Now we're smokin'.....

Smoking, Vaping, and Kicking the Habit

By Tamara Mitchell

Smoking is extremely addictive, for physical, psychological, and social reasons. If you need one more reason to commit to a smoke-free life, smoking has been identified as a risk factor for both Repetitive Strain Injuries (RSI)\textsuperscript{2} and other musculoskeletal disorders (MSD) and it impedes healing from injuries.

The FDA states that it is going to try to reduce the appeal, toxicity, and addictive properties of smoking and vaping. A “deeming regulation” was passed to regulate all tobacco products, which was to be effective on August 8, 2016. There has been a delay on enforcement. The deadline for submitting applications to market both combustible and non-combustible products was extended five years and six years respectively.\textsuperscript{1} The delay was purported to allow more time to explore “clear and meaningful measures” and, in fact, the long-term effects of vaping are not yet well known.\textsuperscript{1} It is clear, however, that damage is being done to health and enough is known to warrant a moratorium on some of the frequent components of e-liquids until more research is completed. It is also clear that with or without government intervention, the responsibility for health belongs squarely with the individual. Neither habit is healthy. There are well-researched health issues and there are lots of unknowns, but breathing chemicals whether they are burned or vaporized, needs to be acknowledged as a risk and a factor in poor health.

In order to understand the whole issue of smoking and vaping, we’ll explore:

- some reasons why people smoke
- what vaping is and why people vape
- smoking and vaping trends
- why people stop smoking
- is vaping OK?
- Smoking and vaping research
  - nicotine
  - carbon monoxide
  - propylene glycol
  - flavorings
- Smoking and musculoskeletal problems
- Kicking the habit
  - Why it is so hard
  - Latest and ongoing research
  - Suggested programs

\textbf{Why do people smoke?}\textsuperscript{2,3,4,5}
If you ask a smoker, they will tell you that:

- Smoking gives them a lot of pleasure.
• It calms them down.
• It is a way to psychologically take a break and pause for a few minutes.
• It has many sensory components: taste, inhaling the smoke, hearing the paper burning
• The social aspect of smoking and chatting with others, possibly having a drink or coffee is very enjoyable.
• They enjoy the ritual of smoking.
• They feel defiant towards society and the anti-smoking campaign.
• They feel glamorous.
• There is a sort-of cult or kinship feeling among smokers
• It suppresses appetite, the sense of taste, and/or affects metabolism and blood sugar levels for some people, so they may fear getting fat if they quit.

For non-smokers, all of this is really hard to understand because to non-smokers:
• It requires considerable effort and continued attempts to get past the dizziness, nausea, coughing.
• It is incredibly unhealthy for not only the smoker, but everybody around them, including their pets.
• Smoking smells really bad and stinks up everything about the smoker, their belongings, their home, and their cars.
• It ages people.
• It costs a lot of money.
• Smokers aren’t a group of people they generally hang around with.
• There isn’t enough anxiety in life to require constant pacification. Yoga or a glass of wine seems like a preferred way to unwind.
• It is an invitation to an early death and likely lung cancer. About 6 million people die every year from smoking-related causes.

What is vaping?
Vape devices go by several names: e-cigarettes, e-cigars, e-hookahs, mods, vape pens, vapes, tank systems, and electronic nicotine delivery systems (ENDS). When you inhale on an e-cigarette or a vape device it forms a vacuum that switches on a battery that shoots a tiny electric current to an atomizer. The atomizer is heated, the liquid is vaporized, and you inhale the vapor from the liquid.

Why do people vape?
There is not enough research on vaping to really understand all the reasons why people vape. Some people, especially adults, probably switch from smoking to vaping in order to quit. E-cigarettes were originally introduced in the U.S. to help people quit smoking and the early e-cigarettes were made to look
a lot like regular cigarettes with a glowing tip and colored filter band.\textsuperscript{9} Youth may vape to experiment, because their friends do it, or because the equipment and flavors are cool and appealing. Vaping is becoming a more harmful option, however, as the equipment and liquids become more sophisticated so the amount of nicotine in the e-liquids can be quite high and the devices can be controlled so more chemicals are released with higher temperatures.

**Smoking and vaping trends**

Smoking rates in the U.S. have been declining fairly steadily, but some populations are still smoking a lot. For instance, nearly 40\% of adults with a G.E.D. smoke while only about 4\% of adults with a graduate degree smoke.\textsuperscript{10} About 24\% of adults with no high school diploma and less than 12 years of education smoke.\textsuperscript{10} Another population with high smoking rates are those with serious psychological disorders. Almost 36\% of that population smokes while about 15\% of adults with no psychological disorders smoke.\textsuperscript{10}

Among adolescents, cigarette smoking has dropped dramatically. While vaping is a concern, the rate of kids using these devices is not high and it appears to be dropping recently as shown in the chart below.\textsuperscript{11} Most adolescents have tried vaping experimentally because they like the taste.\textsuperscript{11} Most didn’t realize there was nicotine in the mist they inhaled. In one study, 65\% thought it was just flavoring and less than 25\% knew it had nicotine.\textsuperscript{11} And most, though they did not approve of vaping on a long-term basis, did not feel that it was as harmful as smoking.\textsuperscript{11} E-cigarettes and vaping devices have caught on with kids because of their appearance, ease of being concealed, lack of smoke, and candy flavorings.\textsuperscript{12} As with many things, what is cool today will be different very quickly and new brands and looks are constantly evolving.\textsuperscript{12}

