Smoking cessation in the oncology population

Smriti Nayan MD, Doron D. Sommer, MD, FRCSC, Michael K. Gupta, MD, FRCSC

Division of Otolaryngology-Head and Neck Surgery, Department of Surgery, McMaster University, Hamilton, Canada
Smoking and the development of malignancies by subsite\textsuperscript{1,2}

<table>
<thead>
<tr>
<th>Head and neck</th>
<th>Lung</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Oral cancer (27 x increase)</td>
<td>5-10 x increase</td>
</tr>
<tr>
<td>• Laryngeal cancer (12 x increase)</td>
<td>• 80% of all lung cancers is related to smoking in developing countries</td>
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<table>
<thead>
<tr>
<th>Gastrointestinal</th>
<th>Genitourinary</th>
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<tbody>
<tr>
<td>• Esophageal</td>
<td>• Bladder (2-3 x increase)</td>
</tr>
<tr>
<td>• Stomach</td>
<td>• Renal</td>
</tr>
<tr>
<td>• Liver</td>
<td>• Cervical</td>
</tr>
<tr>
<td>• Colon</td>
<td>• Ovarian</td>
</tr>
<tr>
<td>• Pancreas (30% of cancers)</td>
<td></td>
</tr>
</tbody>
</table>

| Breast                         | Leukemia                                 |
|                                |                                           |

\textsuperscript{1} World Health Organization. http://www.who.int/tobacco/research/cancer/en/
\textsuperscript{2} Cancer Research UK. http://www.cancerresearchuk.org/cancer-info/healthyliving/smokingandtobacco/
Tobacco smoking and cancer

Tobacco smoking

Development of cancer\(^3,4,5\)

Increases disease severity\(^3,4\)

Increases treatment failure rates\(^6,7\)

Increases treatment complication\(^8-11\)

\(^3\) Chan Y \textit{et al.} J Otolaryngol 2004;33(2):75-81;
\(^4\) Hashibe M \textit{et al.} Head Neck 2013;35(7):914-922;
\(^5\) Parsons A \textit{et al.} BMJ 2010;340:b5569;
\(^7\) Ostroff JS \textit{et al.} Cancer 1995;75(2):569-576;
\(^8\) Sørensen LT. Arch Surg 2012;147(4):373-383;
The effect of tobacco on the pharmacokinetics of anticancer drugs

Tobacco has procarcinogens and carcinogens which can further accelerate and facilitate the proinflammatory state, promoting tumour growth.

Acceleration of CYP450 enzymes such as CYP1A1 and CYP1A2 in the lung and glucoronysltransferases such as UGT1A1 in the liver.

Can result in detoxification of parent drugs or active metabolites and increased concentrations of circulating drug binding proteins.

Tobacco and cancer treatment

Smoking related changes in the clinical pharmacology of antineoplastic drugs may have meaningful clinical implications

Smoking in lung cancer patients
- Smoking history is one of the predictors of erlotinib treatment outcomes in patients with lung cancer
- Cigarette smoking induces CYP1A2 and may be responsible for the reduced systemic exposure of erlotinib observed in smokers

Smoking in head and neck cancer patients
- Patients who were smoking upon initiation of cisplatin + radiation therapy had reduced frequency of local control (hazard ratio 2.8; p 0.004) and shorter overall survival (hazard ratio 1.4; p 0.007)

Cessation challenges

- Despite adverse health effects, patients with **head and neck cancer (23-35%)** and **lung cancer (13-20%)** who smoked prior to diagnosis continue to do so after diagnosis\(^3,5,17-18\)

- Comorbid conditions such as **depression, disease-related anxiety, and alcohol abuse** often make cessation challenging

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3 Chan Y *et al*. J Otolaryngol 2004;33(2):75-81;  
5 Parsons A *et al*. BMJ 2010;340:b5569;  
Smoking cessation and the health care setting

The **health care setting** is an ideal place for health care professionals to **initiate** cessation interventions and **review lifestyle habits** with smokers who are newly diagnosed with a malignancy\(^\text{19-21}\)

**Gritz et al.** emphasise the importance of this opportunity as **“the teachable moment”**\(^\text{22}\)

The ideal health care setting\(^\text{23}\)
- Hospital based
- Community based
- Individual based

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\(^{19}\) Vander Ark W *et al.* Laryngoscope 1997;107(7):888-892;
\(^{20}\) Wewers ME *et al.* Heart Lung 1994;23(2):151-156;
\(^{22}\) Gritz ER *et al.* Cancer 2006;106(1):17-27. Review;
\(^{23}\) Gritz ER *et al.* Cancer Epidemiol Biomarkers Prev 1993;2(3):261-270
Smoking cessation interventions\textsuperscript{3,23-26}

<table>
<thead>
<tr>
<th>Pharmacological</th>
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<tbody>
<tr>
<td>• Nicotine replacement therapy (NRT)</td>
</tr>
<tr>
<td>• Buproprion (norepinephrine-dopamine reuptake inhibitor and nicotinic acetylcholine receptor antagonist)</td>
</tr>
<tr>
<td>• Varenicline (nicotine receptor partial agonist)</td>
</tr>
<tr>
<td>• Champix/Chantix</td>
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<table>
<thead>
<tr>
<th>Non-pharmacological</th>
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<tbody>
<tr>
<td>• Cognitive behavioral therapy/counseling</td>
</tr>
<tr>
<td>• The 5As (ask, assess, advise, assist, arrange)</td>
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<tr>
<td>• The “Ask-Advise-Connect”</td>
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<tr>
<td>• Information pamphlets</td>
</tr>
<tr>
<td>• Telephone help-line</td>
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</tbody>
</table>

\textsuperscript{3} Chan Y \textit{et al.} J Otolaryngol 2004;33(2):75-81;  
\textsuperscript{23} Gritz ER \textit{et al.} Cancer Epidemiol Biomarkers Prev 1993;2(3):261-270;  
\textsuperscript{24} Schwartz JL. Washington, DC: US Department of Health and Human Services Public Health Service, National Institutes of Health; 1987;  
\textsuperscript{25} Fiore MC \textit{et al.} Rockville, MD: US Department of Health and Human Services, Public Health Service; 2008;  
Stead et al.\textsuperscript{27} analysed data on more than 50,000 participants comparing any type of NRT with placebo or a non-NRT control group and reported that NRTs increase the rate of quitting by 50\% to 70\%, regardless of setting.

