Predicting Heart Attacks: Data from the Wisconsin Longitudinal Study

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Background

- Heart disease is the leading cause of death for **both** men and women in the United States.[1]
- About 610,000 people die from heart disease in the United States every year – **that's 1 in every 4 deaths**. [1]
- High blood pressure, high LDL cholesterol, and smoking are key risk factors for heart disease. About **half of Americans** (49%) have at least one of these three risk factors.[2]
- Someone in the United States dies from a heart disease-related event **every minute**.[3]
- In the United States, someone has a heart attack **every 43 seconds.**[3]

Objectives

In this study we examined:

1) how environmental, health, social, behavioral, and genetic factors interact to contribute to heart attack risk
2) whether heart attack risk factors are different between genders
3) whether heart attack risk factors change over a person's lifetime
4) what factors may reduce a person's risk of heart attack

Methods

- This study examined possible risk factors for heart attack using data collected by the Wisconsin Longitudinal Study (WLS), a 58-year-long survey study on the lives of 10,317 Wisconsin high-school graduates.
- 235 environmental , health, and socio-behavioral variables and 77 single-nucleotide polymorphisms (SNPs) were analyzed with heart attack data for 6,198 WLS graduate respondents (2,938 men and 3,260 women).
- Data was analyzed for those having a heart attack up to 72 years of age and for those experiencing a heart attack between 65-72 years of age. This allowed us to determine whether risk factors change over a person's lifetime, and which factors are most important in younger versus older individuals.
- SNPs are genetic variations that occur in a single nucleotide location in DNA. On average there are about 10 million SNPs in the human genome. Studies have shown that specific SNPs may be linked to heart attacks [4, 5], but there is no consensus about which gene(s) are most predictive.
- Statistical analyses included exploring multi-factor interactions using recursive partitioning and random forest, and single-factor effects using Chi-square and logistic regression, with the 'R' online statistical software package.[6]

Results

- Heart attack rates are higher for men than for women in the WLS.
- Heart attack rates are higher than the national average for men and women in the WLS up to age 72, but are lower among those aged 65-72 years.
- Among men to age 72: **high cholesterol, diabetes, stroke, high blood pressure, family history and exposure to dangerous conditions at work** were the highest risk factors for heart attack (Table 1a).
- Among men aged 65-72: **only stroke and diabetes** remained as heart attack risks (Table 1b).
- Among women to age 72: **diabetes, dissatisfaction with financial situation, high blood pressure, high cholesterol, not creating a lifestyle to one's liking, being unmarried, and no physical activity** were the highest risk factors for heart attack (Table 2a).
- Among women aged 65-72: **diabetes, exposure to dangerous work conditions, and being post-menopausal by 53** remained as top heart attack risks (Table 2b).
- Interactions among heart attack risk factors increased risk up to 50% in men (Figure 1), and reduced risk to near 0% in men and women, even when other 'known' risk factors were present (Figures 1 & 2).
- The genetic factors examined in this study were secondary to the environmental factors in terms of predictability of a heart attack.

Results

Table 1: Heart attack risk factors found significant by at least 3 of the 4 statistical analyses employed by this study, listing the 'overall' risks for males a) who ever experienced a heart attack by 72 years of age, and b) who experienced a heart attack between 65-72 years of age.

Table 1a: **Males, 'Heart Attack by 72 Years of Age'** Heart Attack Risk Factor Description (Age at Survey Year)	Random Forest Important Variables	Logistic Regression Odds Ratio (95% Confidence Interval)	Chi-Square (adjusted p-value)	Recursive Partitioning (Tree Nodes)
Have High Cholesterol (65 Years)	Yes	3.29 (2.59-4.18)***	<0.0001[C]	Present
Have High Cholesterol (72 Years)	Yes	3.32 (2.50-4.42)***	<0.0001[C]	Present
Have Diabetes (65 Years)	Yes	3.24 (2.53-4.15)***	<0.0001[C]	Present
Have Diabetes (72 Years)	Yes	2.26 (1.78-2.88)***	<0.0001[C]	
Had a Stroke (65 Years)	Yes	5.01 (3.36-7.48)***	<0.0001[C]	
Have High Blood Pressure (72 Years)	Yes	2.16 (1.67-2.79)***	<0.0001[C]	
Have High Blood Pressure (65 Years)		2.39 (1.92-2.96)***	<0.0001[C]	Present
Parent or Sibling had a Heart Attack before age 55 (65 Years)		1.89 (1.43-2.49)***	<0.0001[C]	Present
Exposed to Dangerous Conditions at Work (65 Years)		1.41 (1.11-1.79)**	0.0080[C]	Present
Table 1b: **Males, 'Heart Attack Between 65-72 Years of Age'** Heart Attack Risk Factor Description (Age at Survey Year)				
Had a Stroke (65 Years)	Yes	4.08 (2.17-7.65)***	0.0002[F]	
Have Diabetes (65 Years)	Yes	2.71 (1.81-4.04)***	<0.0001[C]	

C=Chi-square test; F=Fisher's Exact test; Significance codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1.

Table 2: Heart attack risk factors found significant by at least 3 of the 4 statistical analyses employed by this study, listing the 'overall' risks for females a) who ever experienced a heart attack by 72 years of age, and b) who experienced a heart attack between 65-72 years of age.