![Ever Used E-Cigarettes; National Youth Tobacco Survey (NYTS) 2011–2016](Image)

Adult usage of e-cigarettes shows a different pattern. In a couple of surveys, adults and college students ages 18 to 24 report the highest usage both for those who have ever tried them and those who currently use them, compared to adults over the age of 25.\textsuperscript{13} Another study found the highest usage among adults ages 25 to 34, somewhat lower usage among the ages of 18 to 24, and decreasing usage with adults over the age of 35.\textsuperscript{13} More men use e-cigarettes than women and current users are predominantly Caucasian white people.\textsuperscript{13}
**Why do people stop smoking?**

One personal account reveals that cigarettes were making his allergies and asthma worse, and for some reason it started tasting bad and just not giving the enjoyment it used to. For a lot of smokers, they realize that health problems and addiction develop over a long period of time, so they often feel there is no urgency to stop yet.

Here are some other reasons:

- It costs too much.
- It starts affecting their health or they fear serious illness.
- It starts affecting their relationships.
- It starts affecting their career.
- Social scorn.
- Tired of burning holes in valuable things, furniture, clothes, carpeting, etc.
- Smoking has lost its appeal, its ability to soothe, and is now a source of anxiety with every cigarette smoked.
- They want to prove they can do it.
- They want to be healthier. Smoking and working out or eating a healthy diet are contradictory.
- They want to look younger and healthier.
- They want to set a good example for their children.

**Is vaping OK?**

For smokers, vaping gives them the release they need from nicotine addiction and satisfies most of the social and psychological habits that accompany smoking. For non-smokers, however, although seemingly fairly harmless with fruity, yummy flavors, it secretly delivers a shot of addictive nicotine and several toxic chemicals. It is no wonder that parents and health providers are concerned about their kids taking up this habit. They might not get lung cancer from smoking cigarettes, but it is just another medium for delivering a highly addictive drug.

There is little question that vaping avoids a lot of the toxins that result from burning tobacco. There is a lot of public misunderstanding about smoking and vaping. In England it was found that less than 10% of the public knew that most of the harm from smoking cigarettes is not caused by nicotine. Most people also think that vaping is as harmful to health as smoking. Vaping is considered 95% less harmful to health than smoking cigarettes. Research has shown however, that vaping is far from harmless even though it is much less toxic than cigarette smoking. Since vaping is so new, long-term effects are not known.

The U.S. and U.K government opinions on e-cigarettes are quite different. The U.K. has concluded that they help smokers quit and evidence doesn’t support the theory that vaping is a “gateway” to smoking for young people. In contrast, the CDC in the U.S. concludes that there is not enough evidence to recommend the use of e-cigarettes to quit smoking and it maintains that youth e-cigarette use is associated with the use of other tobacco products and smoking.

Both the U.S. and U.K. agree that:

- completely switching to vaping rather than cigarette smoking is a benefit to health.
- if you aren’t vaping or smoking, avoiding the uses of vape devices is the healthiest choice.

Nicotine is highly addictive and e-cigs deliver a concentrated dose of this drug as well as many other harmful chemicals and flavorings.
Smoking and Vaping research
Previous research on the effects of smoking needs to now be scrutinized in light of the advent of vaping. So much prior research looked at the harmful effects of smoking vs. not smoking without regard to exactly what component of smoking was doing the damage. A lot of things were blamed on nicotine and we now know that this is probably not the primary culprit. Smoking subjects the body to thousands of different compounds that are incinerated and inhaled including not just nicotine, but also carbon monoxide, hydrogen cyanide, nitrogen oxides, and countless other compounds. It is not really known which component of smoking is responsible for the negative impacts on body tissues, healing, and circulatory restriction. We do know that it is extremely harmful to health! We aren’t going to detail every detriment to health posed by smoking. We will discuss the effects on musculoskeletal health specifically. For other harmful effects, refer to the websites below that provide detailed information derived from years of research:

- https://www.healthline.com/health/smoking/effects-on-body#5
- https://smokefree.gov/quit-smoking/why-you-should-quit/health-effects
- https://www.cdc.gov/tobacco/data_statistics/fact_sheets/health_effects/effects_cig_smoking/index.htm
The exact ingredients in vaping liquids are questionable since there has been a historic lack of manufacturing oversight, so concerns about purity and types of ingredients are quite valid. Vaping fluids generally contain nicotine, glycerin, propylene glycol, glycerin, or 1,3-Propanediol, and usually flavorings. The liquids also contain carrying agents, and numerous other chemicals including aldehydes (as carbonyls including formaldehyde), heavy metals, and metal nanoparticles. Breakdown of the heating coils during repeated heating and cooling cycles cause metal nanoparticles to leach into the e-liquid including chromium, manganese, nickel, and lead. More research is needed, but toxicity from breathing metal fumes is well known in the welding industry and animal research indicates that metallic fume exposure results in lung injury, immune suppression, cancer, and reproductive harm. One study found detectable levels of arsenic, nickel, and other metals in the actual e-liquids in addition to traces of lead in the devices, so a lack of quality control and regulation means there is no way of knowing exactly what the consumer is inhaling.

