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The role of smoking in the progressive decline of the body's major systems

A report commissioned by Public Health England

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1. Introduction

The author was commissioned to review the evidence on the role of smoking in the progressive decline of the body's major systems including the respiratory, cardiovascular and musculoskeletal systems, cognitive function, oral health and vision. A brief review established that the evidence on harm to respiratory and cardiovascular health was so well established that there was little value in reciting this and so this report focuses on the latter four systems.

The author was asked, specifically, to determine whether it was justified to describe the effect of smoking as "to rot the body from the inside". This description is considered justified because of the impact on conditions such as peripheral arterial disease and dental caries. In addition, the review describes how smoking causes deterioration and degeneration of a number of body functions due to neglect, in a process akin to rotting, driven by the addictive nature of the habit.

Smoking does progressive harm to the musculoskeletal system. It has a negative impact on bone mineral density, with evidence of damage apparent from the late teens but is particularly pronounced among post-menopausal women. Smoking is associated with more bone fractures and slower healing, and is associated with up to a 40% increase in the risk of hip fractures among men. Smokers and ex-smokers experience 60% more pain in the back, neck and legs and a 114% increase in increase in disabling lower back pain. Smoking is a significant cause of rheumatoid arthritis, especially among men and can also reduce the impact of treatment. Much of the harm and risk caused by smoking arises from smoking in middle years and can be prevented by cessation as a young adult or partially reversed by quitting in later years.

Smoking also does progressive harm to the cognitive system, contributing to a decline in cognitive function as early as middle-age. Current smokers are over 50% more likely to develop cognitive impairment than non-smokers, and the effects are largest among those who smoke more and older age groups. Smoking is one of the main environmental risk factors for dementia, primarily through increasing vascular risk and the risk of dementia increases with increasing cigarette consumption. Heavy smokers are at the greatest risk. Much of the increased risk of dementia and cognitive decline can be reversed by quitting smoking.

Smoking is detrimental to oral health, causing a progressive degeneration of tooth enamel and gum tissue as early as the adolescent years. Current smokers have more than a three times greater risk of developing oral cancers and are three to four times more likely to have periodontal disease than non-smokers. The risk of periodontal disease is higher in heavier smokers, with nearly a six times greater risk than non-smokers and the risk is greater in male than female smokers. Current smokers are four and a half times more likely to experience tooth decay than never smokers, with a greater effect in heavier smokers and adolescent smokers are significantly more likely to experience tooth decay than never smokers. Quitting smoking reduces the risk of oral cancer, periodontal disease and tooth decay.

Smoking is detrimental to visual health, with current smokers having a 78%-358% increased risk of age-related macular degeneration (AMD) and are more likely to develop the disease up to ten years earlier than never smokers. Increasing cigarette consumption (both cigarettes per day and years of smoking) increases both the incidence and progression of AMD in current smokers, with heavy smokers at particular risk. In addition, ever smokers are at a 41%-57% increased risk of age-related cataracts. Quitting smoking decreases the risk of AMD and cataract, although early quitting is more beneficial.

2. Smoking and the musculoskeletal system

2.1 Summary

Smoking does progressive harm to the musculoskeletal system. The damage has been observed to start as early as the late teens and increases with age but both the risk and harm can be partially reversed by quitting.

- smoking has a negative impact on bone mineral density, reducing calcium absorption and lowering levels of vitamin D, changing hormone levels and reducing body mass
- smokers and ex-smokers experience 60% more pain in the back, neck and legs and 114% increase in disabling lower back pain
- smoking appears to be associated with poorer development of the hip, spine and neck and lower bone mineral density among men as young as 18-20
- smoking has a particularly greater impact on reduced bone mineral density among post-menopausal women
- smoking is associated with more bone fractures and slower healing and is associated with up to a 40% increase in the risk of hip fractures among men
- smoking is a significant cause of rheumatoid arthritis, especially among men. Smoking can also reduce the impact of treatment
- much of the harm and risk caused by smoking arises from smoking in middle years and can be prevented by cessation as a young adult or partially reversed by quitting in later years

