



Smoking and VTE

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Abstract

The authors researched the incidence of smoking, its distribution in various age groups, genders, races, and nationalities in the United States, and relationship between smoking and VTE.

There is an increased risk of VTE amongst smokers compared to nonsmokers. One of the major causes of the blood clots is the lack of oxygen in the body, and the intake of carbon monoxide through cigarettes amounts to an overall lack of oxygen in the body. Carbon monoxide in cigarettes causes the heart to work harder to supply oxygen to the tissues. Eventually, when there is not enough oxygen in the body, blood clots start to form.

Several agencies (1-800 Quit Now, North American Quitline Consortium, and Become an Ex) have been working to increase the awareness of risks of smoking. The overall effect of these agencies has been to significantly reduce the incidence of smoking and lung and bronchial cancer.

Introduction:

The Georgia Thrombosis Forum (GTF), an affiliate of the North American Thrombosis Forum (NATF), was founded in 2012 with the main mission to spread awareness for the fatal condition of thrombosis and its prevention methods. GTF has engaged its youth members into various activities and projects including booths, proclamations, articles, and research opportunities. The Smoking and VTE research project was selected as GTF members wanted to investigate the trend of the risk of VTE between smokers and nonsmokers. Already knowing of the fatal impacts of smoking, GTF members became even more intrigued of the possible correlation which could exist between Smoking and VTE. We will now start this article with some brief facts and statistics of smoking followed by how it increases the risk of VTE.

Facts about smoking

Look at these astonishing and scary facts about smoking:

1. More than 16 million people suffer from at least one condition that is caused by smoking.
2. On an average, male smokers die 13.2 years earlier than male nonsmokers and female smokers die 14.5 years earlier than female non-smokers.
3. There have been approximately 2.5 million deaths due to exposure to secondhand smoke

4. Approximately 88 million people are exposed to secondhand smoke, including 54% being children between ages 3-11.
5. Unfortunately, 5.6 million children will ultimately die from smoking, this amounts to one out of thirteen kids living in the U.S.
6. Cigarettes contain over 4,800 chemicals, including 69 carcinogens (cancer-causing) and 400 other toxins.
7. Secondhand smoke contains over 7,000 chemicals, including 70 carcinogens (cancer-causing).
8. Some notable chemicals in a cigarette include nicotine (used as an insecticide/addictive factor), tar (material used to pave roads), lead (used in batteries and mechanical pencils), and arsenic (used in rat poison).
9. The addictive chemical in smoking, nicotine, is just as addictive as heroin and cocaine
10. Cigarette smoke is known to increase the risk of developing arterial thrombosis
11. Everyday approximately 3,450 teens try cigarettes in the U.S. for the first time and 25% of those teens will eventually become regular smokers
12. Tobacco abuse harms every single organ in the body
14. Smoking is the single largest cause of preventable disease and death in the United States

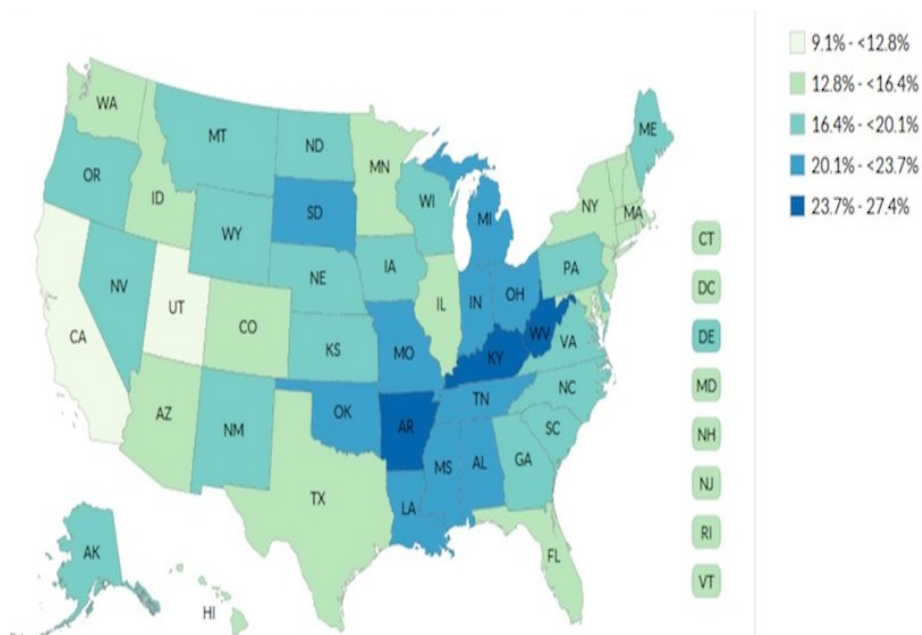
15. More than 80% of adult smokers start regularly smoking before the age of 18

[Incidence of smoking](#)

According to the most recent reports by the United States Center for Disease Control and Prevention (CDC), 15 of 100 Americans smoke cigarettes. This amounts to a total of 36.5 million smokers in the United States alone. Additionally, the CDC statistics show that 16 million Americans live with a smoking-related health condition.