Argentina, Brazil, and Jordan have completely banned the manufacture and sale of vaping devices. The U.S. is working on standards including determining the type of action to take on flavorings, levels of toxicants and impurities in e-liquids, cracking down on marketing to children, and enforcing violations of selling to youth.

Nicotine (cigarettes and vaping).
For many years, nicotine was considered the culprit in problems with wound healing, however some studies have found nicotine to have quite different effects from cigarette smoking as a whole on circulation, blood flow to skin, organs, the intestines, etc. Nicotine infusion in animals has been found to increase blood flow to muscles and intestines, but decrease blood flow to the extremities. Nicotine appears to increase blood flow to the skin and increase skin temperature while smoking reduces blood flow to the skin. The effects of inhaled nicotine on the lungs is not well known, but it appears that difficulty in breathing can be caused by impedance, peripheral airway flow resistance, and oxidative stress in healthy smokers, while it also increases allergen responsiveness, alters the immune system response, increases the strength of infectious bacteria and viruses, triggers smooth muscle contraction, and increases mucus production. So far, it appears that, cigarette smoking is far worse for the lungs than vaping by also greatly increasing the likelihood of cancer, emphysema, COPD, etc. But inhaling nicotine in the form of vaping is also not at all healthy for lung tissues and their functioning, breathing health, and overall potential for lowering defenses to infectious diseases. For people with HIV, this is especially important.

Current research on nicotine with regard to its role in inflammation is difficult to understand. In many cases, nicotine reduces inflammation, but in other cases and doses, it appears to trigger inflammation. The communication involving nicotine receptors in the body and various proteins, steroids, and other signaling systems is very complex and is far from being understood. For certain receptor types (Alpha 7), nicotine and other compounds that also stimulate these same receptors, effects are consistently anti-inflammatory. It is thought that perhaps nicotine also stimulates other receptors that result in different effects from purely anti-inflammatory results. In fact this complex communication system is also involved in a paradoxical effect that can either lead to cell growth or cell death. One study on vaping explored a range of voltages and nicotine concentrations and found that toxicity and release of inflammatory agents (IL-6) were increased with the highest level of nicotine (24 mg/ml), though cell viability was not altered. So, dosage of nicotine may play a part as well, but more research is needed.

One study on live mice exposed them to aerosol saline only or to aerosol nicotine (19 mg/ml) five days a week for four months. This method used compressed air rather than a heating source, so results show the effect of inhaling unheated nicotine. Both solutions contained propylene glycol and vegetable glycerine. Only the solution containing nicotine resulted in airway resistance, increased mucus, increase in inflammatory agents (IL-6 and MCP-1), death of airway and lung cells, and airspace enlargement typical
with emphysema. This result indicates that nicotine alone regardless of whether it is delivered by vaping or smoking, is likely to create lung disease and COPD. Overall, research is conflicting about the effect of nicotine in inflammation.

Nicotine alone actually appears to promote growth of cartilage cells in humans as shown in a laboratory study of normal cartilage and cartilage from Osteoarthritis patients. Type II collagen is the basis for cartilage in joints. Type II collagen was directly affected by nicotine with higher doses stimulating greater cell proliferation in both normal and Osteoarthritis cartilage tissue. Tissues not subjected to nicotine showed no significant cell proliferation. Aggrecan is a type of protein integral to cartilage and it is not affected by nicotine.

Previous studies showed conflicting results that suggested that smoking offered some protection against Osteoarthritis of the knee, foot, hand, and spine, even in overweight people. Another study showed that smokers had greater cartilage loss and more severe knee pain than nonsmokers. A laboratory study showed that nicotine alone was a potent stimulator of bone cell synthesis while a condensation of cigarette smoke was a potent inhibitor of bone growth. It appears that other components of smoke are likely responsible for cartilage and bone damage while nicotine alone may have medically valuable properties.

This is not reason to start vaping, but it shows that if you can eliminate cigarette smoking, a lot of the musculoskeletal problems may be alleviated. With further research, nicotine used alone as a drug may prove to be useful in cartilage and connective tissue repair.

Carbon monoxide (cigarettes only).
Carbon monoxide in cigarette smoke does not seem to affect blood flow, though it does dramatically affect the ability of blood to carry oxygen. Carbon monoxide bonds 200 times more easily to hemoglobin in the blood than oxygen, so it impairs the ability of blood to carry oxygen to the body’s cells. It also appears that carbon monoxide and hydrogen cyanide present in cigarette smoke inhibit the ability of cells to take in nutrients and release waste products.