2.2 Osteoporosis

Osteoporosis is the main disease associated with poor bone health. It is largely associated with older age although can affect people of any age, with almost three million people in the UK suffering with the disease.[1] Osteoporosis results from a loss of bone mineral density (BMD) and degeneration of bone tissue, leading to a weakening of the bone.[2] While the majority (60-80%) of BMD variation is explained by pre-determined factors such as genetics,[3] the remaining 20-40% is attributable to non-modifiable risk factors such as age but also to modifiable risk factors, of which smoking is a long established contributing risk factor.[4]

There are a number of mechanisms by which smoking affects BMD, including decreased calcium absorption, lower levels of vitamin D, changes in hormone levels, reduced body mass, increased free radicals and oxidative stress, higher likelihood of peripheral vascular disease and direct effects of toxic components of tobacco smoke on bone cells.[5-11]

There is little evidence to suggest that smoking at a young age has a physiologic influence on the development of osteoporosis in later life. Indeed, the 2004 Surgeon General's report concludes that the evidence is inadequate to infer a causal relationship between smoking and decreased bone density in pre-menopausal women and younger men.[12] Since smoking patterns established in early life are likely to persist in later life, and the evidence discussed below will highlight the negative effect of smoking on bone health in older individuals, the overall influence of youth smoking should not be ignored. Some evidence has begun to emerge, however, that the development in bone density may be reduced in smokers. One five year longitudinal study investigating the development of BMD in 833 young men aged 18-20 found that those who had started smoking had considerably smaller increases in total body and lumbar spine BMD, and substantially greater decreases at the total hip and femoral neck than men who were non-smokers at both baseline and follow up visits.[13] Another study of 1,068 men aged 18-20 years found a significant mean difference in BMD of 3.3% in the spine and 5% in the trochanter after adjusting for age, height, weight, calcium intake and physical activity. This difference was evident despite the mean duration of smoking being just 4.1 years.[14]

In contrast to findings for younger age groups, smoking has a proven adverse effect on BMD in middle and later years of life. The 2004 Surgeon General's report concluded that there is sufficient evidence to infer a causal relationship between smoking and low bone density in post-menopausal women[12]. The evidence is not as strong for men, with same report concluding that the evidence is suggestive but not sufficient to infer that there is a relationship between smoking and low bone density in older men[12]. A meta-analysis of 29 cross sectional studies published in 1997 reported that bone density was lower in post-menopausal female smokers than non-smokers[15]. The difference increased linearly with age: for every ten year increase in age the BMD in smokers fell below that of non-smokers by approximately two percent of the average bone density at the time of menopause.[15]

A further systematic review published in 2001 reported similar reductions in both men and women, with a significantly lower bone mass in smokers than non-smokers and a particularly pronounced effect at the hip. Effects were greatest in men and smoking had a significant adverse effect in individuals aged over 60 years and in those with a higher smoking exposure (pack years, number of years as a smoker or cigarettes per day).[16] The same review pooled the results of thirteen prospective studies and demonstrated that current and ever smokers had greater rates of bone loss than nonsmokers, independent of factors such as age, gender and body mass[16]. A recent cross sectional study of BMD at the lumbar spine and femoral neck in 41 pairs of female twins discordant for smoking habits showed an average deficit in BMD of 5-10% at the time of menopause in women who had smoked one pack of cigarettes per day throughout adulthood.[17] It has also been suggested that bone loss shows a positive relationship with the daily number of cigarettes smoked and years of exposure, independent from age, sex, weight, BMI and other 'unhealthy' lifestyle factors.[18]

Quitting smoking may have positive effects on BMD. Levels of BMD in ex-smokers fall between those of current and ex-smokers, suggesting that smoking cessation may slow or partially

reverse the deleterious effects of smoking.[16 19 20] In a study investigating the effect of smoking cessation on BMD in postmenopausal women, there was some suggestion of increases in BMD following cessation, although this was limited to a small number of sites.[21]

