



**SMOKING  
CESSATION**  
FOR CANCER PATIENTS

MARCH 2017

# Key Evidence from Peer-reviewed and Grey Literature on Smoking Cessation for Cancer Patients

RAW DATA FILE

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# How to use this resource

- Please refer to the [Key Evidence Slides](#) for details on methods, scope and limitations
- Please refer to the [Key Evidence Data Extraction File](#) for access to complete raw data from all included literature
- This document contains findings from each included study/report by theme, as listed in the [Key Evidence Slides](#)
- Caution should be used when interpreting the findings of included studies given the variations in study design, sample size, limited volume of findings for certain themes, and lack of quality appraisal.

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## PREVALENCE

**Krueger H, Andres E.N., Koot J.M., Reilly B.D. The economic burden of cancers attributable to tobacco smoking, excess weight, alcohol use, and physical inactivity in Canada. *Curr Oncol.* 2016; 23 (4): 241-249.**

- Canada, various cancers
- In Canada in 2013, 15.2% of incident cancer cases were attributable to the risk factor of tobacco smoking. Despite the fact that the proportion of cancers attributable to smoking has declined from 17.9% in 2000, the proportion of cancers attributable to tobacco smoking continues to be higher than those attributable to excess weight, alcohol use and physical inactivity
- “In Canada in 2013, 27.7% of incident cancer cases (95% confidence interval (ci): 22.6% to 32.9%) were attributable to the risk factors (rfs) of tobacco smoking (15.2%; 95% ci: 13.7% to 16.9%), excess weight (5.1%; 95% ci: 3.8% to 6.4%), alcohol use (3.9%; 95% ci: 2.4% to 5.3%), and physical inactivity (3.5%; 95% ci: 2.7% to 4.3%). The proportion and the effect of each rf varied by sex, with 25.6% of cancers in women (95% ci:21.1% to 30.2%) and 29.8% of cancers in men (95% ci: 24.0% to 35.6%) being attributable to the 4 rfs. The effects of smoking and alcohol use are higher in men than in women, and the effects of excess weight and physical inactivity are higher in women.”
- “The proportion of the cancers attributable to the four rfs declined to 27.7% in 2013 (95% ci: 22.6% to 32.9%) from 30.1% in 2000 (95% ci: 24.8% to 35.4%;). The largest proportion of that decline is connected to tobacco smoking [to 15.2% in 2013 (95% ci: 13.7% to

16.9%) from 17.9% in 2000 (95% ci: 16.1% to 19.8%)].

Despite that decline, the proportion of cancers attributable to tobacco smoking continues to be higher than those for the other 3 rfs combined.”

- “The preventable diagnoses include 17,900 lung cancers (95% ci: 17,700 to 18,100), 10,600 colorectal cancers (95% ci: 7,500 to 13,800), 4900 breast cancers (95% ci: 3300 to 6500), and 3900 cancers of the head and neck (95% ci: 3300 to 4400)”

**Krishnamurthy A, Vijayalakshmi R, Gadigi V, Ranganathan R, Sagar TG. The relevance of “Non-smoking-associated lung cancer” in India: a single-centre experience. *Indian J Cancer.* Jan-Mar 2012;49(1):82-88.**

- India, lung cancer patients
- An examination of 258 lung cancer patients at a single cancer centre in India found that 39.5% were never smokers as compared to 60.5% who were ever smokers
- “Although adenocarcinoma was the most common histology seen among both smokers and non-smokers, it was found to occur more among non-smokers (52.7%; 58/110), and squamous cell carcinoma histology was found to occur among smokers (80.4%; 33/41) (P= 0.001).”
- “We found a significant correlation of smokers presenting at advanced age (>60 years) with squamous histology compared to adenocarcinoma histology (P=0.0028)”

Park ER, Japuntich SJ, Rigotti NA, et al. A snapshot of smokers after lung and colorectal cancer diagnosis. *Cancer*. Jun 15 2012;118(12):3153-3164.

- US, lung and colorectal cancer patients
- In a US cohort of lung and colorectal cancer patients, it was found that 90.2% of those with lung cancer and 54.8% of those with colorectal cancer reported ever smoking
- “At diagnosis, 38.7% of patients with lung cancer and 13.7% of patients with colorectal cancer were smoking; whereas, 5 months after diagnosis, 14.2% of patients with lung cancer and 9.0% of patients with colorectal cancer were smoking.”

## POST-DIAGNOSIS TOBACCO USE

### Continued tobacco use after a cancer diagnosis

Burris JL, Studts JL, DeRosa AP, Ostroff JS. Systematic Review of Tobacco Use after Lung or Head/Neck Cancer Diagnosis: Results and Recommendations for Future Research. *Cancer Epidemiol Biomarkers Prev*. Oct 2015;24(10):1450-1461.

- Systematic review, lung and head and neck cancers
- In a systematic review of lung and head and neck cancers aggregated findings showed that among tobacco users who received a diagnosis, a prevalence rate of current tobacco use was 53.8%
- “Among current tobacco users at cancer diagnosis, the mean prevalence rate of current tobacco use (mostly cigarette smoking) was 53.8% (median, 50.3%). In many cases, an operational definition of “current” tobacco use was absent, and biochemical verification of self-reported smoking status was infrequent. These and other observed methodologic limitations in the assessment and reporting of cancer patients’ tobacco use underscore the necessity of uniform tobacco use assessment in future clinical research and cancer care.”

Fujisawa D, Umezawa S, Basaki-Tange A, Fujimori M, Miyashita M. Smoking status, service use and associated factors among Japanese cancer survivors--a web-based survey. *Supportive Care In Cancer: Official Journal Of The Multinational Association Of Supportive Care In Cancer*. 2014;22(12):3125-3134.

- Japan, various cancer survivors
- A survey of Japanese cancer survivors found that 57.1% were still smoking at the time of the survey
- “Of the 168 participants who were smoking at the time of cancer diagnosis, 96 survivors (57.1 %) were still smoking at the time of the survey. Of these 96 continued smokers, 67 survivors (69.8 %) were willing to cut down (n=30; 31.2 %) or to quit smoking (n=37; 38.5 %).”
- “In univariate analyses, marital status (single, widowed or divorced), shorter time after cancer diagnosis, lack of habit of regular physical exercise, lack of participation in social activities, hazardous drinking, lower level of fear of recurrence, and lack of advice on smoking cessation by oncology staff were extracted as possible associated variables for continued smoking (p<0.2).”

Park ER, Japuntich SJ, Rigotti NA, et al. A snapshot of smokers after lung and colorectal cancer diagnosis. *Cancer*. Jun 15 2012;118(12):3153-3164.

- US, colorectal cancer patients
- A cohort of cancer patients highlighted that 5 months after diagnosis, 14.2% of lung cancer patients and 9.0% of colorectal cancer patients continued smoking
- “Overall, 90.2% of patients with lung cancer and 54.8% of patients with colorectal cancer reported ever smoking. At diagnosis, 38.7% of patients with lung cancer and 13.7% of patients with colorectal cancer were smoking; whereas, 5 months after diagnosis, 14.2% of patients with lung cancer and 9.0% of patients with colorectal cancer were smoking.”

**Cooley ME, Finn KT, Wang Q, et al. Health behaviors, readiness to change, and interest in health promotion programs among smokers with lung cancer and their family members: a pilot study. *Cancer Nurs.* Mar-Apr 2013;36(2):145-154.**

- US, lung cancer patients and family members
- A qualitative survey conducted in the US found that lung cancer patients and their family members had high rates of continued smoking (43% and 30%)
- “Lung cancer patients and their family members had high rates of continued smoking (43% vs 30%), low intake of fruits and vegetables (92% vs 95%), and high rates of physical inactivity (84% vs 84%). Patients and family members indicated readiness to change behaviors within the next 6 months ranging from 63% for physical activity, 73% for diet, and 88% to quit smoking for patients and 81% for physical activity, 58% for diet, and 91% to quit smoking for family members.”

#### Factors associated with continued tobacco use

**Tammemägi M.C., Berg C.D., Riley T.L., Cunningham C.R., Taylor K.L. Impact of lung cancer Screening results on Smoking cessation. *JNCI.* 2014; 106 (6): 1-8.**

- Japan, lung cancer patients
- Factors may include: younger age, lower education, being spouseless, lower BMI, history of heavier smoking intensity, longer smoking duration, exposure to second hand smoke at home
- “Our final multivariable logistic model of continued smoking in baseline current smokers found that increased risk of continued smoking was associated with younger age, lower education, being spouseless, lower BMI, history of heavier smoking intensity (cigarettes smoked per day), longer smoking duration, exposure to secondhand smoke at home, and no history of regular pipe or cigar smoking.”

- “In multivariable analysis, continued smoking was statistically significantly associated with screening result from the previous year ( $P < .0001$ ). Compared with having a normal screen, the odds ratio for continuing smoking between T1 and T3 for individuals with screens that had a minor abnormality that was not suspicious for lung cancer was 0.914 (95% CI = 0.859 to 0.974;  $P = .005$ ); for individuals with screens that had a major abnormality that was not suspicious for lung cancer, the odds ratio was 0.811 (95% CI = 0.722 to 0.912;  $P < .001$ ); for individuals with screens that were suspicious for lung cancer but were stable from the previous screen, the odds ratio was 0.785 (95% CI = 0.706 to 0.872;  $P < .001$ ); and for individuals with screens that were suspicious for lung cancer that were new or unstable, the odds ratio was 0.663 (95% CI = 0.607 to 0.724;  $P < .001$ ). The likelihood of continued smoking was inversely associated with severity of screening results.”

**Park ER, Japuntich SJ, Rigotti NA, et al. A snapshot of smokers after lung and colorectal cancer diagnosis. *Cancer.* Jun 15 2012;118(12):3153-3164.**

- US, Lung and colorectal cancer patients
- Factors may include: Coverage by insurance, not receiving chemotherapy, not undergoing surgery, prior cardiovascular disease, lower emotional support and higher daily ever-smoking rates
- “Factors that were associated independently with continued smoking among patients with nonmetastatic lung cancer were coverage by Medicare, other public/unspecified insurance, not receiving chemotherapy, not undergoing surgery, prior cardiovascular disease, lower body mass index, lower emotional support, and higher daily ever-smoking rates (all  $P < .05$ ). Factors that were associated independently with continued smoking among patients with nonmetastatic colorectal cancer were male sex, high school education, being uninsured, not undergoing surgery, and higher daily ever-smoking rates (all  $P < .05$ ).”