[Distribution of smoking by state](#)

1. States that smoke the most include Arkansas, Kentucky, West Virginia, and the Guam territory
2. Kentucky tops the list of smokers (26 %).
3. The Utah population has the least incidence of smoking (approximately 9 out of 100 people)
4. The Southeast region of the U.S. has the highest number of smokers



Distribution of smoking by Race / Ethnicity

American and Indian/Alaskan Natives (21%)

Studies show that most smokers are Americans and Indian/Alaskan Natives. The reasons for this may include a role of ceremonial, religious, sacred, and medicinal roles in the Native culture. Tobacco sold on lands of tribes do not correspond with the state's taxes which lower the cost of tobacco, leading to additional smoking users.

Asians (7%)

Asian Americans living in the U.S. have a wide variety of languages and cultures and have the lowest percentage of smokers in the United States. Many Asians migrate from their homeland into the U.S. from countries where smoking is a norm. However, studies show that Asians who have lived longer in the US and have adopted to the English language are less likely to smoke.

Hispanics (10%)

The prevalence of smoking among Hispanics is generally lower than other racial groups in the US. Research shows that Hispanics that were born in the United States are less likely to smoke than hispanics that have migrated to the U.S., because they have already adopted to the cultural traits and the social patterns of the U.S. In this respect, the

Hispanics are similar to the Asians in the incidence of smoking.

African Americans (Blacks, 16.7%)

Studies imply indicate there are many factors that contribute to the smoking behaviors of African Americans. These include financial situation, occupation and the population density in an area. If an area is heavily populated with the same race, smoking is easily a factor because it may be considered a norm.