Propylene glycol, glycerine, 1,3-Propanediol (vaping only).
Propylene glycol (PG) is classified as Generally Recognized As Safe (GRAS) although there is some indication that inhaling PG over an extended period of time may result in lowered lung function, especially among asthmatics. Some vaping devices allow the user to increase the temperature of the coil which results in vaporizing the liquids at a higher temperature. Temperatures over 300° can be achieved with vape devices on high settings and this results in the breakdown of propylene glycol and glycerine into formaldehyde, acetaldehyde, and acrolein which have been implicated in the development and aggravation of asthma. Propanediol is reportedly easier to inhale and has been found to have virtually no toxicity when inhaled.

Flavorings (cigarettes and vaping).
Artificial and natural flavorings in cigarettes were banned in 2009 with the Family Smoking Prevention and Tobacco Control Act. Only tobacco and menthol flavorings are allowed in cigarettes. It was felt that flavorings would promote smoking by appealing to children and adolescents.

Unfortunately vaping fluids and e-cigarettes are not covered under legislation and as of January 2014 there were 466 e-liquid brands and 7764 unique flavors. The number has continued to grow since then and it is unknown how many brands and flavors exist today. It is important to note that vaping fluids contain no tobacco. If a fluid is tobacco flavored, the flavoring has been added and it is of chemical origin.
The FDA in the U.S. states that flavorings in vaping liquids appear to possibly help some adults quit smoking cigarettes and transition to this less harmful product.\textsuperscript{26} The FDA is continuing to monitor research on flavorings with regard to usage and addiction patterns as well as the flavors which present greater risks to health.\textsuperscript{26} OSHA and the flavoring industry recognize that respiratory damage occurs from flavorings, diacetyl, pentanedione, and acetoin specifically, especially when heated.\textsuperscript{27} These flavorings are present in a huge number of the compounded flavorings of e-liquids. The problem doesn’t stop with respiratory damage. Flavorings are possibly the most pressing issue with regard to e-liquids not only because of the research to date showing numerous severe responses by the body to exposure to these chemicals discussed further below, but also the fact that it is youth and children who are often consumers. U.S. regulatory agencies take more responsibility when it comes to protecting workers than it does to protecting the general public.\textsuperscript{27} The table below shows the estimated mass flavoring content of these three most toxic chemicals.
<table>
<thead>
<tr>
<th>Flavor</th>
<th>Brand</th>
<th>Flavor type</th>
<th>Diacetyl (2,3-butanedione)</th>
<th>2,3-Pentanediene</th>
<th>Acetoin</th>
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<td>&lt;LOD</td>
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<tr>
<td>Allen Blood</td>
<td>H</td>
<td>Fruit</td>
<td>0.4</td>
<td>&lt;LOD</td>
<td>19.4</td>
</tr>
<tr>
<td>Carmel Popcorn</td>
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<td>Brown</td>
<td>0.3</td>
<td>&lt;LOD</td>
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<tr>
<td>Cupcake</td>
<td>H</td>
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<tr>
<td>Energy Drink</td>
<td>H</td>
<td>Other</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>12.2</td>
</tr>
<tr>
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<td>Fruit</td>
<td>0.9</td>
<td>&lt;LOD</td>
<td>114.4</td>
</tr>
<tr>
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<td>Other</td>
<td>2.2</td>
<td>4.2</td>
<td>26.1</td>
</tr>
<tr>
<td>Bubble Gum</td>
<td>I</td>
<td>Other</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
</tr>
<tr>
<td>Cheesecake</td>
<td>I</td>
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<td>&lt;LOD</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
</tr>
<tr>
<td>Cola</td>
<td>I</td>
<td>Brown</td>
<td>&lt;LOD</td>
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<td>3.7</td>
</tr>
<tr>
<td>Cotton Candy</td>
<td>I</td>
<td>Fruit</td>
<td>0.8</td>
<td>&lt;LOD</td>
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<tr>
<td>Tutti Fruiti</td>
<td>I</td>
<td>Fruit</td>
<td>9.3</td>
<td>0.8</td>
<td>24.7</td>
</tr>
</tbody>
</table>

<LOD: detected by the laboratory above the laboratory limit of detection (LOD) but less than the limit of quantification (LOQ); LOD by batch 1 and batch 2 (diacetyl: 2.3 µg, 0.19 µg; 2,3-pentanediene: 0.07 µg, 0.38 µg; acetoin: 1.08 µg, 3.2 µg).
<LOQ: not detected above the laboratory limit of detection (LOD), 0.05 µg.

