

## Nicotine products consideration in the perioperative setting: A narrative review

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Nicotine-containing products, including combustible tobacco, smokeless tobacco, electronic cigarettes (e-cigarettes), and nicotine replacement therapies (NRT), are widely used and have significant implications in the perioperative setting for orthopedic surgery. Smoking has been linked to numerous surgical complications such as delayed wound healing, infection, cardiovascular and pulmonary complications and impaired bone healing. This narrative review aims to provide an overview of the different nicotine-containing products, their nicotine content, and the potential effects observed with their use in orthopedic surgery. A comprehensive literature search was conducted to identify studies reporting on dosage, health effects, and perioperative outcomes associated with various forms of tobacco and nicotine products. The findings reveal that combustible tobacco products contain varying levels of nicotine, ranging from 7.2 to 26.3 mg per gram of tobacco. Smokeless tobacco products have nicotine contents ranging from 7.1 to 23.1 mg per gram. Smokeless tobacco users exhibit better surgical outcomes in terms of bone healing compared to smokers. Nicotine content in e-cigarette liquids varies widely, from 0 to 134.7 mg per milliliter. Limited evidence exists regarding the effects of e-cigarettes on surgical outcomes, but animal studies suggest similar soft tissue healing rates compared to combustible cigarettes due to comparable nicotine levels. NRT, available as gum, nasal spray, lozenges, patches, and inhalers, aims to replace tobacco use and gradually reduce nicotine intake. Dosages range from 0.5 mg per spray to 42 mg in high-dose patches. Understanding the nicotine content, absorption, and route of administration of NRT products is crucial for perioperative management. In conclusion, different nicotine-containing products have varying nicotine levels and potential implications for surgical outcomes. Further research is needed to elucidate the specific effects of e-cigarettes and NRT on bone healing and to establish optimal perioperative management strategies for nicotine users undergoing orthopedic surgery.

**Keywords:** tobacco, nicotine, nicotine containing products, electronic cigarettes, cigarettes, chewing tobacco, smokeless tobacco, nicotine replacement therapy, nicotine pouch, nicotine gum

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Nicotine is a highly addictive chemical that is a byproduct of tobacco. When tobacco products are used, nicotine is released into the bloodstream, resulting in a range of physiological and psychological effects including but not limited to increase in blood pressure, vasoconstriction, appetite suppression, and reduction in anxiety [1]. Tobacco use is also associated with multiple health risks including cardiovascular disease, respiratory problems, and even cancer [2-4].

It also has been well established the detrimental effects of tobacco use on patient's surgical outcomes. Some of these risks include an increase of surgical site infections, delayed wound healing, thromboembolic

events, pulmonary and cardiac complications, and decreased bone healing [2-4]. Although most of the research associated with tobacco examines combustible tobacco products and their effects, there are other nicotine containing products to consider in the perioperative setting [1-8]]. The traditional nicotine-containing products seen have been cigarettes, smokeless tobacco, and nicotine replacement therapies (NRT). In more recent times, we have seen the emergence of electronic cigarettes (e-cigarettes) and nicotine pouches. All these products contain a different amount of nicotine along with different mechanisms of delivery and uptake routes with the most typical being inhaled or absorbed

through the oral mucosa [1]. The goal of this study is to inform the reader of different nicotine containing products, the nicotine amounts seen in those products, and possible effects seen with the use of those products in the perioperative setting for orthopedic surgery.

## **Methodology**

In this narrative review, a literature search was performed using PubMed and Google Scholar to identify studies reporting on dosage, health effects and perioperative outcomes associated with various forms of tobacco and nicotine products. Various combinations of the following search terms were used: smoking, tobacco, health effects, perioperative status, dosages, smokeless, chewing tobacco, nicotine, replacement therapy, vaping, e-cigarettes, pouches, and physiology. Additional studies were located through review of the reference lists of the above articles and through personal searches. The articles were selected based on their relevance to perioperative tobacco/nicotine use, its complications, and dosages.

## **Combustible products**

When considering the many different types of combustible tobacco products that patients may use, we have to also consider the different levels of nicotine in each type. Combustible tobacco products include cigarettes, cigars, pipes, and hookahs. Despite the well-known health risks associated with tobacco use, a survey in 2021 by the National survey on drug use and health showed that 22% (61.6 million people) reported using tobacco products or vaping nicotine and 15.6% (or about 43.6 million people) reported smoking cigarettes in the past 30 days [9,10].