**Li WH, Chan SS, Lam TH. Helping cancer patients to quit smoking by understanding their risk perception, behavior, and attitudes related to smoking. *Psychooncology*. Aug 2014;23(8):870-877.**

- China, various cancer patients
- Factors may include: Patient perceptions that barriers to quitting outweighed the benefits of quitting
- “In general, patients who refused to quit smoking subsequent to a cancer diagnosis thought that the perceived barriers to quitting outweighed the perceived benefits of quitting. In contrast, most cancer patients who quit after their cancer diagnoses thought that the perceived benefits of quitting greatly outweighed the perceived barriers to quitting.”

#### **Tobacco cessation after a cancer diagnosis**

**Cooley ME, Wang Q, Johnson BE, et al. Factors associated with smoking abstinence among smokers and recent-quitters with lung and head and neck cancer. *Lung Cancer*. May 2012;76(2):144-149.**

- US, lung and head and neck cancer patients
- Among US lung and head and neck cancer patients, seven-day-point-prevalence-abstinence rates were 68% at 3 months and 61% at 6 months
- “Seven-day-point-prevalence-abstinence (PPA) rates were 90/132 (68%) at 3 months; 46/71 (65%) among lung and 44/61 (72%) among head and neck cancer patients, whereas 7-day-PPA rates were 74/121 (61%) at 6 months; 31/58 (53%) among lung and 43/63 (68%) among head and neck cancer patients. Continuous abstinence rates were 63/89 (71%) at 3 months; 32/45 (71%) among lung and 31/44 (70%) among head and neck cancer patients, whereas continuous abstinence rates were 46/89 (52%) at 6 months; 18/45 (40%) among lung and 28/44 (64%) among head and neck cancer patients. Lower cancer-related, psychological and nicotine withdrawal symptoms were associated with increased 7-D-PPA abstinence rates at 3 and 6 months in univariate models. In multivariable models, however, decreased

craving was significantly related with 7-day-PPA at 3 months and decreased craving and increased self-efficacy were associated with 7-D-PPA at 6 months. Decreased craving was the only factor associated with continuous abstinence at 6 months.”

**Hawari FI, Obeidat NA, Ayub HS, Dawahrah SS, Hawari SF. Smoking cessation treatment and outcomes in medium to heavy cigarette smokers being treated for cancer in Jordan. *Asian Pac J Cancer Prev*. 2013;14(11):6875-6881.**

- Jordan, various cancer patients
- Among 201 Jordanian cancer patients analyzed, the 3 month abstinence rate was 23.4%
- “A total of 201 smokers were included in the analysis. The 3-month abstinence was 23.4% and significantly associated with older age, being married, and presenting with lower ( $\leq 10$  ppm) baseline carbon monoxide (CO) levels. On a multivariable level, lower CO levels, a higher income (relative to the lowest income group), being older, and reporting severe dependence (relative to dependence reported as ‘somewhat’ or ‘not’) were significant predictors of higher odds of abstinence at three months. Reasons for failing to quit included not being able to handle withdrawal and seeing no value in quitting. Long-term abstinence rates (Ars) did not reach 7%.”

**Farley A, Aveyard P, Kerr A, Naidu B, Dowswell G. Surgical lung cancer patients’ views about smoking and support to quit after diagnosis: a qualitative study. *J Cancer Surviv*. Apr 2016;10(2):312-319.**

- UK, lung cancer surgery patients
- In a qualitative study of lung cancer surgery patients in the UK, it was found that many stopped smoking during hospitalization and that while many wanted to remain quit, relapse occurred shortly after discharge
- “Although diagnosis promoted a successful quit attempt in some, others continued smoking or relapsed after a quit attempt. Most participants wished they were a non-smoker but, in conflict



with this, also felt that smoking was enjoyable, helped with psychological coping or had some health benefits. Some also demonstrated a fatalist attitude towards the potential detrimental health effects. However, all participants felt that it was important for health professionals to address smoking and some wanted cessation support although it was often not provided. Participants wanted support to start as early as possible and to continue for the first weeks after discharge.”

- “Most current smokers at diagnosis reported that they had not smoked whilst an inpatient as they had felt too ill or had not wanted to smoke. Those who relapsed described smoking one cigarette and thereafter limiting their smoking, but this limit gradually increased until most were smoking the same amount as prior to surgery. All relapsed within 3 months of discharge. Participants who resumed smoking on discharge often reported trying to cut down the number of cigarettes they were smoking but that they were not ready to quit completely.”

**Berg CJ, Thomas AN, Mertens AC, et al. Correlates of continued smoking versus cessation among survivors of smoking-related cancers. *Psychooncology*. Apr 2013;22(4):799-806.**

- US, various cancer survivors
- Qualitative analysis of a sample of cancer survivors in the US found that motivators for tobacco cessation included the impact of being diagnosed with cancer, doctor advice to quit, and social influences, and that barriers to cessation included feelings of hopelessness, stress, and addiction
- “Qualitative findings highlighted motivators for cessation (impact of being diagnosed with cancer, doctor advice to quit, social influences) and barriers to cessation (hopelessness, stress, addiction). These findings highlight the need to address depressive symptoms among cancer survivors, particularly those continuing to smoke and the importance of exploring messages cancer survivors are given regarding the need for cessation post cancer diagnosis.”

**TOBACCO USE RELAPSE**

**Simmons VN, Litvin EB, Jacobsen PB, et al. Predictors of smoking relapse in patients with thoracic cancer or head and neck cancer. *Cancer*. Apr 1 2013;119(7):1420-1427.**

- US, thoracic and head and neck cancer surgery patients
- Among 154 US patients undergoing surgery for thoracic and head and neck cancers, relapse rates varied significantly depending on pre-surgery smoking status
  - > 12 months after surgery, 60% of patients who smoked in the week prior to surgery had resumed smoking compared to 13% who were abstinent prior to surgery
- Predictors of relapse for patients who smoked before surgery included:
  - > Lower quitting self efficacy, higher depression proneness, greater fears about cancer recurrence
- Predictors of relapse for patients who were abstinent before surgery included:
  - > Higher perceived difficulty quitting and lower cancer-related risk perceptions
- “Relapse rates varied significantly depending on presurgery smoking status. At 12 months after surgery, 60% of patients who smoked during the week prior to surgery had resumed smoking versus only 13% who were abstinent prior to surgery. Smoking rates among both groups were relatively stable across the 4 follow-ups. For patients smoking before surgery (N = 101), predictors of smoking relapse included lower quitting self-efficacy, higher depression proneness, and greater fears about cancer recurrence. For patients abstinent before surgery (N = 53), higher perceived difficulty quitting and lower cancer-related risk perceptions predicted smoking relapse.”

## RADIATION THERAPY

**Zhang F, Han H, Wang C, et al. A retrospective study: the prognostic value of anemia, smoking and drinking in esophageal squamous cell carcinoma with primary radiotherapy. World J Surg Oncol. Oct 01 2013;11:249.**

- China, esophageal squamous cell carcinoma patients
- Among 79 esophageal squamous cell carcinoma patients in China who underwent radiotherapy, no significant differences were found in the 2 year overall survival and disease free survival between non-smokers and smokers
- “Survival analysis using the Kaplan-Meier method showed that there were no significant differences in the 2-year overall survival (OS) and disease free survival (DFS) between non-smokers and smokers (P = 0.658 for OS; P = 0.939 for DFS)”

**Kawakita D, Hosono S, Ito H, et al. Impact of smoking status on clinical outcome in oral cavity cancer patients. Oral Oncol. Feb 2012;48(2):186-191.**

- Japan, oral cavity squamous cell carcinoma patients
- In a Japanese study, five year overall survival among oral cavity squamous cell carcinoma patients treated with chemoradiotherapy or radiation therapy was 60.4% for non-smokers and 53.6% for heavy smokers. It was found that treatment method did not affect survival
- “For chemoradiotherapy/radiation therapy (CRT/RT), 5 year OS was 60.4% (95% CI: 43.4-73.8) for non-smokers, 93.2% (95% CI: 75.5-98.3) for light smokers, 54.4% (95% CI: 32.8-71.7) for moderate smokers, and 53.6% (95% CI: 13.2-82.5) for heavy smokers.

For surgery, 5 year OS was 86.9% (95% CI: 71.4-94.4) for non-smokers, 79.3% (95% CI: 61.4-89.6) for light smokers, 65.3% (95% CI: 41.9-81.2) for moderate smokers, and 78.6% (95% CI: 47.3-92.5) for heavy smokers.”

- “Although a marginal interaction between smoking status and treatment method was observed (P for heterogeneity = 0.069), treatment method did affect survival, particularly in non-smokers.”

**Hoff CM, Grau C, Overgaard J. Effect of smoking on oxygen delivery and outcome in patients treated with radiotherapy for head and neck squamous cell carcinoma--a prospective study. Radiother Oncol. Apr 2012;103(1):38-44.**

- Denmark, head and neck cancer patients
- Among head and neck cancer patients undergoing radiation treatment in Denmark, the risk of death increased with each additional pack year of smoking, and poor outcomes in loco-regional control can be explained by a reduced tumor oxygen supply caused by the increased carboxy-hemoglobin in smokers
- “The study showed a significant negative impact of smoking when receiving radiation treatment for head and neck cancers. The poor outcomes can in loco-regional control be explained by a reduced tumor oxygen supply caused by the increased carboxy-hemoglobin in smokers. The risk of death was increased with each additional pack year of smoking. The data strongly advocate that smoking should be avoided in order to improve the efficacy of radiotherapy”

**Thomas RJ, Holm M, Williams M, et al. Lifestyle factors correlate with the risk of late pelvic symptoms after prostatic radiotherapy. *Clinical Oncology (Royal College Of Radiologists (Great Britain))*. 2013;25(4):246-251.**

- UK, prostate cancer patients
- Data showed lower late pelvic symptoms after radiotherapy among non-smokers in a questionnaire completed by prostate cancer patients in the UK
- “The data show lower late pelvic symptoms after radiotherapy among non-smokers and physically active individuals with a body mass index <25”
- “8.5% of men smoked during radiotherapy; 6.8% still smoked at the time of the survey. Men smoking more than five cigarettes per day had a significantly higher rectal symptoms scores than non-smokers, and there was also a significant association between smoking and urinary incontinence for all smokers; 26% of smokers had an incontinence score of 2 or more compared to 10% of non-smokers.”