\textsuperscript{27} Stead LF \textit{et al.} Cochrane Database Syst Rev 2012;11:CD000146
Varenicline

- In a recent Cochrane systematic review, Cahill et al.\textsuperscript{28} reported standard dosing of varenicline to increase the chances of successful long-term smoking cessation between 2- and 3-fold when compared with pharmacologically unassisted quit attempts.

- Despite the success of this pharmacotherapy, adverse effects include suicidal ideation and suicide (FDA-issued warning in 2007) and cardiovascular effects (FDA-issued warning in 2011)\textsuperscript{29,30}

- Prescribers must therefore be judicious when evaluating patient suitability for this treatment.

\textsuperscript{28} Cahill K \textit{et al.} Cochrane Database Syst Rev 2012;4:CD006103;
\textsuperscript{29} Food and Drug Administration. 2011 www.fda.gov/Drugs/DrugSafety/ucm259161.htm
\textsuperscript{30} Food and Drug Administration. 2011 www.fda.gov/Drugs/DrugSafety/ucm276737.htm
### Summary of cessation interventions: pharmacological

<table>
<thead>
<tr>
<th>Method of therapy</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
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</table>
| Nicotine replacement therapies (patch, lozenge, gum, combination NRT) | • Easy to use  
• Few side effects  
• Once a day dosing (patch)  
• Constant level of replacement (patch)  
• Can titrate dose (lozenge) | • Cannot titrate dose (patch)  
• May have slow onset of delivery (patch)  
• Risk of nicotine toxicity (combination)  
• Local dermatitis (patch) or cannot eat 15 mins before (lozenge) |
| Bupropion SR      | • Easy to use  
• Few side effects  
• Can treat depression as well  
• Can use with NRT  
• May have better compliance as a pill | • Increased seizure risk  
• Contraindicated with certain medical conditions |
| Combination Bupropion SR + NRT | • Easy to use  
• Two different mechanisms of actions | • May be more expensive because two products  
• No dose titration |
| Varenicline       | • Easy to use  
• May have better compliance as a pill  
• No known drug interactions | • Nausea (1/3 of patients)  
• May have severe neuropsychiatric symptoms  
• Can be expensive |

Timing of cessation intervention

34 Krstev S. Arch Oncol 2006;14(Suppl_1):23-24;
35 Shi Y and Warner DO. Anesthesiology 2010;112(1):102-107;
36 Warner DO. Arch Surg 2009;144(12):1106-1107;
Methods to verify smoking cessation

- Non-invasive biochemical markers:
  - urine cotinine
  - saliva cotinine
  - breath carbon monoxide (CO)

Barriers to cessation interventions

1, 8, 34, 39

Health care provider

Patient

Methods of cessation

Follow-up

1 World Health Organization: http://www.who.int/tobacco/research/cancer/en/
8 Sørensen LT. Arch Surg 2012;147(4):373-383;
34 Krstev S. Arch Oncol 2006;14(Suppl_1):23-24;
Follow-up

- **Regular** follow-up is a critical component of cessation interventions\(^1,^2^4\)

- **Longer** follow-up more accurately reflects the success or failure of an intervention by Fiore *et al.*\(^2^5\)

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Follow-up II

- The **American Society of Clinical Oncologists (ASCO)** survey in 2013 showed:\(^{37}\):
  - Tobacco assessments decrease at follow-up assessments
  - 87% of respondents 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

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The ideal smoking cessation method

- Based on the **systematic review** published in 2013\textsuperscript{32}:

  Initiated in the **preoperative period** prior to **major oncological surgery** and continued in the **postoperative period** (with regular follow-up)

  - **Nonpharmacological interventions** e.g. counseling, therapy, and reading material
  - **Pharmacological interventions**: Varenicline or Buproprion SR + NRT

\textsuperscript{32} Nayan S et al. Otolaryngol Head Neck Surg 2013:149(2):200-211
In summary

- Smoking cessation and cancer prevention methods are essential.

- **Tobacco smoking** is a well-established **risk factor** for the development of many malignancies and increases the risk of oncology treatment failure rates and second primary tumours.

- The **perioperative period** and the **time of cancer diagnosis**, may be an important **teachable moment** for smoking cessation in oncology patients, as demonstrated through the meta-analysis.\(^{32}\)

\(^{32}\) Nayan S *et al.* Otolaryngol Head Neck Surg 2013:149(2):200-211
In summary II

- In theory, tobacco cessation strategies should be an integral part of oncology treatment plans.

- Tobacco cessation remains, however, a challenging issue in the oncology population.

- Collaboration within the health care team is paramount in implementing a smoking cessation intervention.
Future directions

Future research is needed to continue to explore and investigate novel and known methods of smoking cessation to better translate the perceived benefits of tobacco cessation in the oncology population.
Thank you!