When looking at total nicotine content, one study by Penn State showed nicotine content in cigarettes ranges from 7.5-13.4 mg per cigarette with the 5 highest nicotine containing brands being Newport (13.4 mg), Kool Filter (13.0 mg), Virginia Slims (11.7 mg), Red Kamel (11.6 mg), and Cambridge Ultra Light (11.5 mg). The lowest concentration of nicotine by brand was GPC Light and Ultra Light (7.2 mg and 8.0 mg, respectively), Doral Light and Ultra Light (8.3 mg and 7.6 mg, respectively), and Carlton (8.7 mg) [7].

Another study by Lawler, et al., looked at 50 mentholated and non-mentholated cigarettes and 75 cigar brands for their nicotine contents. They found

the average nicotine concentration ranged from 16.2 to 26.3 mg of nicotine per gram of tobacco (mg/g) in the cigarettes. Natural American Spirit had the highest concentration (26.3mg/g) followed by NOW Gold (21.8 mg/g), Carlton White (21.7mg/g), and Kool Green (20.7mg/g). The lowest nicotine concentrations were in the two brands of Basic and Maverick (16.2-17.3 mg/g). The study found a wide range for cigar types (7.88-24.8 mg/g). Large cigars ranged from 9.20-24.8 mg/g, cigarillos ranged from 8.32-17.9 mg/g, and little cigars from 10.3-19.1 mg/g. Pipe tobacco and mini cigarillos were found to have the lowest average with 7.88-9.61 mg/g and 12.2-12.6 mg/g, respectively. The overall mean nicotine concentration found for combustible products going from the least to the most was pipe tobacco, mini-cigarillos, little cigars, cigarillos, large cigars, and cigarettes [8].

Combustible tobacco has been thoroughly researched in its effects on both overall health and complications associated with surgical outcomes. Some of the well-known surgical complications associated with smoking are wound healing complications such as delayed healing and infection, delayed/ non-unions, cardiovascular and pulmonary complications [1-6]. Hawn, et al., compared a total of 393,794 non-smokers to smokers and examined their postoperative complications. They found that smokers had an odds ratio of 1.77 for pneumonia, 1.67 for reintubation for respiratory/cardiac failure, and 1.55 for death within 1 year [4]. A systematic review looking at infection and wound healing associated with smoking found a reduction in tissue perfusion and oxygenation, impairment of inflammatory cell functions and oxidative bactericidal mechanisms, and decreased synthesis and deposition of collagen ultimately leading to higher incidence of wound healing complications and infection in smokers [6].

There have been numerous studies with the focus of looking at bone healing and its association with smoking. One such study looked specifically at the effects of smoking on foot and ankle surgery. In their systemic review they found that any foot and ankle procedure involving arthrodesis, fracture ORIF, or plastic procedures had negative outcomes in patients that smoked while other procedures such as amputations or total ankle arthroplasty did not [11]. A systematic review of which included 1,221 fractures showed that smokers had a 2.32 times more

likelihood of non-union and had a longer time to bony union when looking at fractures [12].

### **Smokeless tobacco**

Another popular form of tobacco use is with smokeless tobacco. The CDC reported that in 2020, more than 2 in every 100 adults reported use of smokeless tobacco products which represents approximately 5.7 million adults. This shows a trend downward with a survey study that showed 8.7 million people ages 12 and old that were using smokeless tobacco. Though the use of smokeless tobacco is trending down, there are still millions of people using it [13].

As with combustible tobacco products, smokeless tobacco products also have a wide range of total nicotine content depending on the brand and type. The estimated amount of nicotine in a can of dip or snuff is 144 mg which is equal to about 80 cigarettes. If a patient uses two cans of smokeless tobacco a week, this is equivalent to about 1 ½ packs of cigarettes a day for a smoker. You also must consider the amount of free/unprotonated nicotine per product as this determines the bioavailability of the nicotine. Studies have shown that smokeless tobacco products absorb a greater amount of nicotine than with smoking tobacco [14,15]. The different types of smokeless tobacco patients may be using include dry snuff, moist snuff, loose-leaf chewing tobacco, and snus.