## CHEMOTHERAPY

**Zheng Y, Cao X, Wen J, et al. Smoking affects treatment outcome in patients with resected esophageal squamous cell carcinoma who received chemotherapy. *PLoS One*. 2015;10(4):e0123246.**

- China, esophageal squamous cell carcinoma patients
- Among 1084 esophageal squamous cell carcinoma patients in China, a decreased overall survival was associated with increased cigarette smoking and overall smoking was found to affect treatment outcomes in patients who received chemotherapy
- “Among 1,084 patients, 702 (64.8%) reported a cigarette smoking history, and the 5-year OS for non-smokers and smokers was 45.8% and 37.3%, respectively. In the surgery and chemotherapy (SC) group, compared with non-smoker, the adjusted HRs of ex-smoker and current smoker were 1.540 (95% CI, 1.1-2.2) and 2.110 (95% CI, 1.4-3.1), respectively;

there is a correlative trend of decreased OS with increased cigarette smoking (Ptrend = 0.001). These associations were insignificant in the S group. In subgroup analysis of the SC group, the lower OS conferred by smoking was not significantly modified by age, gender, body mass index, alcohol drinking, or chemotherapy method (chemotherapy and chemoradiotherapy). Our results suggest that smoking may affect treatment outcome in patients with resected esophageal squamous cell carcinoma who received chemotherapy.”

**Samanta D, Kaufman J, Carbone DP, Datta PK. Long-term smoking mediated down-regulation of Smad3 induces resistance to carboplatin in non-small cell lung cancer. *Neoplasia*. Jul 2012;14(7):644-655.**

- US, non-small cell lung cancer
- A US study suggests that loss of Smad3 expression in cigarette smoke condensate (CSC)-treated cells induces resistance to carboplatin by upregulating the expression of Bcl2, which in part explains the higher chemoresistance rate observed in smokers
- “Long-term CSC treatment increases the half-maximal inhibitory concentration (IC50) of carboplatin and makes cells resistant to carboplatin. The increase in IC50 of long-term CSC-treated cells is due to the reduced induction in apoptosis by carboplatin. The increase in IC50 and decrease in apoptosis in long-term CSC-treated cells is correlated with the expression of Bcl2. We have determined that Bcl2 is both necessary and sufficient to make the cells resistant to carboplatin. We have also shown that Smad3 acts upstream to regulate the expression of Bcl2 specifically and, thus, sensitivity of the cells to carboplatin. This is supported by the inverse correlation between the expressions of Smad3 and Bcl2 in human lung tumors.”
- “These data suggest that loss of Smad3 expression in CSC-treated cells induces resistance to carboplatin by upregulating the expression of Bcl2. This study

explains, at least in part, the higher chemoresistance rate observed in smokers.”

**Kawakita D, Hosono S, Ito H, et al. Impact of smoking status on clinical outcome in oral cavity cancer patients. *Oral Oncol.* Feb 2012;48(2):186-191.**

- Japan, oral cavity squamous cell carcinoma patients
- Five year overall survival among oral cavity squamous cell carcinoma patients treated with chemoradiotherapy or radiation therapy in Japan was 60.4% for non-smokers and 53.6% for heavy smokers. It was found that treatment method did not affect survival
- “For chemoradiotherapy/radiation therapy (CRT/RT), 5 year OS was 60.4% (95% CI: 43.4-73.8) for non-smokers, 93.2% (95% CI: 75.5-98.3) for light smokers, 54.4% (95% CI: 32.8-71.7) for moderate smokers, and 53.6% (95% CI: 13.2-82.5) for heavy smokers. For surgery, 5 year OS was 86.9% (95% CI: 71.4-94.4) for non-smokers, 79.3% (95% CI: 61.4-89.6) for light smokers, 65.3% (95% CI: 41.9-81.2) for moderate smokers, and 78.6% (95% CI: 47.3-92.5) for heavy smokers.”
- “Although a marginal interaction between smoking status and treatment method was observed (P for heterogeneity = 0.069), treatment method did affect survival, particularly in non-smokers.”

## **SURGERY**

**Gajdos C, Hawn MT, Campagna EJ, Henderson WG, Singh JA, Houston T. Adverse effects of smoking on postoperative outcomes in cancer patients. *Ann Surg Oncol.* May 2012;19(5):1430-1438.**

- US, patients with gastrointestinal malignancies
- Among a US veteran population with gastrointestinal malignancies, prior and current smokers were significantly more likely to have surgical site infection, pulmonary complications, and return to the operating room as compared to non-smokers. Current smokers had a significant increase in postsurgical length of stay

- “Compared with never smokers, prior smokers and current smokers with GI malignancies were significantly more likely to have surgical site infection (SSI) (odds ratio [OR], 1.25; 95% confidence interval [95% CI], 1.09-1.44) (OR, 1.20; 95% CI, 1.05-1.38), combined pulmonary complications (combined pulmonary outcome [CPO]: pneumonia, failure to wean from ventilator, reintubation) (OR, 1.60; 95% CI, 1.38-1.87) (OR, 1.96; 95% CI, 1.68-2.29), and return to the operating room (OR, 1.20; 95% CI, 1.03-1.39) (OR, 1.31; 95% CI, 1.13-1.53), respectively. Both prior and current smokers had a significantly higher mortality at 30 days (OR, 1.50; 95% CI, 1.19-1.89) (OR, 1.41; 95% CI, 1.08-1.82) and 1 year (OR, 1.22; 95% CI, 1.08-1.38) (OR, 1.62; 95% CI, 1.43-1.85). Thoracic surgery patients who were current smokers were more likely to develop CPO (OR, 1.62; 95% CI, 1.25-2.11) and mortality within 1 year (OR, 1.50; 95% CI, 1.17-1.92) compared with non-smokers, but SSI rates were not affected by smoking status. Current smokers had a significant increase in postsurgical length of stay (overall 4.3% [P < .001], GI 4.7% [P = .003], thoracic 9.0% [P < .001]) compared with prior smokers.”

**Shiono S, Katahira M, Abiko M, Sato T. Smoking is a perioperative risk factor and prognostic factor for lung cancer surgery. *Gen Thorac Cardiovasc Surg.* Feb 2015;63(2):93-98.**

- Japan, lung cancer patients
- A study of lung cancer patients who underwent surgery in Japan found that postoperative respiratory and cardiac complications developed in 17.1% of past smokers and 21.2% of current smokers, as compared to 11.4% of non-smokers
- “Postoperative respiratory and cardiac complications developed in 107 of 670 patients (15.9 %). These complications developed in 11.4 % of non-smokers, 17.1 % of past smokers, and 21.2 % of current smokers (p = 0.0226). Although other complications were not significantly associated with smokers, more both the past and current tended to develop postoperative

complications than non-smokers”

**Balduyck B, Sardari Nia P, Cogen A, et al. The effect of smoking cessation on quality of life after lung cancer surgery. Eur J Cardiothorac Surg. Dec 2011;40(6):1432-1437; discussion 1437-1438.**

- Belgium, non-small cell lung cancer patients
- In a study examining quality of life after surgery among non-small cell lung cancer patients in Belgium, it was found that non-smokers had a favourable postoperative quality of life evolution, whereas former smokers reported an increase in general and thoracic pain and recent quitters reported longer physical functioning impairment, an increase in dyspnoea, and deficit in role functioning. Current smokers reported a decrease in physical, role and social functioning, increased pain, and shoulder dysfunction
- “The first month after surgery, former smokers reported a temporary increase in general pain and thoracic pain. The other quality of life domains returned to baseline at 1 month after surgery. In contrast to former smokers, recent quitters reported longer physical functioning impairment till 6 months after surgery, an increase in dyspnoea at 1 and 3 months after surgery, but only a temporary deficit in role functioning at 3 months. Current smokers reported a persistent decrease in physical, role and social functioning during the follow-up period. Current smokers reported a temporary decrease in dyspnoea of 6 months; at 6 and 12 months an increase was seen. Current smokers complained of general and thoracic pain after surgery till 6 and 12 months after surgery. Current smokers also complained of shoulder dysfunction, not seen in the other subgroups. Except non-smokers, all patients complained of fatigue the first 3 months after surgery.”

**Kawakita D, Hosono S, Ito H, et al. Impact of smoking status on clinical outcome in oral cavity**

**cancer patients. Oral Oncol. Feb 2012;48(2):186-191.**

- Japan, oral cavity squamous cell carcinoma patients
- Among patients with oral cavity squamous cell carcinoma who were treated with either chemoradiotherapy/radiation therapy or surgery in Japan, five year overall survival was 86.9% for non-smokers and 78.6% for heavy smokers who underwent surgery. The study found marginal interaction between smoking status and treatment method, but treatment method did not affect survival
- “For chemoradiotherapy/radiation therapy (CRT/RT), 5 year OS was 60.4% (95% CI: 43.4-73.8) for non-smokers, 93.2% (95% CI: 75.5-98.3) for light smokers, 54.4% (95% CI: 32.8-71.7) for moderate smokers, and 53.6% (95% CI: 13.2-82.5) for heavy smokers. For surgery, 5 year OS was 86.9% (95% CI: 71.4-94.4) for non-smokers, 79.3% (95% CI: 61.4-89.6) for light smokers, 65.3% (95% CI: 41.9-81.2) for moderate smokers, and 78.6% (95% CI:) 47.3-92.5) for heavy smokers.”
- “Although a marginal interaction between smoking status and treatment method was observed (P for heterogeneity = 0.069), treatment method did affect survival, particularly in non-smokers.”

**Schmidt-Hansen M, Page R, Hasler E. The effect of preoperative smoking cessation or preoperative pulmonary rehabilitation on outcomes after lung cancer surgery: a systematic review. Clin Lung Cancer. Mar 2013;14(2):96-102**

- Systematic review, lung cancer patients
- A systematic review examined the impact of smoking cessation on postoperative outcomes for lung cancer patients, but found that due to methodological limitations no firm conclusions could be drawn.
- “Of the 7 included studies that examined the effect of preoperative smoking cessation (n = 6) and preoperative pulmonary rehabilitation (n = 1) on outcomes after lung cancer surgery, none were randomized controlled trials and only 1 was



prospective. The studies used different smoking classifications, the baseline characteristics differed between the study groups in some of the studies, and most had small sample sizes. No formal data synthesis was therefore possible. The included studies were marked by methodological limitations. On the basis of the reported bodies of evidence, it is not possible to make any firm conclusions about the effect of preoperative smoking cessation or of preoperative pulmonary rehabilitation on operative outcomes in patients undergoing surgery for lung cancer.”