2.3 Fractures/bone repair

One of the main complications of osteoporosis and degeneration of bone tissue is an increased risk of fracture, with over 230,000 resulting fractures per year in the UK.[2] A systematic review comprising nearly 60,000 individuals concluded that current smokers were at a significantly increased risk of any fracture than non-smokers, and that this risk was significantly higher in men than women.[22] Further, ex-smokers were at a significantly increased risk of fracture than never smokers, although this risk was less than for current smokers. Cigarette smoking leads to increased fracture rates of the hip, spine, distal radius and other osteoporosis-related fractures,[23] with reports that this increased risk across all bone sites is approximately 5% in women and 11% in men, with the greatest increases evident at the hip (31% for women, 40% for men) and at the lumbar spine (13% for women and 32% for men).[16] The estimated proportion of hip and lumbar spine fractures attributable to smoking are 6.4% and 2.8% in women and 9.9% and 8.1% in men respectively.[16] One systematic review reported that when comparing women who are current smokers with non-smokers, smokers were at a 17% greater risk of hip fracture at age 60, 41% at 70, 71% at 80 and 108% at 90.[15] The data for men were limited but appear to suggest a similar pattern. It has been concluded that there is sufficient evidence to infer a causal relationship between smoking and hip fractures, although the evidence is inadequate to infer a causal relationship between smoking and fractures at sites other than the hip.[12]

The burden of hip fractures should not be underestimated. Mortality rates of up to 20-24% in the year after a hip fracture have been reported,[24 25] with an increased risk of death persisting for up to five years afterwards.[26] It has been reported that a 50 year old woman has an equal chance of dying from a hip fracture as breast cancer.[27] In addition to the increased risk of fracture, healing time is suggested to be prolonged in smokers.[23 28-31] Smoking is also associated with non-union of fractures, infection and poor wound healing in addition to overall worse health outcomes from both fracture and fracture healing.[23]

The association between smoking cessation the risk of fracture is less widely documented. The largest body of evidence exists for the risk on hip fractures, with a suggestion that successful smoking cessation for at least five years may reduce the risk in men,[32] and a minimum of ten years cessation required to see a benefit in women.[21 33] Current smokers have been reported to be at a 25% increased risk of any fracture, with no difference between males and females.[10]

2.4 Rheumatoid arthritis

Rheumatoid arthritis is a chronic inflammatory disease causing pain, joint stiffness and swelling. The cause is not fully understood but the condition affects an estimated 690,000 people in the UK, most commonly starts between the ages of 40 and 50 and is around three times more common in women than men.[34] It is estimated that smoking contributes to up to 25% of the population burden of rheumatoid arthritis.[35] One systematic review published in 2010 found the overall risk for developing rheumatoid arthritis was 1.35 (95% CI 1.17-1.55) for current smokers and 1.25 (95% CI 1.10-1.40) for past smokers compared to non-smokers.[36] Despite the overwhelming majority (94%) of patients included in the analysis being female, the risk appeared to be highest in males with an overall risk for current smokers of 1.89 (95% CI 1.56-2.28). A dose response relationship has been reported in women.[35 36] A further meta-analysis published in 2012 supported the findings that smoking presents a stronger risk in males and is associated with longer duration of smoking.[37]

After considering the evidence available, the Surgeon General 2014 report concluded that there is sufficient evidence to infer a causal relationship between cigarette smoking and rheumatoid arthritis.[38] Treatment for rheumatoid arthritis often incorporates TNF- α inhibitory drugs, and the evidence is sufficient to infer that cigarette smoking reduces the effectiveness of TNF-alpha inhibitors.[38]

Smoking cessation has been shown to decrease the risk of developing rheumatoid arthritis,[35 37 39] although one study reported that the risk remained elevated in smokers until 20 years or more after cessation.[35] There is insufficient evidence, however, to draw any conclusions as to the potential benefit of smoking cessation on rheumatoid arthritis.[38]

2.5 Soft tissue

A recent review concluded that cigarette smoking is associated with an increased risk of back pain and degenerative disc disease.[23] A meta-analysis of 40 studies showed that current smoking was associated with a 33% increased prevalence of low back pain within the previous 12 months, 79% increased prevalence of chronic back pain and 114% increased prevalence of disabling lower back pain.[40] Results were higher for former smokers than never smokers, suggesting that smoking cessation has a positive effect on incidence. The review reported that the increased risk of low back pain in smokers was stronger in adolescents than adults (82% compared to 16%).[40]