A study looked at different smokeless tobacco products in 2006-2007 and determined their total nicotine and free nicotine content along with the type of smokeless tobacco (Table 1). The some of the brands with the most total nicotine were Railroad Mills with 23.1 mg/g (dry snuff), Bruton with 17.5 mg/g (dry snuff), Catch Dry Licorice and Taboka with 16.7 mg/g (snus), and Levi Garrett with 16.6 mg/g (dry snuff). Other notable brands were Beech-nut with 7.1 mg/g (chew), Copenhagen long cut with 13.9 mg/g (dip), Grizzly long cut

wintergreen with 11.2 mg/g (chew), Kodiak wintergreen with 10.7 mg/g (dip), and Skoal long cut with 13.4 mg/g (dip). When the examined the free nicotine (unprotonated), they found that Kodiak wintergreen long cut 2007 had the most with 8.2 mg/g followed by Copenhagen pouches with 6.8 mg/g, Camel Spice with 6.7 mg/g, Grizzly long cut wintergreen 2006 with 6.6 mg/g, and Kodiak wintergreen 2006 with 6.5 mg/g [16].

Another study in 2003 by Richter, et al., also looked into nicotine, pH, and unprotonated nicotine content found in 18 commonly used smokeless tobacco products (Table 2). They looked at both moist snuff and loose-leaf types of smokeless tobacco. They found the highest nicotine content within the moist snuff tobacco products. The highest amounts were found in Timber Wolf Long Cut Straight (13.54 mg/g), Skoal Long Cut Straight (12.94 mg/g), Copenhagen Snuff (12.71 mg/g), Copenhagen Long Cut (10.35 mg/g), and Kodiak Wintergreen (9.00 mg/g). They also found that the moist snuff products had the highest unprotonated nicotine. The highest containing brands were Kodiak Wintergreen (5.81 mg/g), Skoal Long Cut Straight (3.68 mg/g), Copenhagen Snuff (3.05 mg/g), Copenhagen Long Cut (2.04 mg/g), and Silver Creek Long Cut Wintergreen (1.88 mg/g). The loose-leaf tobacco products overall had lower overall nicotine and unprotonated nicotine [14].

A study out of Sweden wanted to look at surgical outcomes in oral snuff users, specifically on bone healing. They compared surgical outcomes on patients where a tibial osteotomy using hemicallotaxis technique was performed in smokers, snuff users, and non-smokers. They found no cases of delayed healing, shortest time in the external fixator and lowest rates of complications when compared to both smokers and non-smokers. The authors in this study suggested that the delay in bone healing seen in smokers may be the result of smoke components versus actual nicotine [17].

Product	Nicotine	Free Nicotine	Notes
Ariva	3.9	0.7	Dissolvable tobacco
Stonewall	8.2	1.2	Dissolvable tobacco
Beech-nut	7.1	0.02	Chew
Hawken	2.9	0.01	Chew
Lancaster	8.0	0.01	Chew
Levi Garrett	5.3	0.06	Chew
Red Man	8.6	0.08	Chew
Red Man Golden	7.7	0.06	Chew
Stoker's Apple	3.8	0.01	Chew
Taylor's Pride	6.4	0.06	Chew
Cooper Wintergreen	8.0	1.1	Dip
Copenhagen	12.7	3.2	Dip
Copenhagen LC	13.9	5.4	Dip
Copenhagen Pouches	11.2	6.8	Dip
Grizzly LC WG 2006	10.3	6.6	Dip
Grizzly LC WG 2007	11.2	5.9	Dip
Husky FC	12.9	4.8	Dip
Kayak LC WG	11.9	2.3	Dip
Kodiak WG 2006	10.9	6.5	Dip
Kodiak WG 2007	10.7	8.2	Dip
Longhorn LC WG	13.8	5.7	Dip
Red Seal FC	13.2	3.1	Dip
Renegades WG	13.4	2.4	Dip
Skoal FC Original	13.3	3.9	Dip
Skoal LC Cherry	12.7	1.7	Dip
Skoal LC Mint	12.9	3.7	Dip
Skoal LC Straight	13.4	3.9	Dip

**Table 1 (continued on next page)** Concentration of nicotine, free nicotine content per smokeless tobacco product.

Product	Nicotine	Free Nicotine	Notes
Skoal LC Wintergreen	12.8	2.9	Dip
Timber Wolf LC WG	14.1	5.2	Dip
Camel Frost 2006	13.3	4.7	Snus
Camel Frost 2007	14.1	4.7	Snus
Camel Original 2006	13.9	4.7	Snus
Camel Original 2007	13.5	6.2	Snus
Camel Spice 2006	13.2	6.7	Snus
Camel Spice 2007	13.4	5.1	Snus
Catch Dry Eucalyptus	15.9	1.4	Snus
Catch Dry Licorice	16.7	0.7	Snus
General	7.2	1.9	Snus
General Portion	8.5	5.1	Snus
General White Portion	7.9	4.8	Snus
Skoal Dry	11.9	2.4	Snus
Taboka	16.7	0.4	Snus
Taboka Green	13.0	0.5	Snus
Bruton	17.5	0.5	Dry snuff
Dental Sweet	11.1	0.1	Dry snuff
Levi Garrett	16.6	0.1	Dry snuff
Railroad Mills	23.1	0.5	Dry snuff
Red Seal	15.1	0.4	Dry snuff

**Table 1 (continued from previous page)** Concentration of nicotine, free nicotine content per smokeless tobacco product.

