limited) depression by 65 years old, the next MI associated factor was having high cholesterol by 72 years old, although this factor was associated with lower MI prevalence than the preceding factors (2.4% versus 8.6%; see Figure 1). This result is supported by studies showing that the key risk factors for MI become less predictive the older we get [1 2]. That is because the risk for MI increases as we age due to the 'natural' progression of atherosclerosis and narrowing of arteries in the elderly [3-5]. However, for those with high cholesterol by 72 years, consuming more than 5.5 alcoholic drinks per month cut MI prevalence by nearly half and drinking less than 5.5 alcoholic drinks per month was associated with a 3.1-fold increase in the prevalence of MI, supporting results from previous studies (see main text). For those who had no high cholesterol but did have diabetes by 65 years, openness becomes an important factor, with low prevalence among those who were less open and much higher prevalence (9.2-fold increase) among those who were more open (2.9% versus 26.7% respectively). Counter to our results, previous studies have demonstrated an inverse relationship between openness and heart disease risk/mortality [6-8]; therefore, further study should attempt to elucidate this relationship. For those with a higher openness score at 65, MI prevalence is mediated by their genotype at the CYP11B2 gene (rs1799998 SNP). Our study revealed a much higher prevalence of MI among those with the A:G or G:G genotype (30.6%) compared to no prevalence among those with an A:A genotype (0.0%). This is among those males who before the CYP11B2 SNP measurement had an overall MI prevalence of 26.7% (Figure 1). This finding suggests that the A:A homozygous genotype confers a protective effect against MI, supported by studies showing that having a G allele at this polymorphism site is significantly associated with coronary heart disease or its risk factors [9-13]. However, conflicting results in the literature suggest that further study is needed to confirm the association and to determine possible interactions between this SNP and other MI risk factors [14-19].

In addition to the interactions listed above, for those who do have high cholesterol by 65 years, the number of years smoking cigarettes by 54 years, days/month drinking alcohol, dangerous conditions at work, and genotype at the FADS2 gene polymorphism become important interactive associations (see Figure 1). Smoking fewer than 22.5 years by 54 years old interacts with having diabetes by 65 years, a familial history of MI, family worries at work, the most ever weighed, number of years of college completed, total household income, and genotype at the IL6 gene polymorphism site. Among those with high cholesterol by 65 years old who have smoked more than 22.5 years, regular moderate alcohol consumption seems to provide an insulating effect against MI, with a 3.8-fold increase in prevalence of MI among those who drank less than 24.5 days/month (40.9% versus 10.7%; Figure 1). This relationship is mediated by experiencing dangerous conditions in the workplace (at 65 years), with a 2.6-fold increase among those who work under dangerous conditions and half of the men in this group experiencing MI at some point in their lives (50% versus 19.4%). This supports the assertion that this factor may represent a 'new' MI risk, as stated in the main text. For those experiencing no dangerous conditions at work, prevalence increases by having a C:G or G:G genotype at the FADS2 gene polymorphism (rs174575) site, resulting in a 6.6-fold increase in MI prevalence over those with the homozygous C:C genotype (46.7% versus 7.1%). Although one study was identified in which this polymorphism was analyzed against coronary artery disease risk, no association was found [20]. Further study is needed to determine if this gene locus is indeed associated with MI, as supported by this study. Among those who had high cholesterol by 65 years, smoked less than 22.5 years by 54 years, and did not have diabetes by 65 years, a familial history of MI (before age 55) was the next interactive factor associated with MI, with a 3.1-fold increase in prevalence among men in this group (31.5% versus 10.3%; Figure 1).

For those with no familial history of MI, the most ever weighed becomes an important factor with a 3.4-fold increase in prevalence among those who had weighed more than 226.5 lb. at their greatest (17.8% versus 5.3%), which is supported by association studies outlining the risk of MI based on obesity [21-24]. For those who weighed more than 226.5 lb. at their greatest, total household income of less than $130,918 at 65 years old lead to an MI prevalence of 22.6% compared to 0.0% among those with a total household income greater than $130,918 (Figure 1). This suggests that making a higher salary confers a protective effect against MI. However, previous studies looking at socioeconomic factors such as income, education, and occupation have found mixed results [25-27], with lower income as an MI risk factor in developed countries versus the opposite effect in less developed countries [28]. Furthermore, income seems to interact with education, such that those with more education and lower income have a higher risk for MI, while those with more education and higher income are protected from MI [28]. In the U.S., lower income has been strongly associated with all-cause mortality and the disparity has gotten worse over time, specifically for men [29], and is stronger in younger men than in older men [27]. Recent declines in coronary heart disease (CHD) deaths in the U.S. are more prominent

for those in the upper income groups than in the lower income groups, although this trend has changed over the past century, such that the more affluent used to be at a greater risk for CHD whereas now the less affluent are at a greater risk [27]. In addition, it has been shown that those experiencing lower socioeconomic status in childhood are more likely to suffer MI later in life [27], although mixed results have been reported. Survival after MI is greatest among those in the highest income groups, but those in lower income groups are also more likely to smoke, get less physical exercise, and to drink alcohol [excessively or less than one day/week] [25]. Even after taking into account all of the confounding factors associated with MI, income does exhibit an inverse association with all-cause mortality, as well as cardiovascular and MI risk across most studies, suggesting that it is in-fact an independent risk factor for MI.