## DRUGS

**Kajizono M, Saito M, Maeda M, et al. Cetuximab-induced skin reactions are suppressed by cigarette smoking in patients with advanced colorectal cancer. *Int J Clin Oncol.* Aug 2013;18(4):684-688.**

- Japan, colorectal cancer patients
- For colorectal cancer patients in Japan, it was found that cigarette smoking during anticancer treatment with cetuximab-based regimens reduces skin reaction, which in turn lead to a reduction in the benefit of this treatment
- “In the assessment of non-hematologic adverse reactions, however, we found that the incidence of skin reactions (acne-like rash) after cetuximab treatment was lower in the smokers than in the non-smokers (P = 0.0191).”
- “Our findings suggest that cigarette smoking during anticancer treatment with cetuximab-based regimens reduces the skin reaction, which leads to a reduction in the benefit of the treatment”

**Smit EF, Wu YL, Gervais R, et al. A randomized, double-blind, phase III study comparing two doses of erlotinib for second-line treatment of current smokers with advanced non-small-cell lung cancer (CurrentS). *Lung Cancer.* Sep 2016;99:94-101.**

- Multinational, non-small cell lung cancer patients
- Since active smokers with non-small cell lung cancer are known to have increased erlotinib metabolism compared to non-smokers, a multinational RCT was designed to assess the efficacy and safety of an increased dose of erlotinib for smokers, however, no evidence of an efficacy benefit was found in this population
- “The CurrentS study (NCT01183858) assessed efficacy and safety of 300mg erlotinib (E300) as second-line therapy in current smokers with locally advanced or metastatic NSCLC versus the standard 150mg dose (E150)”
- “Despite the difference in erlotinib exposure, there was no evidence of an incremental efficacy benefit of a higher erlotinib dose versus the standard dose in this population of highly active smokers”

## OTHER

**Crivelli JJ, Xylinas E, Kluth LA, Rieken M, Rink M, Shariat SF. Effect of smoking on outcomes of urothelial carcinoma: a systematic review of the literature. *Eur Urol.* Apr 2014;65(4):742-754.**

- Systematic review, urothelial carcinoma patients
- A systematic review of the impact of smoking status on outcomes of urothelial carcinoma, it was found that there was mixed evidence for an effect of tobacco use on the response to intravesical therapy
- “There was mixed evidence for an effect of smoking on the response to intravesical therapy (four of seven studies detected associated measured through disease recurrence)”

## CANCER MORBIDITY

Kroeger N, Klatte T, Birkhauser FD, et al. **Smoking negatively impacts renal cell carcinoma overall and cancer-specific survival.** *Cancer.* Apr 1 2012;118(7):1795-1802.

- US, renal cell carcinoma patients
- Among renal cell carcinoma patients in the US it was found that smokers more commonly presented with pulmonary and cardiac comorbidities than non-smokers
- “Smokers presented more commonly with pulmonary comorbidities (P < .0001) and cardiac comorbidities (P = .014) and with a worse performance status (P = .031) than non-smokers. Smoking was associated significantly with tumor multifocality (P = .022), higher pathologic tumor classification (P = .037), an increased risk of bulky lymph node metastases (P = .031), and the presence of distant metastases (P < .0001), especially lung metastases (P < .0001).”

## CANCER RECURRENCE

Rieken M, Shariat SF, Kluth LA, et al. **Association of Cigarette Smoking and Smoking Cessation with Biochemical Recurrence of Prostate Cancer in Patients Treated with Radical Prostatectomy.** *Eur Urol.* 2015;68(6):949-956.

- Austria and US, prostate cancer patients
- Among prostate cancer patients from Austria and the US, former smoking and current smoking were associated with higher risk of biochemical recurrence compared to non-smokers. Smoking cessation of

≤ 4.9 years and 5-9.9 years was associated with higher risk of biochemical recurrence compared to non-smokers

- “In multivariable Cox regression analysis adjusted for the effects of standard clinicopathologic features, former smoking (hazard ratio (HR) 1.63, 95% confidence interval [CI] 1.30–2.04; p < 0.001) and current smoking (HR 1.80, 95% CI 1.45–2.24; p < 0.001) were associated with higher risk of biochemical recurrence (BCR) compared with non-smokers”
- “In multivariable Cox regression analysis, smoking cessation of ≤4.9 yr (HR 1.86, 95% CI 1.43–2.41; p < 0.001) and 5–9.9 yr (HR 2.01, 95% CI 1.50–2.70; p < 0.001) was associated with higher risk of BCR compared with the risk for men who never smoked.”

Rink M, Xylinas E, Babjuk M, et al. **Impact of smoking on outcomes of patients with a history of recurrent non-muscle invasive bladder cancer.** *J Urol.* Dec 2012;188(6):2120-2127.

- Multinational, non-muscle invasive bladder cancer patients
- A multinational study of the effects of cigarette smoking on patients with a history of recurrent non-muscle invasive bladder cancer found distant former smokers were at significantly decreased risk for disease recurrence compared to current smokers
- “On multivariate Cox regression analysis of ever smokers adjusted for standard clinicopathological features, distant former smokers were at significantly decreased risk for disease recurrence compared to



current smokers (HR 0,4, 95% CI 0.2-0.7, p<0.001). In contrast, recent former smokers were not significantly different from current smokers in disease recurrence.”

**Rink M, Furberg H, Zabor EC, et al. Impact of smoking and smoking cessation on oncologic outcomes in primary non-muscle-invasive bladder cancer. Eur Urol. Apr 2013;63(4):724-732.**

- Multinational, non-muscle invasive bladder cancer patients
- A multinational study of the effects of smoking status and the prognosis of patients with non-muscle invasive bladder cancer showed that among current and former smokers, cumulative smoking exposure was associate with disease recurrence and that smoking cessation of greater than 10 years reduced the risk of disease recurrence
- “Among current and former smokers, cumulative smoking exposure was associated with disease recur-rence (p < 0.001), progression (p < 0.001), and overall survival (p < 0.001) in multi-variable analyses that adjusted for the effects of standard clinicopathologic factors and smoking status; heavy long-term smokers had the worst outcomes, followed by light long-term, heavy short-term, and light short-term smokers. Smoking cessation >10 yr reduced the risk of disease recurrence (HR: 0.66; 95% confidence interval [CI], 0.52–0.84; p < 0.001) and progression (HR: 0.42; 95% CI, 0.22–0.83; p = 0.036) in multivariable analyses.”

**Neslund-Dudas C, Kandegedara A, Kryvenko ON, et al. Prostate tissue metal levels and prostate cancer recurrence in smokers. Biol Trace Elem Res. Feb 2014;157(2):107-112.**

- US, prostate cancer patients
- In a study examining the metal levels among US prostate cancer patients, findings indicated that among ever-smokers with biochemical recurrence, there were significantly lower lead levels and

significantly higher cadmium/lead ratios in tumor tissue, which suggest a potential role for metals in recurrence

- “Compared with cases without biochemical recurrence, those with recurrence had significantly lower median lead (Pb) levels in tumor tissue and a significantly higher Cadmium(Cd)/Pb ratio in tumor tissue. Tumor Pb level was even lower in the smaller group of distant recurrent cases and resulted again in significantly higher Cd/Pb ratios in both tumor and adjacent non-neoplastic tissue of recurrent versus non-recurrent cases (tumor tissue Cd/Pb, 6.36 vs. 1.19, p =0.009, tumor-adjacent normal tissue Cd/Pb, 6.36 vs. 1.02, p =0.038).”

**Andres SA, Bickett KE, Alatoum MA, Kalbfleisch TS, Brock GN, Wittliff JL. Interaction between smoking history and gene expression levels impacts survival of breast cancer patients. Breast Cancer Res Treat. Aug 2015;152(3):545-556.**

- US, breast cancer patients
- A US study that evaluated the interaction between smoking and gene expression levels on breast cancer patients, it was found that CENPN, CETN1, IRF2, LECT2, NCOA1 and COMT were important predictors for recurrence
- “Multivariable analyses revealed CENPN, CETN1, CYP1A1, IRF2, LECT2, and NCOA1 to be important predictors for both breast carcinoma recurrence and mortality among smokers. Additionally, COMT was important for recurrence, and NAT1 and RIPK1 were important for mortality. In contrast, only IRF2, CETN1, and CYP1A1 were significant for disease recurrence and mortality among non-smokers, with NAT2 additionally significant for survival.”

**Kowalkowski MA, Goltz HH, Petersen NJ, Amiel GE, Lerner SP, Latini DM. Educational opportunities in bladder cancer: increasing cystoscopic adherence and the availability of smoking-cessation programs. J Cancer Educ. Dec 2014;29(4):739-745.**

- US, non-muscle invasive bladder cancer survivors
- Among non-muscle invasive bladder cancer survivors in the US, it was found that 89% of smokers were non-adherent to disease recurrence monitoring recommendation, as compared to only 48% of non-smokers
- “More than one half of participants (55.0 %) were non-adherent to AUA guidelines for cystoscopic surveillance. A greater percentage of smokers (89 %) than non-smokers (48 %) were non-adherent (p<0.001).”

## SECOND PRIMARY CANCER

**Hoff CM, Grau C, Overgaard J. Effect of smoking on oxygen delivery and outcome in patients treated with radiotherapy for head and neck squamous cell carcinoma--a prospective study. Radiother Oncol. Apr 2012;103(1):38-44.**

- Denmark, head and neck squamous cell carcinoma patients
- Among a sample of Denmark patients, 20% of smokers had developed a secondary cancer after 10 years, compared to 16% of non-smokers
- “We have also examined the causes of death and development of secondary cancers and at 10-years 20% of the smokers had developed a secondary cancer, compared to 16% of non-smokers.”