A study of nearly 13,000 subjects found that current and ex-smokers experienced up to 60% more musculoskeletal pain (low back, neck upper and lower limbs) than never smokers, and this prevalence was higher in current smokers than ex-smokers[41] (Palmer 2003). One study has found that disc degeneration was 18% greater in heavy smokers than non-smokers, although there was no clinical difference.[42] There is also some suggestion that cigarette smokers may have lower strength than non-smokers. Evidence from one study suggests that

quadriceps strength was reduced by 2.9% in men and 5% in women who smoked 100g tobacco per week.[43]

Tendons are also affected by cigarette smoking: an association has been demonstrated between tendinopathy and persistent shoulder pain[44] and as a risk factor for the development of rotator cuff disease and tears.[44-46] One study reported that among 584 patients presenting for a diagnostic ultrasound for shoulder pain, those with rotator cuff tears were significantly more likely to smoke daily, to have smoked regularly within ten years before attending the clinic, have a higher mean pack per day smoking history, have a longer duration of smoking and larger tobacco exposure than those without rotator cuff tears.[45] Smokers were 74% more likely than non-smokers to have a rotator cuff tear, and this was 424% more likely in those who had smoked within the past ten years and 335% more likely in heavy current smokers. In addition, increasing daily average number of cigarettes and total number of cigarettes smoked has been shown to be associated with the severity of tears.[47]

3. Smoking and cognitive function

3.1 Summary

Smoking does progressive harm to the cognitive system, contributing to a decline in cognitive function as early as middle-age. The impact increases with age and amount smoked, although quitting can reduce the risk and harm caused.

- smoking is one of the main environmental risk factors for dementia, primarily through increasing vascular risk
- the risk of dementia increases with increasing consumption, with the greatest risk in heavy smokers
- current smokers are over 50% more likely to develop cognitive impairment than non-smokers.
- faster declines in verbal memory and lower visual search speeds have been reported in smokers aged between 43 and 53
- the effects of smoking on cognitive decline are largest among those who smoke more
- much of the increased risk of dementia and cognitive decline can be reversed by quitting smoking

3.2 Dementia

Dementia is a syndrome resulting from a progressive deterioration in higher cognitive function (including memory, language, concentration and reasoning) that impairs daily activities.[48] Dementia develops as a result of degeneration and death of brain cells and is caused by a number of diseases. Alzheimer's disease is the most common cause of dementia; brain cells are surrounded by an abnormal protein and their internal structure is damaged. Ultimately, chemical connections between brain cells are lost and some cells die[49] (Alzheimer's Society 2014). Vascular dementia is the second most common type of dementia and results from a reduced oxygen supply to the brain, resulting in damage to or death of brain cells.[49] Dementia has a number of genetic and environmental risk factors, the main ones being those that influence vascular risk including smoking, obesity, high blood pressure and diabetes.[50 51] Two recent reviews calculated that an estimated 13-14% of Alzheimer's disease cases worldwide were potentially attributable to smoking.[50 52]

Two systematic reviews have been published investigating the link between smoking and dementia.[53 54] A meta-analysis of eight studies published in 2008 reported that current smokers were 59% more likely than never smokers to suffer Alzheimer's disease and 35% more likely to suffer vascular dementia.[54] These findings were consistent with a meta-analysis of 19 studies published in 2007 that reported increased risks of 79% and 78% respectively.[53] Three studies

reported exposure-related effects, with the risk of dementia increasing with increasing cigarette consumption, with a marked effect in heavy smokers.[55-57]

There are currently no treatments available to cure or alter the progression of dementia, thus changing modifiable risk factors is of key importance. A recent modelling estimate has suggested that every 5% reduction in smoking prevalence would result in a 2% reduction in the risk of dementia.[58] A further review estimated that if smoking were eliminated, 13.9% of Alzheimer's disease could be prevented.[50]

Two meta-analyses reported no association between former smoking and the risk of dementia, suggesting that smoking cessation could play a role in reducing the incidence of dementia.[53 54]