For men with a lower income, MI prevalence increased among those with a C:C or G:G genotype at the IL6 gene polymorphism (rs1800795) site. Those with a homozygous genotype at this locus showed a 6.2-fold increase in MI prevalence over those with the heterozygous C:G genotype (32.6% versus 5.3%, respectively). However, the results from previous studies are mixed, with some studies demonstrating an association between this polymorphism site and increased cardiovascular risk and others finding no association at all [30-34], therefore additional study is necessary in order to determine what, if any, associations exist between this IL6 gene polymorphism and MI. For men who had high cholesterol by 65 years, smoked less than 22.5 years, and had diabetes by 65 years old, whether one agreed that family worries distracted them from work at 65 years old became an important MI associated factor, demonstrating a 7.4-fold increase in prevalence among those who either strongly agreed or did not agree over those who agreed that family worries distracted from work (39.3% versus 5.3%). Work- and family-related stress has been shown to increase men's risk of MI in prior studies [35 36]; however, here it seems that having distractions at work actually decreased MI prevalence. Kubzansky et al. [37] suggest that only worry in specific 'domains' increases one's MI and CHD risk, while other types of worrying can be considered a constructive problem-solving strategy. The conflicting results here suggest that the 'strongly agreed' outcome is likely an artifact of the way the data was collected and analyzed, and there may be additional interactive effect(s) that we have not illuminated to explain these mixed results. Additional study is needed before conclusions can be drawn concerning this data.

Among the group who did not agree that family worries distracted from work, MI prevalence increased to 53.3% among those who completed less than 5.5 years of college by 54 years old, with no prevalence (0.0%) among those completing more than 5.5 years. Similar to the associations linking income and MI, it has long been acknowledged that education is inversely associated with all-cause mortality including MI across many different countries [25 38-40], and as was found for income the disparity has increased over time, specifically among younger men [27]. For those who have had a MI, less education is associated with increased risk of death and

recurrence of MI [25]. Furthermore, declines in CHD and MI deaths over the past few decades are least evident among those in the lowest SES groups, although again as was found for income these associations are strongest in high-income countries [41 42], and can even be reversed in less developed countries [28]. As stated above, one study showed that education interacts with income such that more education only provides a protective effect against MI if a person also has a higher income [28]. Nevertheless, education has been found to be an independent predictor of MI, regardless of other known risk factors [43]. Surprisingly, in this study years of college education represented the largest gap in prevalence among men who ever had a MI before age 72 (53.3% versus 0.0%; Figure 1). Despite having high cholesterol and diabetes by 65 years old, 2 of the 4 conventional risk factors for MI, men in this group having completed more than 5.5 years of college experienced no MI in the WLS cohort.

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Supplemental Information 9: Additional discussion of recursive partitioning results for females who ever had a MI before age 72 in the WLS cohort.