**Gillison ML, Zhang Q, Jordan R, et al. Tobacco smoking and increased risk of death and progression for patients with p16-positive and p16-negative oropharyngeal cancer. J Clin Oncol. Jun 10 2012;30(17):2102-2111.**

- US, head and neck squamous cell carcinoma
- A US sample of patients found that the risk of developing second primary tumors was increased by 1.5% per pack year
- “Risk of second primary tumors increased by 1.5% per pack-year (HR, 1.015; 95% CI, 1.005 to 1.026)”

## MORTALITY

**Siegel AB, Conner K, Wang S, et al. Smoking and hepatocellular carcinoma mortality. Exp Ther Med. Jan 2012;3(1):124-128.**

- US, hepatocellular carcinoma patients
- While a US study identified in the literature search that examined the association between cigarette smoking and mortality in a hepatocellular carcinoma population did not find that smoking was associated with increased mortality, the majority of the other identified studies did report significant findings
- “Surgery was the dominant predictor of hepatocellular carcinoma (HCC) mortality in our sample. As in previous studies, we found that smoking was not significantly associated with increased mortality in HCC in a multivariate model. Heavy smokers had the best unadjusted 4-year survival rates, whereas non-smokers had the poorest 4-year survival rates.”

## Tobacco use and mortality

**Bostrom PJ, Alkhateeb S, Trottier G, et al. Sex differences in bladder cancer outcomes among smokers with advanced bladder cancer. BJU Int. Jan 2012;109(1):70-76.**

- Canada and Finland, bladder cancer patients
- Among bladder cancer patients from Canada and Finland, smoking was associated with a hazard ratio of 1.4 (95% confidence interval, 1.0-1.9) for bladder cancer specific mortality and 1.4 (95% CI, 1.1-1.8) for overall mortality
- “In a univariate model smoking was associated with a hazard ratio (HR) of 1.4 (95% confidence interval, 1.0-1.9) for bladder cancer specific mortality and 1.4 (95% CI, 1.1-1.8) for overall mortality.”

**Gajdos C, Hawn MT, Campagna EJ, Henderson WG, Singh JA, Houston T. Adverse effects of smoking on postoperative outcomes in cancer patients. Ann Surg Oncol. May 2012;19(5):1430-1438.**

- US, gastrointestinal cancer patients
- A US study of veteran with cancer found that both prior and current smokers had a significantly higher mortality at 30 days (Odds Ratio, 1.50; 95% CI, 1.19-1.89) (OR, 1.41; 95% CI, 1.08-1.82) and 1 year (OR, 1.22; 95% CI, 1.08-1.38) (OR, 1.62; 95% CI, 1.43-1.85) after surgery
- “Both prior and current smokers had a significantly higher mortality at 30 days (OR, 1.50; 95% CI, 1.19-1.89) (OR, 1.41; 95% CI, 1.08-1.82) and 1 year (OR, 1.22; 95% CI, 1.08-1.38) (OR, 1.62; 95% CI, 1.43-1.85). Thoracic surgery patients who were current smokers were more likely to develop combined pulmonary complication(CPO) (OR, 1.62; 95% CI, 1.25-2.11) and mortality within 1 year (OR, 1.50; 95% CI, 1.17-1.92) compared with non-smokers, but surgical site infection rates were not affected by smoking status.”

**Warren GW, Kasza KA, Reid ME, Cummings KM, Marshall JR. Smoking at diagnosis and survival in cancer patients. *Int J Cancer*. Jan 15 2013;132(2): 401-410.**

- US, various cancer patients
- In a US cohort of cancer patients, current smoking was found to increase mortality risks in lung, head/neck, prostate and leukemia in men and breast, ovary, uterus, and melanoma in women

#### Risk of death

**Lin Y, Yagyu K, Ueda J, Kurosawa M, Tamakoshi A, Kikuchi S. Active and passive smoking and risk of death from pancreatic cancer: findings from the Japan Collaborative Cohort Study. *Pancreatology*. May-Jun 2013;13(3):279-284.**

- Japan, pancreatic cancer patients
- Among Japanese pancreatic cancer patients it was found that current smokers had a significantly increased risk of death as compared to non-smokers with a relative risk of 1.7 (1.33-2.19). Former smokers had a 1.36 fold increase in risk as compared to non-smokers

- “Overall, current smokers had a significantly increased risk of death from pancreatic cancer compared to non-smokers, with a relative risk (RR) of 1.70 (1.33-2.19). This positive association was observed for both women and men. Former smokers had a 1.36-fold increase in risk compared with non-smokers. In current smokers, there was a clear dose-response relationship between the number of cigarettes smoker per day and risk of death from pancreatic cancer. The multivariable adjusted RR was 2.29(95% CI 1.30-4.05) for men who had smoked more than 40 cigarettes per day, and 2.53 (95% CI 1.25-5.12) for women who had smoked more than 20 cigarettes per day. Years of smoking and cumulative amount of smoking are associated with increased risk of death from pancreatic cancer in men.”

**Gawron A, Hou L, Ning H, Berry JD, Lloyd-Jones DM. Lifetime risk for cancer death by sex and smoking status: the lifetime risk pooling project. *Cancer Causes Control*. Oct 2012;23(10):1729-1737.**

- US, various cancers
- A cohort of US cancer patients showed that risk for cancer death remains significantly higher for smokers compared to non-smokers, and that the risk of death for male smokers at 45 years of age is 27.7% compared to 15.8% for non-smokers. Similarly, the risk of cancer death for female smokers is 21.7% compared to 13.2% for non-smokers at age 45
- “There were a total of 11,317 cancer-related deaths. At age 45 years, the lifetime risk of cancer death for male smokers is 27.7 % (95 % CI 24.0-31.4 %) compared to 15.8 % (95 % CI 12.7-18.9 %) for male non-smokers. At age 45 years, the lifetime risk of cancer death for female smokers is 21.7 % (95 % CI 18.8-24.6 %) compared to 13.2 % (95 % CI 11.0-15.4 %) for female non-smokers. Remaining lifetime risk for cancer death declined with age, and men have a greater risk for cancer death compared to women. Adjustment for competing risk of death, particularly representing cardiovascular mortality, yielded a

greater change in lifetime risk estimates for men and smokers compared to women and non-smokers.”

**Gillison M, Zhang Q, Jordan R, et al. Tobacco use treatment in the U.S. National Cancer Institute’s designated Cancer Centers. J Clin Concol. 2012;30(17):2102-2111.**

- US, head and neck squamous cell carcinoma patients
- Head and neck squamous cell carcinoma patients in the US demonstrated that risk of death doubled (hazard ratio, 2.19; 95% CI, 1.46-3.28) for those who smoked during radiotherapy
- “Risk of death doubled (HR, 2.19; 95% CI, 1.46 to 3.28) among those who smoked during radiotherapy after accounting for pack-years and other factors. Risk of oropharyngeal cancer progression and death increases directly as a function of tobacco exposure at diagnosis and during therapy and is independent of tumor p16 status and treatment.”

**Braithwaite D, Izano M, Moore DH, et al. Smoking and survival after breast cancer diagnosis: a prospective observational study and systematic review. Breast Cancer Res Treat. Nov 2012;136(2):521-533.**

- Systematic review and cohort study, breast cancer patients
- A systematic review of breast cancer studies found significantly increased risk of breast cancer death with current smoking, but little evidence was found of an association between former smoking and breast cancer mortality
- “Compared with never smokers, women who were current smokers had a twofold higher rate of dying from breast cancer [hazard ratio (HR) = 2.01, 95 % confidence interval (CI) 1.27-3.18] and an approximately fourfold higher rate of dying from competing (non-breast cancer) causes (HR = 3.84, 95 % CI 2.50-5.89). Among seven studies that met the inclusion criteria in the systematic review, three studies and our own reported significantly increased

risk of breast cancer death with current smoking. We found little evidence of an association between former smoking and breast cancer mortality (HR = 1.24, 95 % CI 0.94-1.64). Consistent with findings from our prospective observational study, the systematic review of seven additional studies indicates positive association of current smoking with breast cancer mortality, but weak association with former smoking. Women who smoke following breast cancer diagnosis and treatment are at higher risk of death both from breast cancer and other causes.”

## Other

**Jerjes W, Upile T, Radhi H, et al. The effect of tobacco and alcohol and their reduction/cessation on mortality in oral cancer patients: short communication. Head Neck Oncol. Mar 12 2012;4:6.**

- UK, oral squamous cell carcinoma patients
- A cohort of oral squamous cell carcinoma patients in the UK showed that reduction in tobacco use and tobacco cessation led to a reduction in mortality at 3 and 5 years
- “Reduction of tobacco smoking and smoking cessation led to a significant reduction in mortality at 3 (P < 0.001) and 5 (P < 0.001) years.”

**Andres SA, Bickett KE, Alatoum MA, Kalbfleisch TS, Brock GN, Wittliff JL. Interaction between smoking history and gene expression levels impacts survival of breast cancer patients. Breast Cancer Res Treat. Aug 2015;152(3):545-556.**

- US, breast cancer patients
- A study exploring the impact of smoking on gene expression breast cancer in the US found that CENPN, CETN1, CYP1A1, IRF2, LECT2, and NCOA1 were predictors for recurrence and mortality among smokers, but only IRF2, CETN1, and CYP1A1 were significant among non-smokers
- “Multivariable analyses revealed CENPN, CETN1, CYP1A1, IRF2, LECT2, and NCOA1 to be important

predictors for both breast carcinoma recurrence and mortality among smokers. Additionally, COMT was important for recurrence, and NAT1 and RIPK1 were important for mortality. In contrast, only IRF2, CETN1, and CYP1A1 were significant for disease recurrence and mortality among non-smokers, with NAT2 additionally significant for survival.”

## **SURVIVAL**

### **Mixed or non-significant findings**

**Poullis M, McShane J, Shaw M, et al. Smoking status at diagnosis and histology type as determinants of long-term outcomes of lung cancer patients. Eur J Cardiothorac Surg. May 2013;43(5):919-924.**

- UK, lung cancer patients
- A study of lung cancer patients in the UK found that smoking status at the time of surgery did not effect long-term survival in patients with squamous cell carcinoma, but it did significantly effect long-term outcomes of patients with adenocarcinoma
- “Smoking status did not affect long-term survival in patients with squamous cell carcinoma.”
- “Cox multivariate analysis revealed that patients with adenocarcinoma who were current smokers had a significantly worse long-term survival compared with ex-smokers and non-smokers (hazard ratio: 1.26, 95 confidence interval: 1.01-1.56), P = 0.04.”