Table courtesy of Reference 27
Flavorings can cause lung and airway damage. The use of food flavorings in e-liquids is problematic because the flavors are not consumed, but inhaled. It is well known that the buttery/creamy flavoring of diacetyl (2,3-butanedione) causes irreversible obstructive lung disease when inhaled. A test found this toxicant in 69% of the e-liquid products tested with a large portion of those containing well over the amount allowed by the National Institute for Occupational Safety and Health (NIOSH) and the Centers for Disease Control (CDC). The Flavor and Extract Manufacturers Association (FEMA) of the U.S. has identified 1037 flavoring agents as potential respiratory hazards. Among the flavorings on the FEMA list which are used in e-liquids in addition to the buttery flavors are minty, cherry, almond, cinnamon, clove, leathery, medicinal, chocolate, banana which are all either naturally occurring or chemical food flavorings. These flavorings can not only cause respiratory problems and asthma, but also often cause skin, mucous membrane, and/or eye irritation. Benzaldehyde is used to create a cherry or fruit flavor and it has been found in a large number of e-liquids. Mint flavorings are allowed in both cigarettes and e-liquids, though with the e-liquids the quantity is not controlled, so manufacturers can add whatever amount they choose, even changing the quantity from batch to batch. There have been a few reported cases of allergy and respiratory problems associated with mentha-based flavorings and it has cough-suppressing properties, so it may mask early symptoms of respiratory disease. Two types of nerve receptors (TRPV1 and TRPA1) are involved in inflammation and respiratory irritation. Pepper (capsaicin) and vanilla-type compounds, cinnamon, cannabis, floral/spicy flavor, mint, clove, citrus, and ginger are all agents that activate those nerve receptors and are likely to cause breathing problems and inflammation of airways to sensitive individuals.

Flavorings can cause DNA damage to the smoker and unborn babies in pregnancy, oxidative stress, as well as chronic inflammation (at least in the mouth and lungs). Since there are a multitude of flavorings used, each research study is generally limited to one or a few flavorings. Though flavorings probably all have their own unique toxicities, the research has been in agreement that DNA damage both in gene expression (DNA methylation) and cell aging (senescence), oxidative stress, and inflammation incur from breathing flavorings.

Flavorings can cause inflammation. Research has been showing that flavorings result in the release of pro-inflammatory agents in the body (IL-8), especially diacetyl, acetoin, and 2,3-pentanedione. In another study, diacetyl, pentanedione, o-vanillin, maltol, coumarin, and cinnamaldehyde all resulted in a significant increase in pro-inflammatory agents (IL-8) in the lab. Interestingly, acetoin resulted in a dose-dependent decrease in pro-inflammatory agents (IL-8) in contrast to some other research. It was conjectured that perhaps this was due to immune system suppression, but not enough is known to clearly understand this yet. It is clear that a few commonly used chemicals in flavorings produce a significant effect of increasing pro-inflammatory agents.

Flavorings can cause cell toxicity and oxidative stress. Laboratory tests have found that some flavorings result in cell toxicity and, in the case of cinnamaldehyde, cell death. Cinnamaldehyde, o-vanillin, and pentanedione showed significant toxicity. Mixing flavorings gave rise to the highest cell toxicity measures indicating that users who inhale a variety of e-fluids are possibly more prone to greater toxic effects. Significant oxidative stress was measured with a wide variety of flavorings and, as with cell toxicity, mixing flavors resulted in higher oxidative stress than individual flavors.

Smoking and musculoskeletal problems
A thorough recent review of all qualified research on the effects of smoking and musculoskeletal problems concluded:

- Wound healing is impaired because smoking can damage blood vessels, decreases the amount of blood flowing to wounds, and decreases oxygen in the blood. Even one cigarette a day can impair the ability to heal.
• Smoking can decrease the strength of scar tissue and reduce the chance that skin grafts will be successful.
• Smoking can make some conditions more painful such as back pain, headaches, rheumatoid arthritis, gum pain, and fibromyalgia.
• There is a large and consistent body of research showing adverse effects of Bone Mineral Density (BMD) across all age categories and sex. Bone mass, measured as bone mineral content has not been studied as much and there is less consistency of results. Increased risk of bone fracture and delayed fracture healing both have a large and consistent body of research showing a strong negative effect of smoking.
• Dental health suffers consistently in smokers. This includes increased bone loss, poor health of tooth supporting structures, and increased failure of implants through bone implant failure and tissue deterioration.
• Rheumatoid arthritis is negatively affected by smoking with a high degree of association in disease activity and poor response to therapies.
• As mentioned earlier, the response of Osteoarthritis in smokers is somewhat inconsistent and has not been studied sufficiently. The prevalence of OA and the risk for total joint replacement show inconsistent association. Two things do show consistent associations are increased pain with OA and an increased risk for complications after total joint replacement in OA.
• Spondyloarthritis shows a consistent association with smoking, but more research is required to verify this.
• Pain associated with temporomandibular joint disorder has a fairly consistent association with smoking, but more research is needed.
• There is a strong and consistent association between smoking and decreased muscle strength, though decreased maximal muscle voluntary contraction shows little consistency.
• There is both an increase in the volume and increased defects in knee joint cartilage in smokers, so as mentioned previously, perhaps nicotine encourages cartilage growth, but other factors in cigarette smoke result in poor quality cartilage. Smoking is strongly and consistently associated with poor outcomes for knee surgeries.
• Spinal surgeries are less successful in smokers with high risk for needed repeated operations and decreased fusion rates.
• Rotator cuff tears are much worse and outcome after reconstructive surgery is poor with smokers. Results are consistent, though more research is needed.
• Stability and function following Anterior Cruciate Ligament (ACL) surgery is poor with smokers. Research is moderately consistent, though more research is needed.
• Research has found that smoking negatively affects ligaments of the knee mechanically, molecularly, and clinically and there some studies have found that it also negatively affects knee cartilage. There have been no studies to determine the effect of smoking on the knee meniscus.