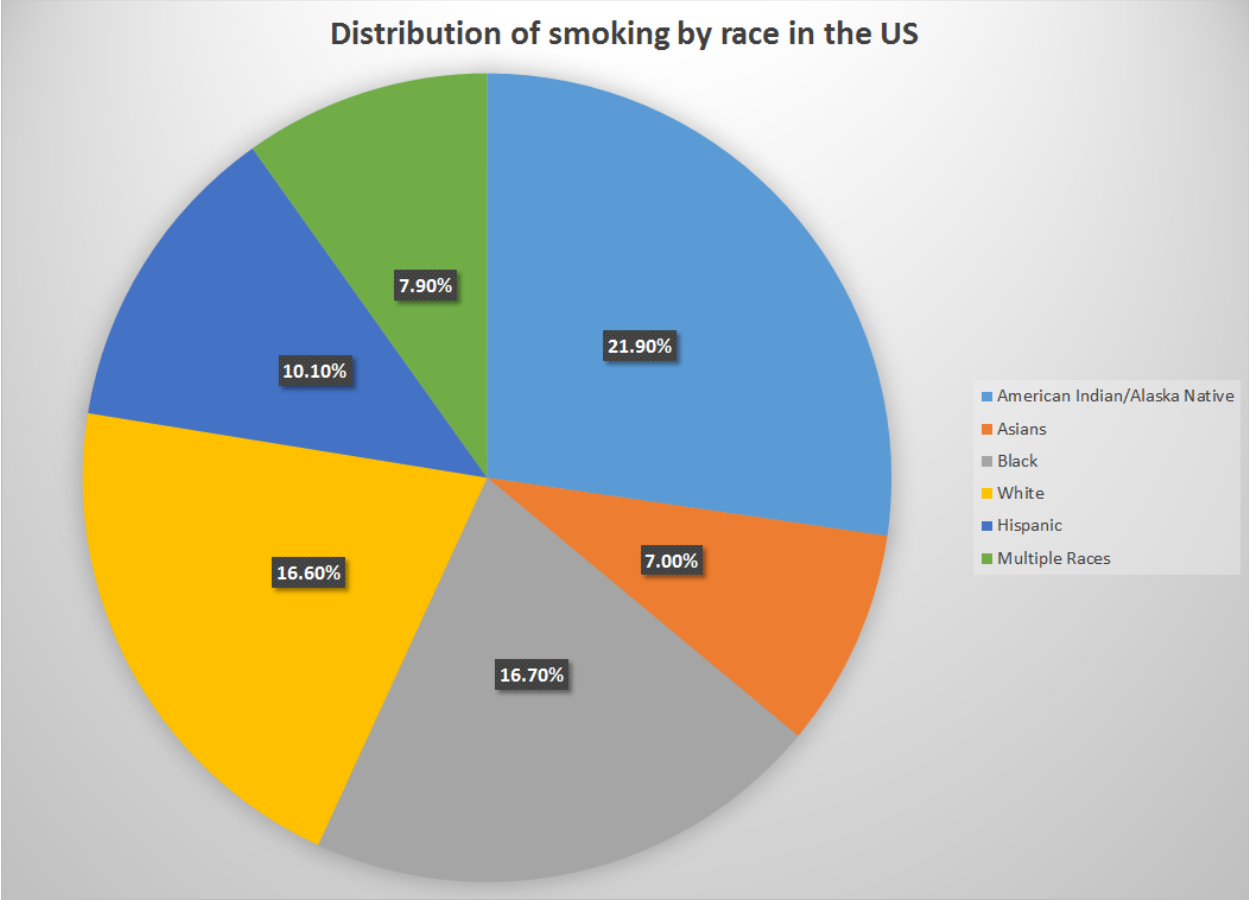
Whites

Many whites choose to smoke due to social influences, trends, and low income.

Current cigarette smoking is highest among non-Hispanic American Indians/Alaska Natives and people of multiple races and lowest among Asians.

- Nearly 22 of every 100 non-Hispanic American Indians/Alaska Natives (21.9%)
- More than 20 of every 100 non-Hispanic multiple race individuals (20.2%)
- Nearly 17 of every 100 non-Hispanic Blacks (16.7%)
- More than 16 of every 100 non-Hispanic Whites (16.6%)
- More than 10 of every 100 Hispanics (10.1%)
- 7 of every 100 non-Hispanic Asians (7.0%)

The pie chart on the next page indicates distribution of smoking stratified by race in the U.S. The following races were chosen for this pie chart: American Indian / Alaska Native, Asians, Blacks, Whites, Hispanics and multiple races.



Distribution of smoking by age

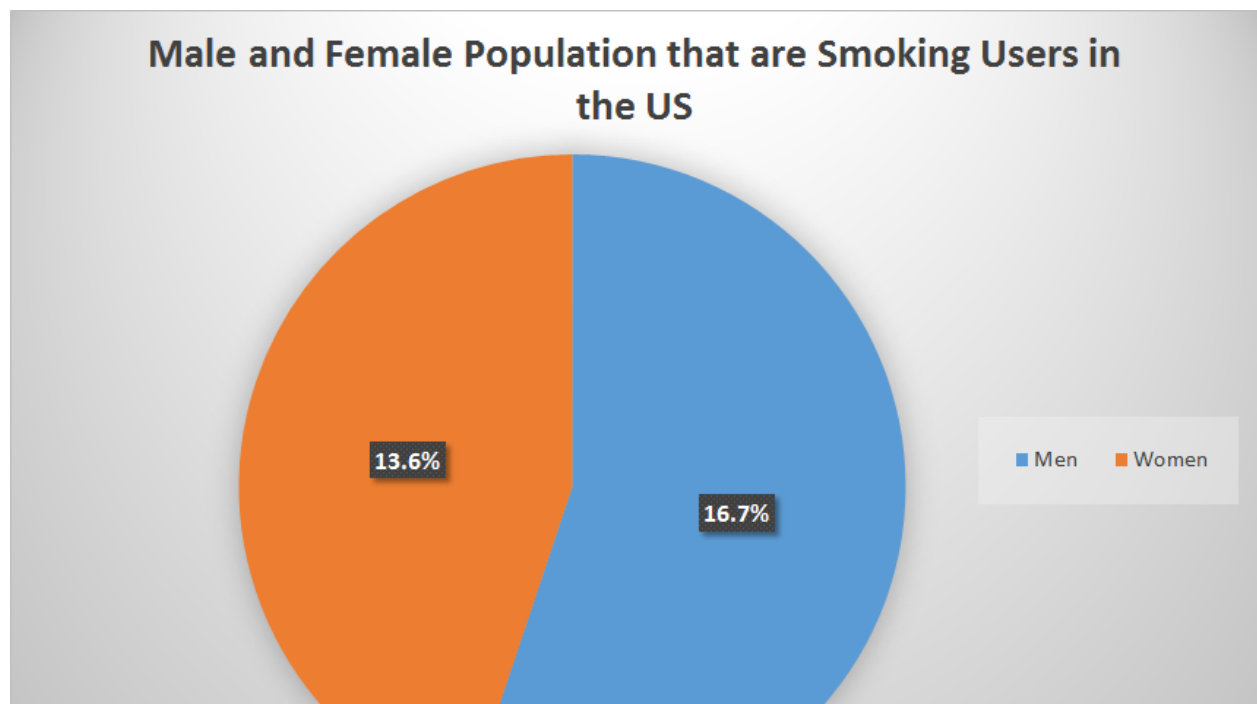
The age group where smoking is most prevalent is the adults in the 25-44-year group (17.7%).