Brand	Nicotine mean (mg/g)	Unprotonated nicotine (mg/g)
<b>Moist snuff</b>		
Hawken Wintergreen	4.28	.01
Skoal Bandits Mint	8.49	.97
Timber Wolf Long Cut Straight	13.54	1.58
Silver Creek Long Cut Wintergreen	6.39	1.88
Copenhagen Long Cut	10.35	2.04
Copenhagen Snuff	12.71	3.05
Skoal Long Cut Straight	12.94	3.68
Kodiak Wintergreen	9.00	5.81
<b>Loose leaf tobacco</b>		
Chattanooga Chew Premier Flavor	8.26	.02
Beech-nut Wintergreen	4.06	.02
H.B. Scott's Private Blend	4.11	.02
Beech-nut	6.79	.03
Taylor's Pride	4.69	.03
Red Man	7.44	.04
Red Man Golden Blend	6.23	.06
Red Man Select	3.73	.06
Granger Select	4.90	.10
Levi Garrett	4.45	.11

**Table 2** Nicotine means concentration per brand name of chewing tobacco.

**E-cigarettes**

Electronic cigarettes are composed of a battery unit that heats a coil around a wick containing the e-liquid solution, which aerosolizes it into a dense, white vapor [18]. E-cigarettes first appeared in the United

States in 2007 and have increased in popularity since. With an initial surge of use once it first became available, increase in use has been slowed but still increasing. Between 2017 and 2020, Boakye, et al., survey found an increase in use from 4.4% to 5.1% of the total population surveyed and a high prevalence of 14.5% in adults between the ages of 21-24 [19].

Although some e-cigarettes do not contain nicotine, the majority (99%) of e-cigarette use liquids in their cartridges that contain nicotine [20]. Multiple studies have been performed that show a range of nicotine content. Voos, et al., looked into some of these studies and found nicotine content ranging from 0-24 mg/ml typically but had nicotine concentration as high as 134.7 mg/ml in pure nicotine liquids. Some of these concentrations are close to or over the estimated lethal dose of nicotine (30-60 mg/ml) for adults. They also looked at the amount of nicotine that is aerosolized in the puffs. They found studies showing a range of 0.27 to 2.91 mg per 15 puff in 1st generation e-cigarettes and 1.01 to 10.61 mg per 20 puffs in 2nd and 3rd generation e-cigarettes. Overall they found that the nicotine produced by e-cigarettes were equal to or greater compared to cigarettes (1.76 to 2.20 mg per one cigarette) but also had few toxins and on average, less free base nicotine [21].

Another variable to consider with e-cigarettes with perioperative management is lack of regulations. Nicotine content in e-cigarettes can vary from the listed concentration. Raymond, et al., study found that 37% of the 70 samples tested had a greater than 10% deviation from the listed nicotine amount and 23.6% of the samples listed had a deviation of greater than 20%. They also found that approximately 92% of the samples listed as 0% nicotine content had trace amounts [18]. With trends still increasing, especially in the younger population, understanding the effects e-cigarettes have on surgical outcomes is important.

The current literature on e-cigarette effects on surgical outcomes is very limited. Most of the current literature shows its effects on soft tissue healing in animal models. Toriano, et al., studied cutaneous skin flap survival comparing cigarette and e-cig smoke in 45 rats. Their results showed that cigarette and e-cigs had similar skin flap necrosis (68.7% and 65.9%, respectively) along with similar cotinine levels before and after surgery. Their conclusion was that due to nicotine's vasoconstrictive effects that there was no difference in skin flap survival rates between the two cigarettes and e-cigarettes as they contain

approximately the same amount of nicotine [22]. Kenney, et al., examines the effects of achilles tendon healing with 54 rats that were exposed to either cigarette smoke or e-cigarette smoke. They were exposed to the smoke 6 days a week for 4 weeks leading up to surgery. There was an equivalent amount of nicotine between the two groups. They continued with the smoke exposure for two weeks after the achilles tendon repair and found that both groups had lower tensile strength when compared to the control group but it was not of significance [23]. There is also no current literature specifically looking at e-cigarettes effects on bone healing though this is ample amount of literature discussing the effects of smoking and nicotine on bone healing. Future studies are needed to determine if there is a difference between combustible tobacco products and e-cigarettes on bone healing.