**Siegel AB, Conner K, Wang S, et al. Smoking and hepatocellular carcinoma mortality. Exp Ther Med. Jan 2012;3(1):124-128.**

- US, hepatocellular carcinoma patients
- Among hepatocellular carcinoma patients at a single US center, it was found that smoking was not independently associated with survival in a multivariate model
- “As in previous studies, we found that smoking was not significantly associated with increased mortality in hepatocellular carcinoma in a multivariate model.”

**Zhang F, Han H, Wang C, et al. A retrospective study: the prognostic value of anemia, smoking and drinking in esophageal squamous cell carcinoma with primary radiotherapy. World J Surg Oncol. Oct 01 2013;11:249.**

- China, esophageal squamous cell carcinoma patients
- No significant differences were found for overall survival and disease-free survival between non-smokers and smokers among a sample of patients with esophageal squamous cell carcinoma in China
- “Survival analysis using the Kaplan-Meier method showed that there were no significant differences in the 2-year overall survival (OS) and disease-free survival (DFS) between non-smokers and smokers (P = 0.658 for OS; P = 0.939 for DFS)”

**Rink M, Xylinas E, Babjuk M, et al. Impact of smoking on outcomes of patients with a history of recurrent nonmuscle invasive bladder cancer. J Urol. Dec 2012;188(6):2120-2127.**

- Multinational, nonmuscle invasive bladder cancer patients
- While a multinational study of patients with nonmuscle invasive bladder cancer found that current smokers had worse survival than former smokers, who in turn had worse survival than never smokers, these differences were not statistically significant
- “Overall 113 (29%) patients died of any cause and 40 (10%) dies of urothelial cancer of the bladder (UCB). Current smokers had worse survival than former smokers, who in turn had worse survival than never smokers. However, these differences were not statistically significant.

### **Smokers vs. non-smokers**

**Bostrom PJ, Alkhateeb S, Trottier G, et al. Sex differences in bladder cancer outcomes among smokers with advanced bladder cancer. BJU Int. Jan 2012;109(1):70-76.**



- Canada and Finland, bladder cancer patients
- Among bladder cancer patients from Canada and Finland, it was found that 10-year disease specific survival (DSS) was significantly worse for smokers at 52% versus 66% for non-smokers, and overall survival (OS) was 37% for smokers and 62% for non-smokers
- “The 10-year disease-specific survival (DSS) was 52% vs 66% for smokers and non-smokers, respectively (P = 0.039). Smokers also had significantly worse overall survival (10-year overall survival 37% vs 62%; P = 0.015).”
- “Smoking affected significant DSS among men (P = 0.012), although no effect was observed among women.”

**Hoff CM, Grau C, Overgaard J. Effect of smoking on oxygen delivery and outcome in patients treated with radiotherapy for head and neck squamous cell carcinoma--a prospective study. *Radiother Oncol.* Apr 2012;103(1):38-44.**

- Denmark, head and neck cancer patients
- A study in Denmark with head and neck cancer patients reported that heavy smokers had significantly worse DSS and OS compared to non-smokers (DSS 56% vs 77%, and OS 39% vs 66%)
- “Actuarial 5-year univariate analysis showed that heavy smokers had a significantly reduced probability of loco-regional control (44% vs. 65%, p = 0.001), disease-specific (56% vs. 77%, p = 0.003) and overall survival (39% vs. 66%, p = 0.0004) compared to non-smoking patients.”

**Linam JM, Chand RR, Broudy VC, et al. Evaluation of the impact of HIV serostatus, tobacco smoking and CD4 counts on epidermoid anal cancer survival. *Int J STD AIDS.* Feb 2012;23(2):77-82.**

- US, epidermoid anal cancer patients
- Medical records of epidermoid anal cancer patients in the US showed that a history of smoking significantly decreased OS (75.4% OS at two years for patients

with a history of smoking vs 87.1% OS for patients with no history of smoking)

- “Table 3 Results: Overall survival at 2 years for those with history of smoking (75.4% (63.1-09.0)) and overall survival at 2 years for those with no history of smoking (87.1% (71.8-100.0))”
- “Disease-free survival was similar at two-years (77.4% versus 80.8%, respectively), but ever-smokers trended towards poorer disease-free survival over the follow-up period. A history of smoking significantly decreased overall survival (P<0.05, log-rank test)”

**Liu M, Jiang G, Ding J, et al. Smoking reduces survival in young females with lung adenocarcinoma after curative resection. *Medical Oncology* (Northwood, London, England). 2012;29(2):570-573.**

- China, lung adenocarcinoma patients
- The 5-year OS of young female lung adenocarcinoma patients in China was 20% for current smokers and 36.6% for non-smokers
- “The 5-year OS of current-smokers and non-smokers were 20 and 36.6%, respectively (P = 0.03). As for patients with stage I disease, the 5-year OS of current-smokers and non-smokers were 50 and 68.8%, respectively, (P = 0.02).”

**Qu Y, Chen Y, Yu H, et al. Survival and Prognostic Analysis of Primary Nasopharyngeal Carcinoma in North China. *Clin Lab.* 2015;61(7):699-708.**

- China, nasopharyngeal carcinoma patients
- A study of nasopharyngeal carcinoma among Chinese patients found that non-smokers had significantly higher survival rates compared to smokers
- “Higher survival rates (1, 3, 5, and 10 year) were found in nasopharyngeal carcinoma patients who were female, non-smokers, early clinical phase (p < 0.05).”

**Kroeger N, Klatte T, Birkhauser FD, et al. Smoking negatively impacts renal cell carcinoma overall and**

**cancer-specific survival. *Cancer*. Apr 1 2012;118(7):1795-1802.**

- US, renal cell carcinoma patients
- Among renal cell carcinoma patients in the US, OS (62.37 months vs 43.64 months) and cancer-specific survival (CSS) (87.43 months vs 56.57 months) were significantly worse in patients who were smokers vs non-smokers
- “Both overall survival (OS) (62.37 months vs 43.64 months; P = .001) and cancer-specific survival (CSS) (87.43 months vs 56.57 months; P = .005) were significantly worse in patients who smoked. The number of pack-years was retained as an independent predictor of CSS and OS in patients with nonmetastatic disease.”

**Ferketich AK, Niland JC, Mamet R, et al. Smoking status and survival in the national comprehensive cancer network non-small cell lung cancer cohort. *Cancer*. Feb 15 2013;119(4):847-853.**

- US, non-small cell lung cancer patients
- A study of non-small cell lung cancer patients from the US showed that never smokers had better survival than current smokers (hazard ratio 0.47 vs. 0.51)
- “Among patients with stage I, II, and III disease, only never smokers had better survival than current smokers (hazard ratio, 0.47 [95% confidence interval, 0.26-0.85] vs 0.51 [95% confidence interval, 0.38-0.68], respectively).”

**Zheng Y, Cao X, Wen J, et al. Smoking affects treatment outcome in patients with resected esophageal squamous cell carcinoma who received chemotherapy. *PLoS One*. 2015;10(4):e0123246.**

- China, esophageal squamous cell carcinoma patients
- A study examining survival of esophageal squamous cell carcinoma patients at a Chinese institution found that 5 year OS for non-smokers and smokers was 45.8% and 37.3% respectively

- “Among 1,084 patients, 702 (64.8%) reported a cigarette smoking history, and the 5-year OS for non-smokers and smokers was 45.8% and 37.3%, respectively.”

**Survival in various types of smokers**

**Kawakita D, Hosono S, Ito H, et al. Impact of smoking status on clinical outcome in oral cavity cancer patients. *Oral Oncol*. Feb 2012;48(2):186-191.**

- Japan, oral cavity squamous cell carcinoma patients
- Among oral cavity squamous cell carcinoma patients in Japan, it was found that 5-year overall survival was 72.9% for non-smokers, 85.5% for light smokers, 59.9% for moderate smokers and 69.0% for heavy smokers
- “Five-year overall survival for non-, light, moderate, and heavy smokers was 72.9% (95% confidence interval CI): (61.4-81.5), 85.5% (74.0-92.2), 59.9% (44.3-72.4) and 69.0% (42.8-85.0).”

**Shiono S, Katahira M, Abiko M, Sato T. Smoking is a perioperative risk factor and prognostic factor for lung cancer surgery. *Gen Thorac Cardiovasc Surg*. Feb 2015;63(2):93-98.**

- Japan, lung cancer patients
- A Japanese study that examined the effect of smoking on survival after lung cancer surgery found that the 5-year survival rates for non-smokers, past and current smokers was 81.4%, 65.4%, and 68.8% respectively
- “The 5-year survival rates for non-smokers, past, and current smokers were 81.4, 65.4, and 68.8 %, respectively (p = 0.0003).”

**Cao W, Liu Z, Gokavarapu S, Chen Y, Yang R, Ji T. Reformed smokers have survival benefits after head and neck cancer. *Br J Oral Maxillofac Surg*. Sep 2016;54(7):818-825.**

- China, head and neck cancer patients



- In a sample of head and neck cancer patients in China, there was a significant difference in survival in reformed and non-smokers on the one hand, and current smokers on the other
- “A total of 521 patients were treated for head and neck cancer, and there was a significant difference in survival between reformed and non-smokers on the one hand, and current smokers on the other ( $p=0.02$ ). The significance increased when reformed smokers were grouped according to their duration of abstinence and time of diagnosis of cancer ( $>15$  and  $\leq 15$  years,  $p<0.01$ ).”
- long-term smokers having the worst outcomes
- “Among current and former smokers, cumulative smoking exposure was associated with disease recurrence ( $p < 0.001$ ), progression ( $p < 0.001$ ), and overall survival ( $p < 0.001$ ) in multi-variable analyses that adjusted for the effects of standard clinicopathologic factors and smoking status; heavy long-term smokers had the worst outcomes, followed by light long-term, heavy short-term, and light short-term smokers.”