The least prevalent age group for smoking is 65 years and older (8%). This might have to do with the fact that regular smokers might not be alive after they are 65 years of age, that by the time they are 65, or they realize the dangers of smoking, or they were asked to quit smoking by their physicians due to health reasons.

Age (yrs)	Prevalence (%)
18–24	13.0
25–44	17.7
45–64	17.0
>65	8.4

Distribution of smoking by gender

Men smoke more cigarette (17%) than women (14%, see the pie chart below).



Risk of VTE in smokers

The risk of VTE in smokers is significantly higher than in non-smokers. A study conducted by Sun-Yatsen University breaks down the risk of VTE in former, current, and ever (former and current combined) smokers.

The study involved about 4 million participants.

The results of the study show that former smokers were 10% more likely to develop VTE than non-smokers, current smokers were 23% more likely to develop VTE than non-smokers while ever smokers were 17% more likely to develop VTE than non-smokers. These statistics clearly indicate a pattern and co-relation between smoking and VTE. The findings of this study show that any association of smoking directly increases the risk of that individual to develop a blood clot (VTE).

3.8. How does smoking increase the risk of VTE?

Smokers are at a very high risk to develop blood clots. Factors that increase the risk for developing Venous Thromboembolism include Cancer, Obesity, Surgery, Clotting disorders, Smoking, Pregnancy, Oral contraceptives, and Immobility.

Findings by the Sun-Yatsen University indicate that smoking increases the risk of VTE. There are 2 major

reasons why smoking amounts to an increase in risk of VTE.

One major reason being that smoking contains the chemical nicotine. Once an individual starts smoking, nicotine enters the body, and this results in a higher heart rate and blood pressure.

Nicotine also causes narrowing of the body's blood vessels, resulting in the heart working extra to push blood to the body, since it is harder to transport blood through the narrow constricted blood vessels. Over the time, these blood vessels become so narrow that blood cannot be transported in them. A long term smoker thus might get a blood clot.

Smoking contains carbon monoxide, which is considered a silent killer. One of the major causes of blood clots is lack of oxygen in the body, and the intake of carbon monoxide through cigarettes amounts to an overall lack of oxygen in the body. The carbon monoxide in cigarettes causes the heart to work harder to supply oxygen to the tissues. Eventually, when there is not enough oxygen in the body, blood clots start to form.

[Smoking and pregnancy](#)

Smoking during pregnancy is very risky to both the mother and to the fetus.



Smoking and VTE

Two studies indicate that smoking does increase VTE risk, but only if other risk factors are present.

In a single-center, prospective, population-based, cohort trial (the Tromsø study), investigators in Norway enrolled >24,000 persons and followed them for a median of 12.5 years. Compared with nonsmokers, heavy smokers (>20 pack-years) had higher risk for VTE (hazard ratio, 1.46; 95% confidence interval, 1.04–2.05). The elevated risk in smokers occurred only with provoked VTE (in conjunction with surgery, cancer, or other acute medical conditions) and increased with more pack-years of smoking. As expected, the incidence rates and hazard ratios for myocardial infarction and cancer were significantly related to smoking intensity ($P < 0.001$).

In the second study, the Danish case-cohort trial, investigators recorded 641 incident VTE episodes in >56,000 persons during a follow-up of 10.2 years. The study included assessment of several risk factors for VTE, including age, sex, blood type, and factor V Leiden. After adjustment for age, sex, and hormone replacement, the hazard ratios for VTE were elevated only in those with non-O blood type for smokers.

These studies show that smoking is a risk for VTE, only if other risk factors, such as MI, cancer are present simultaneously.