### **Nicotine Replacement Therapies**

Nicotine replacement therapies (NRT) first appeared in the United States in 1984 with nicotine gum. The goal of NRT is to replace tobacco product use with a slow discontinuation of nicotine all together. Since the release of NRT, there have been multiple alternatives to gum such as nasal spray, lozenges, patches, and inhalers. Each product has variability of dosage and route of administration. Table 3 shows all the dosages for the different types of NRT. Dosages differ from 0.5 mg per spray per nostril to 42 mg with high dose transdermal patches. Understanding the route, duration and absorption of each product is important in understanding possible effects that each may have on surgical outcomes [24].

Benowitz, et al., compared nicotine levels obtained through nicotine nasal spray, transdermal patches and cigarettes. They looked at 12 adults over the course of 21 days and gave each standardized doses of cigarettes (16 per day for 5 days), transdermal patch (15 mg over 16 hours for 5 days), nasal spray (1 mg dosed 24 times a day over 16 hours for 5 days), and a placebo nasal spray (dosed the same as the nicotine nasal spray for 5 days). They found that mean plasma concentrations of nicotine in the nasal spray and transdermal patch were similar (10.5 ng/mL and 9.2 ng/mL) while levels found during cigarette smoking were twice as high (16.3 ng/mL) [25]. Azzopardi, et al., study of 34 patients found nicotine absorption concentrations of nicotine gum (4 mg) and nicotine lozenge (4 mg) to be 4.4 ng/mL and 8.3 ng/mL respectively.

In that study they also examined the nicotine content left in the gum after 30 minutes of use and found that approximately 67% of the nicotine remained in the gum [26]. So even though the gum and lozenge contain the same amount of nicotine, the nicotine in the gum is not completely absorbed as it is with the lozenge.

There is limited research available on direct effects of NRT with surgical outcomes. Most of the studies available are either animal models or look specifically at just pure nicotine which can skew the results depending on the route of administration and absorption as seen with Azzopardi, et al., study. Donigan, et al., evaluated 22 adult rabbits and the effects of transdermal nicotine patches on fracture healing. The rabbits had a 10.5 mg transdermal patch applied to their ear daily starting first on postoperative day 1 of after a midshaft tibial osteotomy was performed and fixated. After 21 days, they euthanized the rabbits and performed a biomechanical test to both the fractured and unfractured tibias.

The average torque to failure in the nicotine group was 36% (0%-83%) when compared to the unfractured side. In the control group they found an average torque to failure to be 69% (25%-146%). They also noted 3 nonunions within the nicotine group and none in the control group [27]. Other studies evaluating nicotine in animal studies showed similar results but had plasma concentrations exceeding that found in a smoker and 3-6 times as much found in a nicotine patch user while others have shown that nicotine given in lower dose showed greater needing stiffness and fusion rates when compared to their control group [28,29]. There is still a lack of evidence showing whether NRT contributes to higher rates of complications in the perioperative setting.

Type of NRT	Dosage
Gum	2 mg, 4 mg
Transdermal Patch	5 mg, 10 mg, 15 mg doses worn over 16 hours 7 mg, 14 mg, 21 mg doses worn over 24 hours High dosage- 42 mg dose worn over 24 hours
Nasal Spray	0.5 mg per nostril per spray
Lozenges/Sublingual tablets	1 mg, 2 mg, 4 mg
Inhaler	10 mg cartridge

**Table 3** Nicotine dosage per NTR.

### Nicotine pouches

In 2016, nicotine pouches became available for sale in the United States as the newest form of a nicotine containing product and have seen substantial increase in popularity. Nicotine pouches are prefilled microfiber pouches containing nicotine powder which is dissolved in the mouth and absorbed similarly to snus and chewing tobacco but does not require one to spit. One of the main selling points for these products is that they are less harmful than using tobacco containing products. In 2016 the total units sold was 163,178 and in the first 6 months of 2020, the total amount of units sold was 45,965,455 [30]. The top three brands currently in the United States market include Zyn, On!, and Velo with each brand having a variety of strengths. As per each companies websites, Zyn, which currently is the most popular brand, have 1.5 mg, 3 mg, 6 mg, and 9 mg strength pouches, On! with 2 mg, 4 mg, and 8 mg strength pouches, and Velo with 2 mg, 4 mg, and 7 mg strength pouches. As with all other nicotine containing products, the rate of absorption is the most important aspect to consider in the perioperative setting.