3.3 Cognitive impairment

Cognitive impairment (as opposed to degeneration and death of brain cells) is a natural part of ageing[59] but may develop into dementia and this decline is suggested to be accelerated in current smokers.[60] A recent study reported that current smokers were 53% more likely to develop cognitive impairment than non-smokers.[61] When looking at differential effects by gender, it has been reported that a significant effect was only present in women; female smokers were 62% more likely to develop cognitive impairment than never-smokers, and those with high pack years were more than twice as likely to develop cognitive impairment than never-smokers.[61] Other studies have reported a stronger effect in men, with reports that middle aged male smokers experienced faster declines in global cognition and executive function than never smokers.[60] Further, smoking was consistently associated with lower performance on cognitive outcomes in adults aged 50 and over.[62]

There is evidence to suggest a significant dose-response relationship between amount smoked and rate of decline in cognitive function in smokers with a higher cigarette pack-year exposure.[61 63] One study also reported higher rates of decline in male and female smokers aged over 65.[60] Faster declines in verbal memory and lower visual search speeds have been reported in male and female smokers aged between 43 and 53, with the effect largest in those who smoked more than 20 cigarettes per day, independent of other potentially confounding factors.[64] It has been demonstrated that ex-smokers who have not smoked for at least ten years were at no increased risk of cognitive decline as a result of their past smoking.[60]

4. Smoking and oral health

4.1 Summary

Smoking is detrimental to oral health, causing a progressive degeneration of tooth enamel and gum tissue as early as the adolescent years. The risk and harm can, however, be reduced by quitting.

- current smokers have more than a three times greater risk of developing oral cancers than non-smokers
- current smokers are three to four times more likely to have periodontal disease than non-smokers
- the risk is higher in heavier smokers, with nearly a six times greater risk than non-smokers
- male smokers are at a greater risk of periodontal disease than female smokers
- current smokers are four and a half times more likely to experience tooth decay than never smokers, with a greater effect in heavier smokers
- adolescent smokers are significantly more likely to experience tooth decay than never smokers
- quitting smoking reduces the risk of oral cancer, periodontal disease and tooth decay

4.2 Oral cancers

Cancer is a disease caused by changes in normal cells so that they grow in an uncontrolled way; oral cancer includes cancers of a number of sites including the lip, tongue, mouth, oral cavity and pharynx.[65] The 2004 Surgeon General's report on the health consequences of smoking concluded that smoking is the major cause of oral cancer.[12] Smoked and smokeless tobacco use are linked to a wide range of cancerous, precancerous and non-malignant conditions affecting the soft and hard tissues of the oral cavity.[66] It is estimated that current smokers have more than three times greater risk of developing oral cancers[67] and an estimated 65% of oral and pharangeal cancers in the UK are linked to smoking.[68] Oral cancer is two to three times more common in men than women, however, trends over the last 15 years showed an increase in oral cancer mortality rates in women in industrialised countries.[69-71]

Cases of oral cancer in the UK have increased by 32% from 2000-2002 to 2009-2011.[65] Incidence increases with age in both genders and across countries with smokers aged 50 and above having a higher risk of developing oral cancers. Socioeconomic inequalities were found to influence the mortality rates in oral cancer with nearly doubled mortality rates in blacks compared to whites.[69 70] Alcohol consumption is a risk factor for oral cancer in smokers[70-72] and is almost tripled in alcohol drinkers who smoke.[65]

Smoking cessation has major and immediate health benefits for smokers of all ages and both genders.[73 74] A cohort study of over 12,000 smokers and former smokers with a ten year follow up found that cessation of tobacco use lead to a substantial decrease in incidence of mucosal lesions in smokers who ceased tobacco use, implying a reduced risk for oral cancer.[75] Findings from the Australian National Survey of Adult Oral Health also confirmed that smoking cessation may reduce the prevalence of oral mucosal lesions in the population following tobacco cessation interventions.[76]

4.3 Periodontitis and tooth loss

Peridontitis is an inflammatory response that causes inflammation, bleeding gums and ultimately the degeneration of gum, bone and connective tissue that support the teeth, ultimately leading to tooth loss.[77 78] In addition to the impact on oral health, it has also been shown that individuals with periodontal disease are at a 1.24-1.35 times greater risk of coronary heart disease[79] and 1.47-2.63 times greater risk of stroke,[80] independent of other risk factors. Smokers are more likely than non-smokers to develop periodontitis,[81] indeed the 2004 Surgeon General's report on the health consequences of smoking concluded that there is a causal relationship between smoking and periodontal disease.[12] Adult smokers are suggested to be approximately three to four times as likely as non-smokers to have periodontitis[82 83] and among post-menopausal women, heavy smokers were 82% more likely to report tooth loss than never smokers.[84] Smoking appears to have considerable adverse effects on the inflammatory process, thereby, promoting the progression of periodontal disease in smokers.[85]