Table 2a: **Females, 'Heart Attack by 72 Years of Age'** Heart Attack Risk Factor Description (Age at Survey Year)	Random Forest Important Variables	Logistic Regression Odds Ratio (95% Confidence Interval)	Chi-Square (adjusted p-value)	Recursive Partitioning (Tree Nodes)
Have Diabetes (65 Years)	Yes	5.62 (4.08-7.75)***	<0.0001[C]	Present
Have Diabetes (54 Years)	Yes	6.93 (4.18-11.49)***	<0.0001[C]	
Have Diabetes (72 Years)	Yes	4.24 (3.04-5.91)***	<0.0001[C]	
(Not at All) Satisfied with Financial Situation (72 Years)[‡]	Yes	4.00 (1.94-8.27)***	0.0002[F]	
(Somewhat) Satisfied with Financial Situation (72 Years)[‡]		2.02 (1.31-3.12)**	--	
Have High Blood Pressure (72 Years)	Yes	3.37 (2.23-5.09)***	<0.0001[C]	
Have High Cholesterol (72 Years)	Yes	2.03 (1.38-3.00)***	0.0007[C]	
Agree (Slightly) that You Created Lifestyle to Your Liking (72 Years)	Yes	1.67 (1.00-2.78)*	0.0253[F]	
Not Married (72 Years)	Yes	1.59 (1.16-2.18)**	0.0070[C]	
(Often Engaged in) Vigorous Physical Activity Alone 5 Years Ago (72 Years)	Yes	0.53 (0.32-0.89)*	0.0330[C]	
Have High Blood Pressure (65 Years)		3.21 (2.34-4.39)***	<0.0001[C]	Present
(Often Engaged in) Light Physical Activity with Others 5 Years Ago (72 Years)		0.34 (0.21-0.57)***	0.0002[C]	Present
Table 2b: **Females, 'Heart Attack Between 65-72 Years of Age'** Heart Attack Risk Factor Description (Age at Survey Year)				
Have Diabetes (65 Years)	Yes	4.25 (2.50-7.24)***	<0.0001[C]	Present
Exposed to Dangerous Conditions at Work (54 Years)	Yes	2.24 (1.36-3.69)**	0.0030[C]	
Had Menstrual Period in last 12 Months (54 Years)		0.46 (0.23-0.91)*	0.0324[C]	Present

[‡] = Multiple Coefficients Found Significant for this Variable using Logistic Regression; C=Chi-square test; F=Fisher's Exact test;
Significance codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1.

Discussion

- Although there are shared risk factors between men and women, there are also key differences in heart attack risk factors between the genders.
- Heart attack risk factors become less predictive and change with age in both genders (Tables 1 & 2).
- For most of the factors identified, exposure time had a large effect on overall heart attack risk (Tables 1 & 2).
- Interactions among factors greatly affects one's risk of heart attack, therefore it is essential to consider these interactions when predicting heart attack risk.
- New heart attack risk factors identified included exposure to dangerous working conditions, for both men and women, and having created a lifestyle to one's liking in women.
- Factors that lowered heart attack risk included physical activity for women (when about 67 years old) and still having her menstrual period at 53 years of age.

Results

Figure 1

Males, Risks for 'Heart Attack by 72 Years of Age'

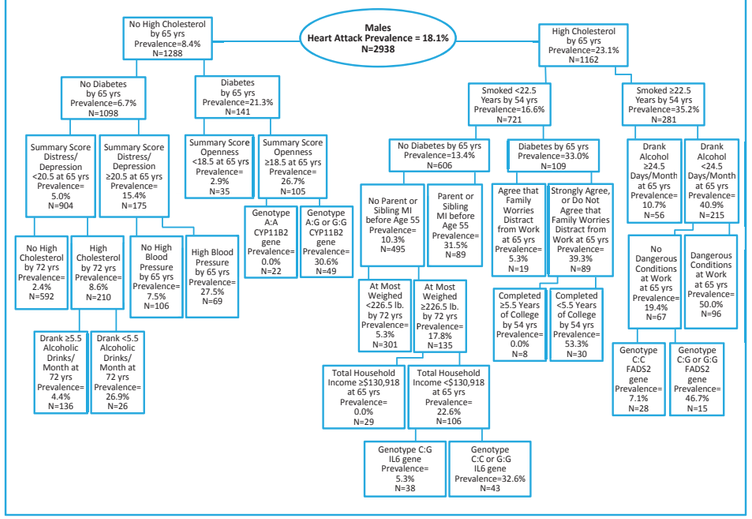
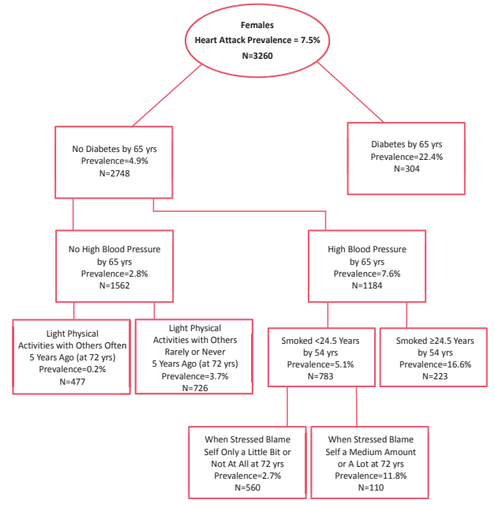


Figure 2

Females, Risks for 'Heart Attack by 72 Years of Age'



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