Kicking the smoking habit.
It isn’t simply nicotine addiction.
The point can be made that biggest reason smoking is so pleasant is the addiction to nicotine, otherwise people would be smoking all sorts of non-addictive plants and herbs. As soon as one cigarette is finished, the level of nicotine in the blood starts to drop and withdrawal symptoms start. As time progresses, a fidgety, edgy, craving becomes more and more uncomfortable so that after ½ hour to one hour, the smoker really craves a cigarette pretty badly. Smoking a cigarette gives the smoker an immediate hit of nicotine that relieves this anxious feeling quickly. They feel comforted by the cigarette and all that anxiety is reduced. Over time, smoking becomes attached to every emotion in life. Whenever a difficult emotion arises, the smoker grabs a cigarette and feels better.
So, in reality, smoking may not calm you down. The nicotine addiction makes you progressively more anxious due to an almost constant state of withdrawal. The only thing that relieves that feeling is smoking, so the smoker doesn’t realize that people who don’t smoke don’t feel that anxiety and craving most of the time.\textsuperscript{5}

But, it really isn’t that simple. Research at Duke University’s Center for Smoking Cessation has studied smoking since 1989 and they have found that out of the more than 5000 components in tobacco smoke, there are some with psychoactive effects other than just nicotine.\textsuperscript{34} There is also a very powerful habitual sensorimotor aspect and cue conditioning related to smoking.\textsuperscript{34} Consistent with reports by smokers, they miss the actual act of smoking. This has been shown in several studies. Smoking behavior among habitual smokers can be maintained by denicotinized cigarettes alone. Clearly nicotine addiction is powerful, but so is the entire habit of smoking. Smoking denicotinized cigarettes has been shown to suppress withdrawal symptoms and reduce cravings.\textsuperscript{34} Smokers aren’t just addicted to nicotine. Reduced blood flow to the brain is associated with symptoms of withdrawal, specifically craving, negative affect (emotions), and habit withdrawal.\textsuperscript{34} Blood flow to the brain was also found to be reduced for smokers who did not smoke even with a nicotine patch.\textsuperscript{34} The act of smoking denicotinized cigarettes resulted in significantly increased regional cerebral blood flow as well as reduced reported withdrawal symptoms.\textsuperscript{34} Other research has shown that strong cravings may be part of a cognitive and emotional memory circuit involving the fronto-temporo-cerebellar regions of the brain.\textsuperscript{34} If a smoker refrains from smoking, this memory circuit may trigger craving as blood flow to the brain is reduced, totally independent from the absence of nicotine.

Clearly, although nicotine is an addictive drug, the other aspects of smoking and probably other components of cigarette smoke are also a very large factor in making quitting very difficult.

**Research on quit attempts**

There are two aspects to attempting to quit smoking. There is the actual *effort* to make a quit attempt and then there is the actual *success* of the quit attempt or not. Both are important. Even getting to a mental state where a smoker considers quitting is a landmark, but we also want to understand what tends to make that attempt stick.

One study did not provide any treatment or intervention, but simply measured the data on people who tried to quit on their own.\textsuperscript{35} They used a group of people who responded that they planned to quit sometime in the next three months, so there was at least a desire on the part of the individuals to stop smoking. Participants phoned into an automated system and answered questions about their smoking habits that day and intentions for the next day by using a touchtone phone every night for 12 weeks. What this study found was interesting in understanding the success of fairly motivated smokers with no intervention other than nightly reporting to an automated, non-human, non-judgemental system.

- Most smokers made several attempts to stop smoking, often in rapid succession.
- Only 16\% of the intentions to stop smoking the next day resulted in a quit attempt, but over 60\% of the intentions to quit the next week or month resulted in a quit attempt.
- Setting a quit date only happened 21\% of the time and it did not predict greater abstinence.
- 60\% of the smokers attempted to quit or reduce smoking during the 12 week period.
- In 48\% of the quit attempts lasted less than a day, but 38\% of the quit attempts lasted more than 7 days. Only 18\% of the smokers were abstinent at the end of the study for more than 7 days. 15\% were abstinent from their first quit attempt to the end of the study.
- 72\% of the quit attempts were unplanned and not preceded the previous day by an intention to quit the next day.
- Planned quit attempts lasted 25 days whereas unplanned attempts lasted 1 day.
• Use of treatments was common, but it was not significantly associated with greater abstinence: 14 days vs. 3 days.
• Quitting early in the study was a predictor of repeated quit attempts (86%). 67% of the people who waited until later in the study attempted to quit. Repeat attempts were not a predictor of the success in quitting, however the fourth attempt at quitting resulted in a significantly longer quit length.
• After the study was completed, it was determined that 17% of the smokers did not report brief quit attempts.

The following demographics were found NOT to be associated with regard to likelihood that an attempt to quit will be made nor that attempts will be successful:
• Gender (men vs. women)
• Education level
• Age
• Income
• Smoking ban at work

Dependence on cigarettes appears to be negatively associated with quit attempts as well as successful quitting, with higher dependence/heavier smokers less likely to make a quit attempt or to have it last.