Using recursive partitioning (RP), this study found that the most important interactive effects among factors associated with MI in females who ever had a MI by 72 years old was first having diabetes by 65 years old (see Figure 3). For those who did not have diabetes by 65, the next most important factor was having high blood pressure by 65, with a 2.7-fold increase in prevalence among those women who did have high blood pressure by 65 (7.6% versus 2.8%), followed by how often one engaged in light physical activity with others when about 67 years old (asked at 72 years) for those who did not have high blood pressure by 65. For those who engaged in light physical activity with others often, prevalence decreased from 2.8% to 0.2%, with MI nearly disappearing among this group in the WLS cohort. However, for those who engaged in light physical activity with others rarely or never when about 67, prevalence increased from 2.8% to 3.7%, demonstrating an 18.5-fold increase over those who engaged in light activity often (Figure 3). This result supports what is already understood about the effect of physical inactivity on MI risk (see main text). For those who did have high blood pressure by 65 years old, important interactions included the number of years one had smoked by 54 and whether one blames themselves when stressed (at 72 years old). For women, diabetes, high blood pressure, and smoking all act to increase one's MI risk, which (as in men) represent 3 of the 4 key or conventional risk factors for MI [1-6]. Smoking more than 24.5 years by 54 years old increased the prevalence of MI by 3.3-fold within this group (16.6% versus 5.1%; see Figure 3). Additionally, those who blamed themselves a medium amount or a lot when stressed showed a 4.4-fold increase in MI prevalence over those who blamed themselves only a little bit or not at all (11.8% versus 2.7%; Figure 3). This factor represents (a facet of) one's coping strategy and it has been shown in prior studies that an unhealthy coping strategy, such as blaming oneself when under stress can lead to an increase in overall ill-health, as well as increased risk for MI [7 8]. Blaming oneself when under stress has also been linked to depression [9 10], which is associated with increased MI risk, and one's general state of mind after MI can affect post-MI risk for recurrent MI or death [11-16]. The largest gap in prevalence was seen between those who reported engaging in light physical activity with others often versus those who reported rarely or never; although, this factor was associated with lower MI prevalence than the above listed factors. Furthermore, only women diagnosed with diabetes by 65 years old had a MI prevalence higher than that demonstrated among men in the WLS cohort. And even considering interactions among all other factors in the RP tree, no other group of women who ever had a MI by 72 years old (nodes in the tree) reached the prevalence achieved by those who had diabetes by 65 years old. This suggests that diabetes truly is the single most important factor associated with MI for women in the WLS, and points to this as a potentially important predictor for whether a woman will have a MI in her lifetime.

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Supplemental Information 10: Additional discussion of recursive partitioning results for females who had a MI between 65-72 years of age in the WLS cohort.

Using recursive partitioning (RP), this study found that the most important interactive effects among factors associated with MI in females between 65-72 years of age was first having diabetes by 65 years old (see Figure 4), with a 3.9-fold increase in MI incidence among those with diabetes by 65 years (7.8% versus 2.0%), suggesting that this is the most important MI associated factor for women in the WLS. For those who did have diabetes by 65, the next most important factor was their summary score for agreeableness at 65 years, and then whether they had menstruated in the last 12 months at 54 years old. Those women who had an agreeableness score < 32.5 at 65 had a 10.9% MI incidence rate, while those whose agreeableness score was ≥ 32.5 at 65 years reported no MIs (0.0% incidence; Figure 4), which is supported by previous studies in which agreeableness was shown to have an inverse relationship with CHD risk [1 2]. Among those women whose agreeableness score was <32.5 at 65 years old, MI incidence increased further for those who had not menstruated in the last 12 months at 54 to 14.0%, while those who had menstruated in the last 12 months at 54 saw incidence once again drop to 0.0% (Figure 4). Therefore, even for those women who were diagnosed with diabetes by 65, the top factor associated with MI for women in the WLS cohort, and who reported a lower agreeableness score at 65, still having their menstrual cycle at 53 years old seems to have provided a protective effect against MI. Further research is needed to confirm this finding, but prior research on hormonal imbalance due to menopause and MI risk in women lends support [3-10]. Among those women who did not have diabetes by 65 years old, the factors that interacted to affect MI incidence were IQ, genotype for the Inhibin Beta B gene, and whether her work required physical effort at 54 years old. Women with an IQ < 112.5 had an incidence rate 4.0-fold higher than women with an IQ ≥ 112.5, although incidence was relatively low among both of these groups (2.4% versus 0.6%; Figure 4). Prior studies have shown that IQ relates to CVD, CHD, and all-cause mortality, however there are mixed results in the literature suggesting the association is linked with socioeconomic status in adulthood and other known risk factors [11-15]. For those with a higher IQ (≥ 112.5), having a G:A or G:G genotype for the Inhibin Beta B gene polymorphism (rs11902591 SNP) resulted in an increased MI incidence of 4.7% compared to no incidence (0.0%) among those with the A:A genotype at this polymorphism site. This suggests that the A:A genotype confers a protective effect against MI, or at least that the G allele may leave someone at risk. However, there are no prior studies linking MI to the Inhibin Beta B gene, therefore further investigation is necessary. For those women carrying the G allele at the Inhibin Beta B polymorphism site, whether her work required physical effort at 54 years mediated the (above) proposed effect (Figure 4). Incidence among those women whose work required physical effort frequently was 25%, while those whose work required physical effort always, sometimes, rarely or never reported no MIs (0.0%

incidence). Although previous research has supported an association between physical activity and MI, this result may be an artifact of the way the data was collected (ie. survey) and how participants chose to answer the question. Sedentary behavior has been shown to increase one's risk of all-cause mortality, including CVD and CHD mortality and incidence, specifically when one is sedentary in their occupation as well as at home [16-20]. However, it has been suggested that physical activity in the workplace does not have the same effect as physical leisure activity when it comes to MI, and may in fact increase one's risk of MI if the occupational activity is highly strenuous or repetitive [21-25]; therefore, further study is warranted.