The severity of periodontal disease increases with the number of cigarettes smoked per day and the duration of the habit[86] and is more evident after ten years of smoking.[87] One study reported that in those smoking less than nine cigarettes per day, the risk of developing periodontal disease more than doubled but was nearly six times higher in those who smoked more than 31 cigarettes per day.[83] The effect of tobacco on periodontal tissues seem to be more pronounced in men than women.[87] Smoking is a risk indicator for missing teeth in older adults in both current and previous smokers,[88] and the progression of periodontal disease and tooth loss is independently influenced by smoking and disadvantaged socioeconomic status.[89]

Tobacco cessation is associated with improvement in periodontal status and former smokers have lower rates of periodontal disease than current smokers[82 87 90] and respond significantly better to non-surgical periodontal therapy after quitting compared to those who continue to smoke.[91] While the rate of periodontal disease progression is suggested to be faster in smokers,[92] it decreases to that of a nonsmoker following tobacco cessation.[82] The elevated risk for tooth loss in smokers who quit also decreases over time. A longitudinal cohort study on tobacco use and tooth loss in 43,112 male health professionals found that risk decreased with the increase in time since cessation but remained elevated by 20% for smokers who had quit ten or more years before.[93] Similarly, another study reported that individuals who had quit smoking for between 0 and 2 years were almost three times more likely experience periodontitis than non-smokers, compared to just 15% more likely more among those who had

quit smoking for more than 11 years[83] Although the risk of experiencing tooth loss declines with time since smoking cessation, the effects of smoking may persist for at least 30 years. [94]

4.4 Dental caries

Dental caries (or tooth decay) is an infection where bacterial produced acids dissolve enamel,[95] leading to a degeneration of hard tissues of the teeth. There are a limited number of research studies investigating the relationship between smoking and dental caries. Based on 16 studies, the 2014 Surgeon General's Report concluded that the evidence is suggestive but not sufficient to infer a causal relationship between smoking and dental caries.[38] Four studies have reported a significantly higher prevalence of untreated dental caries in smokers than non-smokers but no significant difference in the overall prevalence of dental caries.[96-99] One study that investigated the relationship between smoking and tooth decay found that current smokers were around four and a half times more likely to experience tooth decay than never smokers, with former smokers over two and a half times more likely.[100] Smoking is also shown to have an effect in adolescents, with one study showing significantly higher proportions of decayed, missing and filled teeth than non-smokers,[101] with another showing that among those adolescents with at least four decayed, missing or filled tooth surface 85% more likely to be current smokers than those with no history of dental caries in their permanent teeth.[102] The data also indicate that the prevalence of dental caries in smokers increases with the increase in daily consumption of cigarettes.[101 103 104] Although the association between smoking and prevalence of dental caries can be attributed to poor dental care and oral hygiene,[105] a cross–sectional study with a four-year follow-up found that daily smoking independently predicts caries development in smokers.[106]

5. Smoking and visual health

5.1 Summary

Smoking is detrimental to visual health, contributing to visual impairment earlier and to a greater severity in smokers than non-smokers. Quitting smoking can decrease the risk, although early quitting is more beneficial.

- current smokers have a 78%-358% increased risk of age-related macular degeneration (AMD), and are more likely to develop the disease up to ten years earlier than never smokers
- increasing cigarette consumption (both cigarettes per day and years of smoking) increases both the incidence and progression of AMD in current smokers, with heavy smokers particularly at risk
- ever smokers are at a 41%-57% increased risk of age-related cataracts
- quitting smoking decreases the risk of AMD and cataract, although early quitting is more beneficial