Restrictions on smoking at home did make a difference in quit attempts and in their success in Western cultures, but not in East Asian cultures.

The issue of multiple quit attempts is an interesting issue. Whereas past quit attempts is a good predictor of more quit attempts, the results from various studies were mixed with regard to that as a predictor of successful quitting. It appears that multiple quit attempts is associated with longer abstinence, but not necessarily with totally kicking the habit. Short periods of abstinence, less than a week, predicted less success in quitting than smokers who had never tried quitting.

Motivation and intention to quit are also variables that have interesting mixed results. While both motivation and intention to quit are predictors that a smoker will make a quit attempt, they are either not associated or negatively associated with actually quitting successfully.

Health effects and negative opinions about smoking are also factors that differ in their effect. While concerns about the effect of smoking on health, looking forward to the benefits to health of stopping, as well as having a negative opinion about smoking are all good predictors that a smoker will make a quit attempt, these factors have little effect on quitting success or even a negative association.

Smokers who are confident that they will succeed in quitting are more likely to make a quit attempt, but in 3 out of 4 studies, there was no association between initial confidence and actual success, though one study found success at 2 to 3 times the rate of those who were not at all sure they would succeed.

Genomic links and drug treatments
Genetic research has been used to determine risk for cancer and other congenital diseases, but now research funded by the National Institutes of Health, the Centers for Disease Control and Prevention, and private companies are beginning to broaden their focus and are including aspects of behavioral medicine. The goal is to personalize approaches to disease prevention and treatment by determining genetic biomarkers and to find drug treatments that are specific to these.
There are two strong genomic expressions that have been identified already that play a role in heavy smoking, lung cancer, and COPD (chronic Obstructive pulmonary disease). One (CHRNA5) predicts smoking heaviness, later age of smoking cessation, lung cancer, COPD and early mortality. The other (CYP2A6) is the gene encoding the primary enzyme that metabolizes nicotine and also predicts heavier cigarette smoking, failed smoking cessation, hypertension, lung cancer, and other smoking-related illnesses.

One of the strongest predictors of failed smoking cessation is the level of dependence on nicotine. Pharmacogenomics is the use of genomic variation to predict the success of a specific drug with a specific gene expression. There are currently three FDA-approved medications: nicotine replacement therapy (nicotine patch), varenicline, and bupropion. A review of current research concluded that there may be a connection between these treatments and the known genetic biomarkers, but results have not been clearcut. People vary with regard to the speed that they metabolize nicotine and different treatments appear to work better depending on this factor.

People who metabolize nicotine slowly have been found to have greater quit rates using a nicotine patch. People who metabolize nicotine faster appear to have better treatment response on varenicline than with the nicotine patch. One study found that slow metabolizers also had more side-effects from varenicline than faster metabolizers. One study found for high nicotine metabolizers, bupropion was significantly more effective that a placebo both at the end of the study and at a 6-month followup. For people with moderate or low nicotine metabolism, bupropion was not significantly more effective than the placebo. The people with the slowest nicotine metabolism did well with counseling alone and achieved no benefit from bupropion where as the people with the fastest nicotine metabolism did not benefit from counseling alone.

Research seems to indicate that people who metabolize nicotine quickly have stronger cravings to smoke, but aren’t generally more dependent on nicotine. Dependence is a multifaceted issue.

Smoking cessation programs
According to authorities at Duke University, a leader in smoking research, the best first step is to seek professional help by getting a referral to a smoking-cessation program through a physician, psychologist, or pharmacist.

As noted above, if you can find a program that can test your nicotine metabolism (NMR or nicotine metabolism ratio), it will help design a program that is more tailor-made to your genetic makeup and will increase the odds of quitting success. Programs that use multiple approaches such as nicotine replacement or other drug therapies, behavior training, and hypnosis, have a higher success rate, but even with these programs many people return to smoking within a year. As we have pointed out, it isn’t simply a matter of craving nicotine or nicotine addiction. Most people report that after about two weeks, physical cravings are mostly gone with the first few days being the worst. It is all the habits and cues that are such powerful stimuli: a cup of coffee first thing in the morning, a friend lighting up and offering a cigarette, a stressful day. Good quit-smoking programs need to have support in place that will be there when you are ready to cave or at least arm you with strategies to cope.

Effective counseling
There are various studies that have looked at types of counseling that may be more or less effective in helping people to quit. In England, pharmacies have been assigned the responsibility for smoking cessation counseling, offloading the task from primary care physicians. The effectiveness of the community pharmacy services as measures by self-reported quit rates after 4 weeks has been found to be close to that of physician counseling (44% vs. 49%), though neither reaches the desired goal of 70%. One study recorded and categorized the topics covered during counseling sessions for both the counselor
and the smoker attempting to quit.\textsuperscript{40} The topics and feedback had some association with successful quitting or non-quitting.\textsuperscript{40} All counselors had attended training and were certified by the National Centre for Smoking Cessation and Training (NCSCT) program.