### Survival and level of tobacco use

**Gillison ML, Zhang Q, Jordan R, et al. Tobacco smoking and increased risk of death and progression for patients with p16-positive and p16-negative oropharyngeal cancer. J Clin Oncol. Jun 10 2012;30(17):2102-2111.**

- US, head and neck squamous cell carcinoma patients
- Among a study of head and neck squamous cell carcinoma patients in the US, it was found that risk of death (overall survival) increased by 1% per pack-year or 2% per year of smoking
- “After adjustment for p16 and other factors, risk of progression (PFS) or death (OS) increased by 1% per pack-year (for both, hazard ratio [HR], 1.01; 95% CI, 1.00 to 1.01;  $P = .002$ ) or 2% per year of smoking (for both, HR, 1.02; 95% CI, 1.01 to 1.03;  $P < .001$ ) in both trials.”

**Rink M, Furberg H, Zabor EC, et al. Impact of smoking and smoking cessation on oncologic outcomes in primary non-muscle-invasive bladder cancer. Eur Urol. Apr 2013;63(4):724-732.**

- Multinational, urothelial carcinoma patients
- A multinational study of urothelial carcinoma patients reported that cumulative smoking exposure among current and former smokers was associated with overall survival in multivariable analysis, with heavy

# Impact of Tobacco Use/Cessation on Quality of Life Outcomes for Patient Survivors

## QUALITY OF LIFE OUTCOMES FOR POST-OPERATIVE PATIENTS

**Kruskemper G, Handschel J. Smoking affects quality of life in patients with oral squamous cell carcinomas. Clin Oral Investig. Oct 2012;16(5): 1353-1361.**

- Germany, Austria, Switzerland, oral squamous cell carcinoma patients
- Oral squamous cell carcinoma patients in Germany, Austria and Switzerland were administered a quality of life (QoL) questionnaire before, immediately after surgery, and 6 months later. It was found that during therapy and rehabilitation quality of life scores were higher in non-smokers
- “Significant differences were found between smokers (80%) and non-smokers (20%) with respect to diagnosis, therapy and rehabilitation. Disabilities and impairments in speech, appearance, chewing/swallowing, pain and QoL were examined. Smokers were more often and more severely affected. Differences were found in the size of the tumour, scar tissue, ingestion, functionality of the facial muscles and a numb feeling in the head and shoulder area. Smoking has a severe effect on the oral cavity. Non-smokers suffer far less from the effects of squamous cell carcinoma and the ensuing therapy. During therapy and rehabilitation, the QoL is much higher in non-smokers.”

**Balduyck B, Sardari Nia P, Cogen A, et al. The effect of smoking cessation on quality of life after lung cancer surgery. Eur J Cardiothorac Surg. Dec 2011;40(6):1432-1437; discussion 1437-1438.**

- Belgium, non-small cell lung cancer patients

- Non-small cell lung cancer patients from Belgium were administered post-operative QoL questionnaires and it was found that while non-smokers had QoL scores that returned to baseline 3 months after surgery, former smokers experienced a 3 month decrease in physical function and a 12 month decrease on role functioning, recent quitters had a longer impairment in physical functioning (6 months) and a 3 month burden of dyspnoea, and current smokers experienced no return to baseline physical, role and social functioning
- “In non-smokers, all QoL scores returned to baseline 3 months after surgery. Former smokers complained of a significant 3-month decrease in physical functioning (3 months post-operatively (MPO),  $p = 0.01$ ) and a 12-month decrease in role functioning (12 MPO,  $p = 0.01$ ). Former smokers complained of a significant increase in dyspnoea (6 MPO,  $p = 0.001$ ) during the first 6 months after surgery. Recent quitters had a longer impairment in physical functioning (6 MPO,  $p = 0.01$ ) and a 3-month burden of dyspnoea (3 MPO,  $p=0.02$ ). In current smokers, no return to baseline in physical (12 MPO,  $p = 0.01$ ), role (12 MPO,  $p = 0.01$ ) and social functioning (12 MPO,  $p = 0.02$ )”

## QUALITY OF LIFE OUTCOMES FOR CANCER SURVIVORS

**Chen J, Qi Y, Wampfler JA, et al. Effect of cigarette smoking on quality of life in small cell lung cancer patients. Eur J Cancer. Jul 2012;48(11):1593-1601.**

- US, small-cell lung cancer survivors
- In small-cell lung cancer survivors from the US, former smokers reported the best QoL profile, late or never quitters reported the worst profile, and recent quitters showed an improving trend
- “Small cell lung cancer survivors consistently showed a significant deficit in QoL profile; e.g., mean overall QoL in patients was 17.5 points worse than the controls ( $p < 0.0001$ ). Among all smokers, former smokers reported the best QoL profile, while late or never quitters reported the worst. The recent quitters showed an improving trend in QoL profile and lower percent of reduced appetite (an average of 43% compared to the late or never quitters (58%).”

**Gopalakrishna A, Longo TA, Fantony JJ, Van Noord M, Inman BA. Lifestyle factors and health-related quality of life in bladder cancer survivors: a systematic review. J Cancer Surviv. Oct 2016;10(5):874-882.**

- Systematic review, bladder cancer survivors
- A systematic review in bladder cancer survivors identified two studies with mixed findings. Health-related QoL was not found to be associated with tobacco use in one study, whereas higher psychological distress, traumatic stress, fear of recurrence, social constrain, illness intrusiveness and impact of repeated treatments was found in the other study among current smokers versus non-smokers
- “Two studies, by Blanchard et al. and Kowalkowski et al., offered data regarding the association between smoking status and health-related quality of life (HRQOL). Blanchard et al. found that HRQOL was not associated with smoking status. In contrast, Kowalkowski et al. reported higher psychological distress ( $d = 0.5$ ), traumatic stress ( $d = 0.5$ ), fear of recurrence ( $d = 0.6$ ), social constraint ( $d = 0.7$ ), illness intrusiveness ( $d = 0.4$ ), and impact of repeated treatments ( $d=0.7$ ) among current smokers compared with non-smokers. However, there was no reported relationship between overall HRQOL and smoking status.”

**Shen MJ, Coups EJ, Li Y, Holland JC, Hamann HA, Ostroff JS. The role of posttraumatic growth and timing of quitting smoking as moderators of the relationship between stigma and psychological distress among lung cancer survivors who are former smokers. Psychooncology. Jun 2015;24(6): 683-690.**

- US, non-small cell lung cancer
- Among US survivors with non-small cell lung cancer, those who quit smoking prior to diagnosis, stigma had a positive association with psychological distress at high levels of posttraumatic growth. Among those who quit smoking after diagnosis, stigma had a positive association with psychological distress among those with low levels of posttraumatic growth, indicating that posttraumatic growth buffers against the effects of stigma among post-diagnosis quitters
- “Hierarchical linear regression and simple slope analyses indicated that among those who quit smoking prior to diagnosis (pre-diagnosis quitters), stigma had a positive association with psychological distress at high levels of posttraumatic growth ( $p = 0.003$ ) and had a positive (but non-significant) association with psychological distress among those with low levels of posttraumatic growth ( $p = 0.167$ ). Among those who quit smoking after diagnosis (post-diagnosis quitters), stigma had a positive association with psychological distress among those with low levels of posttraumatic growth ( $p = 0.004$ ) but had no relationship among those with high levels of posttraumatic growth ( $p = 0.880$ ).”
- “Findings indicate that posttraumatic growth buffers against the negative effects of stigma on psychological distress but only among post-diagnosis quitters.”

## STATE OF CLINICAL PRACTICE

Vaidya V, Hufstader-Gabriel M, Gangan N, Shah S, Bechtol R. Utilization of smoking-cessation pharmacotherapy among chronic obstructive pulmonary disease (COPD) and lung cancer patients. *Curr Med Res Opin.* Jun 2014;**30(6):1043-1050.**

- US, lung cancer patients
- A US study examining the prevalence of smoking and consequent cessation agent use among lung cancer patients found that few smokers used tobacco cessation agents with only 12.6% reporting use of such agents during a 5 year period
- “Around 16.8% of COPD patients and 15.1% of lung cancer patients reported smoking after diagnosis. Out of the total smokers, 8.8% patients with COPD and 12.6% patients with lung cancer reported use of smoking cessation agents during the 5 year period.”

### Positive efficacy of tobacco cessation interventions

de Bruin-Visser JC, Ackerstaff AH, Rehorst H, Retel VP, Hilgers FJ. Integration of a smoking cessation program in the treatment protocol for patients with head and neck and lung cancer. *Eur Arch Otorhinolaryngol.* Feb 2012;**269(2):659-665.**

- Netherlands, lung and head and neck cancer patients
- Lung cancer and head and neck cancer patients from the Netherlands experienced favourable long-term success by participating in a nurse-managed smoking cessation programme, with 40% of patients who had stopped smoking at 6 months and 33% at 12 months

- “At 6 months, 58 patients (40%) had stopped smoking and at 12 months, 48 patients (33%) still had refrained from smoking. There were no differences in smoking cessation results between patients with head and neck and lung cancer. The only significant factor predicting success was whether the patient had made earlier attempts to quit smoking. A nurse-managed smoking cessation programme for patients with head and neck or lung cancer shows favourable long-term success rates.”

Warren GW, Marshall JR, Cummings KM, et al. Automated tobacco assessment and cessation support for cancer patients. *Cancer.* Feb 15 2014;**120(4):562-569.**

- US, various cancer patients
- A US automated tobacco assessment and cessation program that was incorporated into an electronic health record found that of patients who were identified and referred to the cessation service, 4.5% of patients contact by mail and telephone reported no tobacco use within the past 30 days, whereas only 1.2% of patients contacted by mail reached out to the program for assistance
- “In referred patients, 1381 of those patients received only a mailed invitation to contact the cessation service, and 1384 received a mailing as well as telephone contact attempts from the cessation service. In the 1126 (81.4%) patients contacted by telephone, 51 (4.5%) reported no tobacco use within the past 30 days, 35 (3.1%) were medically unable to participate, and 30 (2.7%) declined participation.

Of the 1381 patients who received only a mailed invitation, 16 (1.2%) contacted the cessation program for assistance.”

**Price S, Hitsman B, Veluz-Wilkins A, et al. The use of varenicline to treat nicotine dependence among patients with cancer. *Psychooncology*. May 24 2016.**

- US, various cancer patients
- Among cancer patients in the US treated with 12 weeks of varenicline and five brief behavioural counselling sessions, it was found that the rate of biochemically verified abstinence at week 12 was 40.2%
- “Retention was 84.1% over 12 weeks. The rate of biochemically verified abstinence at week 12 was 40.2%. Expected side effects were reported (e.g. sleep problems, nausea), but there were no reports of elevated depressed mood, suicidal thoughts, or cardiovascular events. Abstinence was associated with improved cognitive function and reduced negative affect over time ( $p < 0.05$ ).”