In another study involving about 4 million participants and more than 35,000 patients with VTE from 32 observational studies, a slightly increased risk of VTE for smokers compared with non-smokers. The risk was higher in studies adjusted for conventional cardiovascular risk factors, especially for BMI. The risk of developing VTE was greater for current smokers than for former smokers, and a dose-response relationship was found for daily smoking and pack-years smoked.

Mechanism of VTE in smokers

Several potential mechanisms involving inflammation, fibrinogen synthesis, clotting factors, and impaired fibrinolysis are suggested as possible causes.

Factors causing increased risk of blood clots

Research shows that certain conditions and actions make an individual more prone to blood clots through smoking. Such conditions include obesity, pregnancy, hormonal therapy, use of oral contraceptives, and many more.

Most of the conditions which increase the risk of VTE through smoking are not gender specific with the possible exception of a few including pregnancy and other related conditions. For this reason, it is reasonable to conclude

that the risk of smoking and VTE is not affected directly by gender, rather it is affected by the condition and actions of an individual.

In a large population-based case-control study (The MEGA Study), the authors evaluated smoking as a risk factor for venous thrombosis and the joint effect with oral contraceptive use and the factor V Leiden mutation. Current and former smoking resulted in a moderately increased risk of venous thrombosis, compared with non-smoking. A high number of pack-years resulted in the highest risk among young current smokers compared with young nonsmokers. Women who were current smokers and used oral contraceptives had an 8.8-fold higher risk (OR 8.79, CI95 5.73-13.49) than nonsmoking women who did not use oral contraceptives. In conclusion, smoking appears to be a risk factor for venous thrombosis with the greatest relative effect among young women using oral contraceptives.

[Impact on the U.S. economy by smoking and VTE](#)

The cost of smoking and all of its the related conditions it causes on the U.S. economy is above \$300 billion per year.

In addition to this, the cost of VTE and blood clots on the U.S. economy amounts to an additional \$69 billion per year. In total, when both of these are combined together, the cost of smoking and VTE is above about \$369 million dollars per year (this includes direct costs due to hospitalization, physician costs, loss of job, family stress)

National and Statewide Programs to manage smoking



There are a few major nationwide tobacco prevention programs:

1. 1-800 Quit Now

This is a free telephone call line that connects people with tobacco quitting coaches that can give them tips and encouragement on how to quit tobacco.

2. Become an Ex: This is a national campaign launched in 2008 that helps smokers create personalized plans on how they can stay away from tobacco.

3. North American Quitline Consortium

This is a group of professionals from health, service, research, and national organizations both from the U.S. and Canada that work together to give help needed for smokers across North America.

4. Smoke-free Families

This is a nationwide program that funds innovative research about smoking during pregnancy and helps families across the nation know about the harms of smoking during pregnancy.

[Funding for the tobacco funding, by state](#)

It is rather unfortunate that most states are spending less than 2 cents for every dollar of tobacco revenue towards state tobacco cessation programs. Altogether, the states are giving only 14.8 percent of the recommended CDC funding

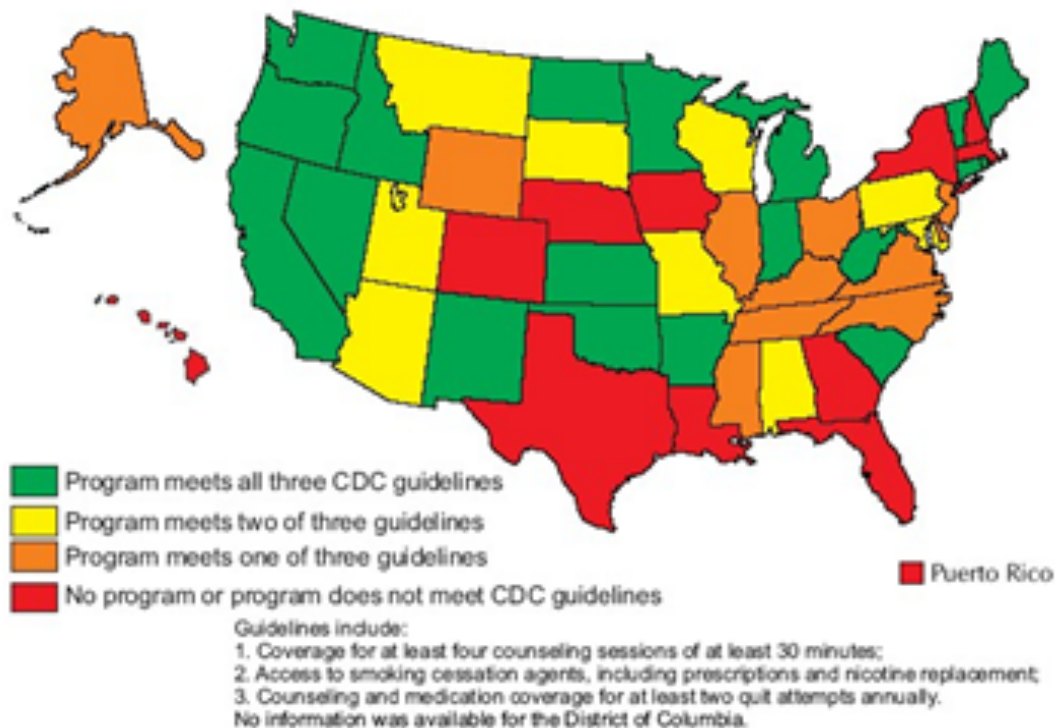
[Tobacco Cessation Programs](#)