- Lifeworld talk between the advisor and the smoker was common for both quitters and non-quitters, though it was a bit more with the quitters. These were interchanges where the advisor learned about the smoker’s life situation, experiences, and context which enabled them to better understand the smoker’s difficulties and stresses allowing them to understand and discuss approaches to quitting that takes their individual situation into consideration.
- Excessive praise, especially when the smoker made some effort, but did not actually quit, was detrimental to quitting. Quitters received limited, brief praise while non-quitters received extensive praise from the counselors even when they hadn’t achieved the goal of “not one puff”. While praise was well-intentioned to cheer a smoker on, it actually was counterproductive when they had not achieved the desired goal.
- Biomedical information and advice was given to all of the smokers, but it was heavier in the cases where smokers succeeded in quitting.
- The need for the smoker to primarily use their own willpower to quit with support from the advisor was emphasized with the quitters, but less often with the non-quitters.
- Advisors inviting the smoker to stop in for support or advice any time the pharmacy was open was offered to fewer of the eventual non-quitters and it was less effective for them. This opportunity is one advantage to the program of having pharmacists and their assistants oversee quitting programs. Their availability is much higher than physicians.
- Health reasons were cited by more than half of the smokers, but slightly more of the non-quitters used this as a reason, so it may not be a strong factor in success.
- Under 1/3 of the smokers used expense as a reason for smoking even though financial savings was used often by advisors as a reason they might want to quit. The study was conducted in an impoverished area, but money was not a factor in deciding to quit or quitting success.
- Quitters were twice as likely to mention their families and children as motivating factors, though this still was only a factor in less than 1/3 of the quitters.

Using e-cigarettes to quit
Are e-cigarettes or other vaping methods effective in helping smokers quit? That is what they were originally developed for. They deliver nicotine and they provide most of the behavioral and habitual aspects of smoking without all the toxic and cancer-causing effects of smoking. A survey in the U.K. has concluded that yes, e-cigarettes have helped tens of thousands of people quit smoking in England.\textsuperscript{41} E-cigarettes alone or in combination with other prescription medications appears to be helpful, at least in the short term.\textsuperscript{41} The usefulness is very inconclusive, however. Of 7 reviews with statistical analysis, 2 found that e-cigarettes had a positive effect on quitting, 4 found an inconclusive effect, and 1 found a negative effect.\textsuperscript{41} Stop-smoking programs often do not use e-cigarettes as a method of quitting as opposed to the use of medications.\textsuperscript{41} E-cigarettes are certainly not a risk-free method of quitting and are still a crutch keeping smokers reliant on nicotine and continuing reinforcement of all the behavioral habits and rituals of smoking. It is too soon to determine if e-cigarettes or other vaping methods are effective in long-term quit attempts.\textsuperscript{39,41}

Quitting conclusions
There is so much more information about quitting smoking and programs, it is best for the smoker to try to find a local program that is appealing and convenient to them personally. Quitting “cold turkey” by yourself with no medications or support has only a 3–10% chance of success.\textsuperscript{43} Some people can do it, but it is generally a lot more difficult. If possible, get a test to find out what the individual nicotine metabolic rate is and work with a knowledgeable professional to use that information to tailor a plan that works best for your profile. In areas where there is no professional help with cutting edge knowledge or technology,
it is up to the individual to attempt an approach that they feel might be something that will help them. Local hospitals often have smoking cessation programs that are offered free to the public. If you’d rather have something 24/7 or use this as part of your program, check Facebook or the links below for information and support online. For some people technology is appealing, but for others personal interaction, support, and accountability are important.

Part of the issue is physical and part is mental. “If at first you don’t succeed, try, try again” is very apropos in the case of quitting smoking. Don’t give up. Keep trying different approaches until you find what works best for you.

**Online Resources:**

- Smokefree.gov, U.S. All aspects of quitting smoking with unique tabs for Veterans, women, teens, seniors, and Spanish language. Texting tips, advice, and motivation available. Also available, using nicotine replacement, managing cravings, dealing with slips, and a “build your own quit plan” section. [https://smokefree.gov](https://smokefree.gov)
- National Centre for Smoking Cessation and Training, U.K. Lots of information on all aspects of smoking, research, quitting, medications, behavioral interventions, community interventions, etc. [http://www.ncsct.co.uk/index.php](http://www.ncsct.co.uk/index.php)
- Centers for Disease Control and Prevention Quit Program. Stories, tools, 800 Quitline, videos, tips and tools, and much more. [https://www.cdc.gov/tobacco/campaign/tips/](https://www.cdc.gov/tobacco/campaign/tips/)
- American Cancer Society “Quit for Life” Program. [https://www.quitnow.net/Program/](https://www.quitnow.net/Program/)
- Nicotine Anonymous (Smokers Anonymous) is a 12-step support group program with fellow smokers and former smokers. In cases where there is no local group established, there is phone and online members that are available [https://nicotine-anonymous.org](https://nicotine-anonymous.org)

Sept. 26, 2018

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40. **Determining counselling communication strategies associated with successful quits in the National Health Service community pharmacy Stop Smoking programme in East London: a focused ethnography using recorded consultations.** By Rivas, C. et al. BMJ, Vol. 7(10), [https://bmjopen.bmj.com/content/7/10/e015664](https://bmjopen.bmj.com/content/7/10/e015664).