**Klemp, I., Steffenssen, M., Bakholdt, V., Thygesen, T., Sorensen, J.A. Counselling is effective for Smoking Cessation in Head and Neck Cancer Patients - A Systematic Review and Meta-analysis. *Oral and Maxillofacial Surgery*. 2016; 74 (8): 687-694.**

- Systematic review, head and neck cancer patients
- A systematic review examining the efficacy of smoking cessation counselling in patients with head and neck cancer found compiled data from the studies show that patients receiving counseling had a higher quit rate compared with controls
- “Eight studies involving 1,239 patients were included (3 randomized controlled trials, 3 cohorts, and 2 case series). Smoking cessation was achieved considerably more often in patients who received smoking cessation counseling compared with those who received usual care.”
- “Meta-analysis (relative risk (RR) = 0.76; 95% CI,

0.59-0.97) showed a statistically relevant increase in quit rate in the intervention group compared with the controls.”

**No improved effect of tobacco cessation interventions**

**Ostroff JS, Burkhalter JE, Cinciripini PM, et al. Randomized trial of a presurgical scheduled reduced smoking intervention for patients newly diagnosed with cancer. *Health Psychol*. Jul 2014;33(7):737-747.**

- US, various cancer patients
- A US randomized clinical trial (RCT) including newly diagnosed cancer patients compared the efficacy of hospital based ‘best practices’ treatment (including cessation counselling and nicotine replacement therapy) and ‘best practices’ enhanced by a behavioural tapering regimen. It was found that 7-day-point prevalence abstinence rates at 6 months for both treatment arms was 32% and the behavioural tapering regimen did not improve abstinence rates
- “Overall, 7-day-point prevalence, confirmed abstinence rates at 6 months for BP (Best Practices including cessation counseling and nicotine replacement therapy) alone (32%) and BP + SRS (Best Practices and a behavioural tapering regimen called scheduled reduced smoking) (32%) were high; however, no main effect of treatment was observed. Patients who were older and diagnosed with lung cancer were more likely to quit smoking.”
- “Compared to best practices for treating tobacco dependence, a pre-surgical, scheduled reduced smoking intervention did not improve abstinence rates among newly diagnosed cancer patients”

**Hawkes AL, Chambers SK, Pakenham KI, et al. Effects of a telephone-delivered multiple health behavior change intervention (CanChange) on health and behavioral outcomes in survivors of colorectal cancer: a randomized controlled trial.**

**J Clin Oncol. Jun 20 2013;31(18):2313-2321.**

- Australia, colorectal cancer survivors
- Among Australian colorectal cancer survivors, an RCT found no significant differences between participants assigned to the telephone delivered health coaching intervention and usual care for smoking behaviours, while the intervention was effective for improving other lifestyle behaviours
- “No significant group differences were found at 6 or 12 months for health-related quality of life, cancer-related fatigue, fruit, fiber, or alcohol intake, or smoking.”

**Nayan S, Gupta MK, Strychowsky JE, Sommer DD. Smoking cessation interventions and cessation rates in the oncology population: an updated systematic review and meta-analysis. Otolaryngol Head Neck Surg. Aug 2013;149(2):200-211.**

- Systematic review, various cancer patients
- A systematic review to evaluate tobacco cessation interventions and cessation rates in an oncology population found interventions such as counselling, nicotine replacement therapy, bupropion and varenicline do not significantly affect cessation rates, however the perioperative period may represent an important teachable moment regarding tobacco cessation
- “The therapeutic interventions included counseling, nicotine replacement therapy, bupropion, and varenicline. Smoking cessation interventions had a pooled odds ratio of 1.54 (95% confidence interval [CI], 0.909-2.64) for patients in the shorter follow-up group and 1.31 (95% CI, 0.931-1.84) in the longer follow-up group. Smoking cessation interventions in the perioperative period had a pooled odds ratio of 2.31 (95% CI, 1.32-4.07).”
- “Our systematic review and meta-analysis demonstrate that tobacco cessation interventions in the oncology population, in both the short-term and long-term follow-up groups, do not significantly affect cessation

rates. The perioperative period, though, may represent an important teachable moment with regard to smoking cessation.”

**Zeng L, Yu X, Yu T, Xiao J, Huang Y. Interventions for smoking cessation in people diagnosed with lung cancer. Cochrane Database of Systematic Reviews. 2015(12).**

- Systematic review, lung cancer patients
- A systematic review to evaluate tobacco cessation programmes for lung cancer patients found that due to the lack of RCTs there was insufficient evidence to determine whether interventions are effective and whether one programme is more effective than another
- “There were no RCTs that determined the effectiveness of any type of smoking cessation programme for people with lung cancer. There was insufficient evidence to determine whether smoking cessation interventions are effective for people with lung cancer and whether one programme is more effective than any other. People with lung cancer should be encouraged to quit smoking and offered smoking cessation interventions. However, due to the lack of RCTs, the efficacy of smoking cessation interventions for people with lung cancer cannot be evaluated and concluded.”

## **PROVIDER LEVEL FACTORS**

### **Advice to quit tobacco use**

**Emmons KM, Sprunck-Harrild K, Puleo E, de Moor J. Provider advice about smoking cessation and pharmacotherapy among cancer survivors who smoke: practice guidelines are not translating. Transl Behav Med. Jun 2013;3(2):211-217.**

- US and Canada, childhood or young adult cancer survivors
- Among US and Canadian participants who were childhood or young adult cancer survivors, 55%



of those who smoke reported receiving advice to quit smoking from their regular provider and only 36% reported discussing pharmacotherapy with their provider during the study period

- “This is a longitudinal study that included 329 smokers who were childhood or young adult cancer survivors, recruited from five cancer centers in the USA and Canada. Fifty-five percent of smokers reported receiving advice to quit smoking from their regular provider during the study period, and only 36 % of smokers reported discussing pharmacotherapy with their provider. Receipt of advice was associated with being female and having a heavier smoking rate. Pharmacotherapy discussions were associated with readiness to quit, heavier smoking rate, and previous provider advice to quit”

**Simmons VN, Litvin EB, Unrod M, Brandon TH. Oncology healthcare providers’ implementation of the 5A’s model of brief intervention for smoking cessation: patients’ perceptions. Patient Educ Couns. Mar 2012;86(3):414-419.**

- US, lung and head or neck cancer patients
- A questionnaire of lung and head or neck cancer patients at a cancer center in the US found that patients reported partial implementation of the Public Health Service guidelines recommended “5A’s” model of brief intervention with only half reporting that their interest in quitting had been assessed and limited reported assistance in quitting or follow-up
- “Results indicate partial implementation of the 5A’s model. The majority of patients reported that their providers had asked about smoking and advised them to quit, however; only half reported that their interest in quitting had been assessed, and few reported assistance in quitting or follow-up. Delivery of the 5A’s was greater among patients who requested cessation advice from their health care providers.”

**Goldstein AO, Gillison ML, Zhang Q, Jordan R, et al. Tobacco smoking and increased risk of death and progression for patients with p16-positive and p16-negative oropharyngeal cancer. J Clin Oncol. Jun 10 2012;30(17):2102-2111.**

- US, various cancer patients
- In a study examining the availability of tobacco use treatment services at cancer centers in the US, it was found that only 62% of centers reported routinely providing tobacco education materials to patients
- “All 58 Cancer Centers participated. Twelve (20.7%) Centers reported no tobacco use treatment (TUT) services for their patients. Of the remainder, 34 (58.6%) reported a TUT program within their Center and 12 (20.7%) reported external tobacco use treatment (TUT) services in their health care system or affiliated university. Only 62% of Centers reported routinely providing tobacco education materials to patients, just over half reported effective identification of patient tobacco use, and less than half reported an employee dedicated to providing TUT services or a clear commitment to providing TUT services from Center leadership.”

#### Physician views of tobacco and tobacco cessation

**Warren GW, Marshall JR, Cummings KM, et al. Practice patterns and perceptions of thoracic oncology providers on tobacco use and cessation in cancer patients. J Thorac Oncol. May 2013;8(5):543-548.**

- Multinational, International Association for the Study of Lung Cancer members
- A survey of International Association for the Study of Lung Cancer members found that at the initial visit, 90% asked patients about tobacco use, 81% advised patients to stop tobacco use, but only 40% discussed medication options, 39% actively provided cessation assistance, and few addressed tobacco at follow-up. 58% reported pessimism regarding their ability to help patients quit tobacco use and 67% were



concerned about patient resistance to treatment. Only 33% felt themselves to be adequately trained to provide cessation interventions

- “More than 90% of physician respondents believe current smoking affects outcome and that cessation should be a standard part of clinical care. At the initial patient visit, 90% ask patients about tobacco use, 79% ask patients whether they will quit, 81% advise patients to stop tobacco use, but only 40% discuss medication options, 39% actively provide cessation assistance, and fewer yet address tobacco at follow-up. Dominant barriers to physician cessation effort are pessimism regarding their ability to help patients stop using tobacco (58%) and concerns about patient resistance to treatment (67%). Only 33% report themselves to be adequately trained to provide cessation interventions.”

**Warren GW, Marshall JR, Cummings KM, et al. Addressing tobacco use in patients with cancer: a survey of American Society of Clinical Oncology members. J Oncol Pract. Sep 2013;9(5):258-262.**

- US, American Society for Clinical Oncology members
- A survey of American Society for Clinical Oncology members reported similar findings to Warren et al. 2013 with only 29% indicating adequate training in tobacco cessation interventions
- “At initial visit, most respondents routinely ask patients about tobacco use (90%), ask patients to quit (80%), and advise patients to stop using tobacco (84%). However, only 44% routinely discuss medication options with patients, and only 39% provide cessation support. Tobacco assessments decrease at follow-up assessments. Most respondents (87%) agree or strongly agree that smoking affects cancer outcomes, and 86% believe cessation should be a standard part of clinical cancer care. However, only 29% report adequate training in tobacco cessation interventions. Inability to get patients to quit (72%) and patient resistance to treatment (74%) are dominant barriers to cessation intervention, but only 8% describe cessation as a waste of time.”

# SMOKING CESSATION

FOR CANCER PATIENTS

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