5.2 Age-related macular degeneration

Age-related macular degeneration (AMD) is an eye condition that leads to a gradual loss of central vision.[107] Based on a review of evidence the 2014 Surgeon General's report concluded that there is a causal relationship between cigarette smoking and neovascular and atrophic forms of AMD[38]. A recent meta-analysis reported significant increases in AMD risk for current versus never smokers of between 78% and 358%, depending on the study design[108] (Chukravarthy et al 2010). In addition, smokers are more likely to develop the disease ten years earlier than non-smokers.[109] The number of cigarettes and a greater number of pack-years smoked increased the risk of both incidence and progression of AMD in current smokers.[110 111] The findings of a large French case-control study confirmed that heavy smokers (at least 25 pack-years of smoking) were particularly at risk.[112] A recent longitudinal study reported that current smoking was associated with a 36% increased risk of transitioning from minimal to moderate early AMD, and a greater number of pack-years smoked was associated with a 3% increased risk of developing early AMD and transitioning from severe early AMD to late AMD.[110]

Evidence suggests, but is not sufficient to infer, that smoking cessation decreases the risk of age-related macular degeneration.[38] The results of a number of studies showed that in former smokers the risk of AMD after quitting remained high compared to never smokers and only began to decrease after more than 20 years after quitting.[112 113] Early quitting, therefore, is more beneficial.

5.3 Cataract

Cataracts are cloudy patches that develop in the lens of the eye, causing blurred vision and sometimes stopping some light reaching the back of the eye. Cataracts become progressively worse over time and often require surgery to remove and replace the affected lens (cataract extraction).[114]

It has been concluded that there is sufficient evidence to infer a causal relationship between smoking and nuclear cataracts[12]. Findings from cohort and case-control studies showed that ever smoking was associated with a statistically significant 41%-57% increased risk of age-related cataracts; in current smokers, this increased risk is between 47% and 55%.[115] Age and gender have been found to be independent risk factors for the development of mixed lens opacity.[116]

Smoking cessation reduces risk over time, however, the larger the exposure the longer it takes for the risk to reduce and this risk is unlikely to return to that of a never smoker,[117 118] although one study just in women has demonstrated this possibility.[119]

Male and female smokers who had quit for at least 25 years had a 20% lower risk of cataract extraction than current smokers after adjusting for other risk factors, although this risk did not decrease to the level of never smokers.[118] A prospective cohort study of 20,907 men found that those who quit smoking were at a 21-27% reduced risk of cataract, with the lowest reduction in risk evident in those who had quit smoking less than ten years previously although the risk did not reduce to that of never smokers in any category.[120] Similar results have recently been reported by Lindblad and colleagues, who found that smoking cessation in men significantly decreased the risk of cataract extraction with time, although risks did not reduce to that of never smokers.[117] The effect of smoking cessation was observed earlier in lighter smokers ($\leq$15 cigarettes per day) than heavy smokers.[117]

In a prospective cohort study of 34,595 women, smoking cessation was associated with decreasing risk over time.[119] For women with a moderate intensity of smoking (6-10 cigarettes/day), the risk of cataract extraction after ten years of smoking cessation decreased to the same level as that among never smokers. Risk among women with a higher smoking intensity (>10 cigarettes/day) also decreased significantly over time but it took 20 years of cessation until the risk was no longer significantly increased in comparison with never smokers.

5.4 Other eye conditions

There are a number of other eye conditions that have a very limited evidence base addressing their relationship with smoking. Glaucoma is a condition usually caused by a build up of pressure within the eye which can damage the optic nerve.[121] The evidence is inadequate to infer a relationship between smoking and glaucoma,[12] with a small number of studies reporting no association between smoking and glaucoma.[122-125] However, there is a strong link between

smoking and high blood pressure, cataracts and diabetes all of which are risk factors for glaucoma.

Retinal vein occlusion (RVO) is a major cause of vision loss. A basic risk factor for RVO is age, although cigarette smoking increases the risk of RVO as do systemic conditions such as arteriosclerosis and vascular cerebral stroke (both of which are increased in smokers).[126] Smoking is significantly related to vision loss from retinal vasculitis (inflammation of the vascular branches of the retinal artery), and cigarette smoking predicted vision loss in a study of 56 patients followed for 25 years.[127] A cohort study of the association of smoking cessation on the retinal vessels in women found that the impact of smoking on the retinal vessel calibre is reversible after ten or more years of smoking cessation.[128]

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