Among those women who did not have diabetes but had a lower IQ (< 112.5), one's summary score for extraversion at 54 years, how many hours/month she engaged in light physical activities alone at 65, how many alcoholic drinks she consumed per month at 65, body mass index at 65, genotype for the A2M gene polymorphism, how often she worked under the pressure of time at 54, and the age at which she last menstruated (reported at 65 years old) become important interactions associated with MI (see Figure 4). Each of the aforementioned factors interacted with its preceding factor to either increase MI incidence, or drop it down to zero (or nearly zero), suggesting a potential protective effect against MI. For women whose summary score for extraversion at 54 years was ≥ 17.5, incidence was 2.8%, while for those whose summary score for extraversion was < 17.5, incidence was 0.0%. Although our study demonstrated a positive relationship between extraversion and MI, results produced by previous studies suggest a negative association [26], therefore more study is needed. Among those women who demonstrated a higher score for extraversion, MI incidence increased to 3.0% among those who engaged in light physical activities alone ≥ 11 hours/month at 65, a 7.5-fold increase over those who engaged in light physical activities alone < 11 hours/month at 65 (0.4% incidence). However, it is widely agreed that more physical leisure activity reduces one's MI risk, and runs counter to the results produced by this study's analysis of women who ever had a MI by 72 (see Figure 3) in which those women who often engaged in light physical activities with others when ~ 67 years old (asked at 72) showed a reduced incidence of MI compared to those who engaged in these activities rarely or never. Therefore we suggest that there may be an effect of women feeling they participated in activities 'alone' versus 'with others' during this time period in their lives, as it has been shown that a woman's MI risk is increased when she feels she lacks a strong social support or a strong social network [27 28], but this remains an anomaly amongst our results. For women who drank < 20.5 alcoholic drinks/month at 65 years, MI incidence was increased to 3.6%, while dropping to 0.0% among those who drank ≥ 20.5 alcoholic drinks/month at 65, once again supporting that regular, moderate alcohol consumption helps protect against MI. A body mass index of ≥ 22.5 at 65 years interacted to increase MI incidence among women to 4.3%, while a body mass index < 22.5 at 65 years resulted in an incidence of 0.0% (Figure 4). Body mass index interacted with a

woman's genotype for the A2M gene polymorphism (rs669 SNP) site, such that those with a G:A or G:G genotype experienced an increase in MI incidence to 5.9%, an 8.4-fold increase over those with the A:A genotype (0.7% incidence). However, there are no prior studies linking MI to the A2M gene, therefore further study concerning this association is warranted. One's genotype at the A2M gene polymorphism interacted with how often a woman worked under the pressure of time at 54 years old, such that those who did always, sometimes, rarely, or never showed a MI incidence of 9.4%, while those who worked under the pressure of time frequently at 54 years experienced no MIs (0.0% incidence; Figure 4). Working under the pressure of time has not specifically been associated with MI in prior studies; however, other types of job stress have been linked to increased MI [29-33]. Unfortunately, the results from the current study are unclear about whether the identified association is positive or negative, and again may be an artifact of the way the data was collected and how participants chose to answer the question; therefore, additional study is necessary. Finally, working under the pressure of time interacted with the age at which a woman last menstruated, such that those who had last menstruated at < 50.5 years (reported at 65 years old) showed a MI incidence of 13.8%, while those who last menstruated at ≥ 50.5 years of age had no MIs (0.0%) by 72 years old. This result is supported by previous studies (concerning hormonal imbalance, as described in main text) and by other results in this study, for example, whether a woman had not menstruated in the last 12 months at 54 years old (14% incidence; see above). This finding lends support to the assertion that a woman's MI risk increases inversely to the age at which she stops menstruating, at which time her hormonal levels become out of balance. It seems that for women, the state of her hormonal balance in her younger years (< 65) becomes a stronger factor for MI as she ages and may affect who experiences a MI in their later years (between 65-72 years old). Each of the interactions listed above was associated with either an increased MI incidence or no incidence, suggesting that these are critical (interactive) factors for MI among women between 65-72 years old in the WLS cohort. Even among those women who appeared in the 'riskier' group for each factor listed, the next factor could interact to drop MI incidence down to 0.0% (or close to zero) for these women (Figure 4).

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Reported on Page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	8-9
Study size	10	Explain how the study size was arrived at	6

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	8-9
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	8-9
		(*e*) Describe any sensitivity analyses	8-9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5-6, 10
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Supplemental Table 1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Tables 2, 3
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Tables 2, 3
		Cross-sectional study—Report numbers of outcome events or summary measures	NA
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-15
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-15
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20-21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21-22
Generalisability	21	Discuss the generalisability (external validity) of the study results	16-20
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.