The following states have excellent Tobacco Cessation Programs: California, Florida, Massachusetts, North Dakota and Washington.

The following programs have proven to be very helpful:

1. California has reduced lung and bronchial cancer four times faster than the rest of the U.S.
2. Florida's high school smoking rate fell to 6.9% which is well below the national average.
3. Massachusetts cigarette consumption has decreased 36 percent between 1992 and 2000 and smoking during pregnancy has decreased by 50 percent from 1990 to 1999.
4. North Dakota's adult smoking rate has lowered 3.2% from 2011 to 2015 and high school smoking went from 22.4 percent to 11.7 percent between 2009 and 2015.
5. Washington has prevented 13,000 premature deaths

State Employee Tobacco Cessation Coverage



Conclusions

1. In the United States, smoking is most prevalent in the southeast region. Statistically, Americans, Indians, and Alaskans have the most incidence of smoking.
2. With respect to gender, males have the most incidence of smoking. Unfortunately, smoking also has a high incidence amongst the young in ages ranging from 25-44.
3. A number of agencies and organizations are already established in society to help smokers understand the consequences of smoking and to help them stop the bad habit altogether.
4. Smoking is very prevalent and widespread across the world.
5. From our research, statistics and observations we can conclude that the risk of having VTE as a smoker is significantly higher than a nonsmoker.
6. Smoking increases the risk of the formation of blood clots thus leading to serious conditions such as thrombosis.

References:

Campbell, Robert A., Kellie R. Machlus, and Alisa S. Wolberg, Smoking Out the Cause of Thrombosis,

Arteriosclerosis, Thrombosis, and Vascular Biology, American Heart Association, 2010

Cheng Y-J, Liu Z-H, Yao F-J, Zeng W-T, Zheng D-D, et al, Current and Former Smoking and Risk for Venous Thromboembolism: A Systematic Review and Meta-Analysis. PLoS Med 10(9), 2013

Grosse, SD; Nelson, RE; Nyarko, KA; Richardson, LC; Raskob, GE, The economic burden of incident venous thromboembolism in the United States: A review of estimated attributable healthcare costs, Thromb Res, 137:3-10, 2016

Moore, Lisa; Bilello, Kathryn & Murin, Susan, Sex and gender issues and venous thromboembolism. Clinics in Chest Medicine, 25, 281-297, 2004.

“Morbidity and Mortality Weekly Report (MMWR).” *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, 17 Aug. 2017, www.cdc.gov/mmwr/volumes/65/wr/mm6544a2.htm?s_cid=mm6544a2_wv.

“Smoking & Tobacco Use.” *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, 24 Sept. 2018, www.cdc.gov/tobacco/data_statistics/fact_sheets/adult_data/cig_smoking/index.htm.

“Smoking & Tobacco Use.” *Centers for Disease Control and Prevention*, Centers for Disease Control and

Prevention, 4 May 2018,
www.cdc.gov/tobacco/data_statistics/fact_sheets/economics/econ_facts/index.htm.

SEVERINSEN, M. T., et al. "Smoking and Venous Thromboembolism: a Danish Follow-up Study." *The Canadian Journal of Chemical Engineering*, Wiley-Blackwell, 30 June 2009,
onlinelibrary.wiley.com/doi/full/10.1111/j.1538-7836.2009.03490.x.

"Tips From Former Smokers ®." *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, 23 Apr. 2018,
www.cdc.gov/tobacco/campaign/tips/resources/data/cigarette-smoking-in-united-states.html#by_race.