The study by Azzopardi, et al., also examined the amount of absorption of 4 mg Velo nicotine pouch within in his study. During the study, each subject that received the nicotine pouch left it in for 60 minutes. They found the mean rate of absorption in these subjects was 8.5 ng/mL. This was both higher than the nicotine Lozenges and gum [26].

Product	Maximum Nicotine Concentration (ng/mL)
Cigarette	13.9
Lyft nicotine pouch 10 mg	17.1
Zyn nicotine pouch 10 mg	11.9
Nordic Spirit nicotine pouch 9 mg	18.4
On! nicotine pouch 6 mg	17.5
Skruf nicotine pouch 8 mg	13.0

**Table 4** Nicotine concentration (ng/mL) per nicotine pouch brand.

Another study compared 5 nicotine pouch products against cigarettes and looked at the nicotine absorption. The 5 nicotine pouches were Lyft 10 mg, Zyn 10 mg, Nordic Spirit 9 mg, On! 6 mg, and Skruf 8 mg. Like in the previous study, they had each subject hold the nicotine pouch in their mouth for 60 minutes. The cigarette group were allowed to only smoke 1 cigarette. They then analyzed each subject's blood for nicotine concentration. The maximum concentration of nicotine found for each product is listed in table 4. Interestingly, 3 of the 5 nicotine pouches were found to have higher concentrations of nicotine (Lyft 10 mg, Nordic Spirit 9 mg, and On! 6 mg) [31]. In the study, they had the subject use the nicotine pouches for 60 minutes which is double the length of time that the manufacturers recommend so it is likely that the maximum concentrations would be lower in normal daily users. As with other pure nicotine products, there is still a lack of research to determine their effects on surgical outcomes.

### Discussion

Smoking and tobacco use in the perioperative setting has been extensively researched. It is well known the health effects that smoking has on a person and also the complications seen with surgical outcomes. It is well established that smoking can cause complications such as wound healing, non-union and contribute to systemic diseases such as pulmonary and cardiovascular diseases. There is a significant lack of evidence seen in human models when looking at non-combustible tobacco products. There has been a multitude of studies looking into animal models but this has not been well translated into the effects seen



in humans in the perioperative setting. There also appears to be a switch from tobacco products to just pure nicotine product use as the public becomes more informed on the major health effects seen with tobacco use and the emergence of newer nicotine products. Though there is more research being done on the exact effects that nicotine has on surgical outcomes, this still is a lack seen on human models with most of the research being performed on animal models.

When looking at animal model studies, it appears that tobacco as a whole may have a negative effect on bone healing when compared to just nicotine. One study looked at fracture strength and torque between rats given tobacco extract and nicotine. They found that the rats given the tobacco extract had decreases in both fracture site strength and torque after 21 days of healing, but they did not observe this in the group that was given just nicotine, even when nicotine levels reached those seen in a daily smoker [32]. Hastrup, et al., found that rats given just nicotine were found to have higher strength and torque when compared to the control group [33]. Daffner, et al., studied the effects of just nicotine with spinal fusions in rabbit models. They found that doses at a lower end of a daily smoker had a 30% increase in fusion rates compared to their control group. Doses that were higher had similar fusion rates compared to the control group [28]. Although these studies looked at animal models, it is something to consider whether it's the other chemicals found in tobacco causing the bone healing complications versus nicotine itself. Another consideration is that these were all performed in animal models and research is still needed to examine the effects that pure nicotine products have on surgical outcomes.

## Conclusion

There is overwhelming evidence that shows tobacco products and their delirious effects it has on patients overall health and surgical outcomes. There is still a severe lack of evidence based medicine that looks at the overall health effects nicotine products have and its effects on surgical outcomes. The current animal model research has conflicting evidence on whether nicotine actually increases complications with surgery. Another consideration one must consider is the differences seen in the absorption of nicotine between each product. Some of the research shows that lower levels of nicotine may actually enhance bone and wound healing but at higher levels it

increases complications. Overall, there is still a need for further research into human models on the exact effects nicotine has on surgical outcomes, specifically looking at the effects different doses of nicotine has on bone and wound healing.

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**Conflict of Interest:** None

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