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Smoking cessation in the oncology population

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Smoking and the development of malignancies by subsite[1,2]

Head and neck

- Oral cancer (27 x increase)
- Laryngeal cancer (12 x increase)

Lung

5-10 x increase

- 80% of all lung cancers is related to smoking in developing countries

Gastrointestinal

- Esophageal
- Stomach
- Liver
- Colon
- Pancreas (30% of cancers)

Genitourinary

- Bladder (2-3 x increase)
- Renal
- Cervical
- Ovarian

Breast

Leukemia

[1] World Health Organization. http://www.who.int/tobacco/research/cancer/en/
[2] Cancer Research UK. http://www.cancerresearchuk.org/cancer-info/healthyliving/smokingandtobacco/

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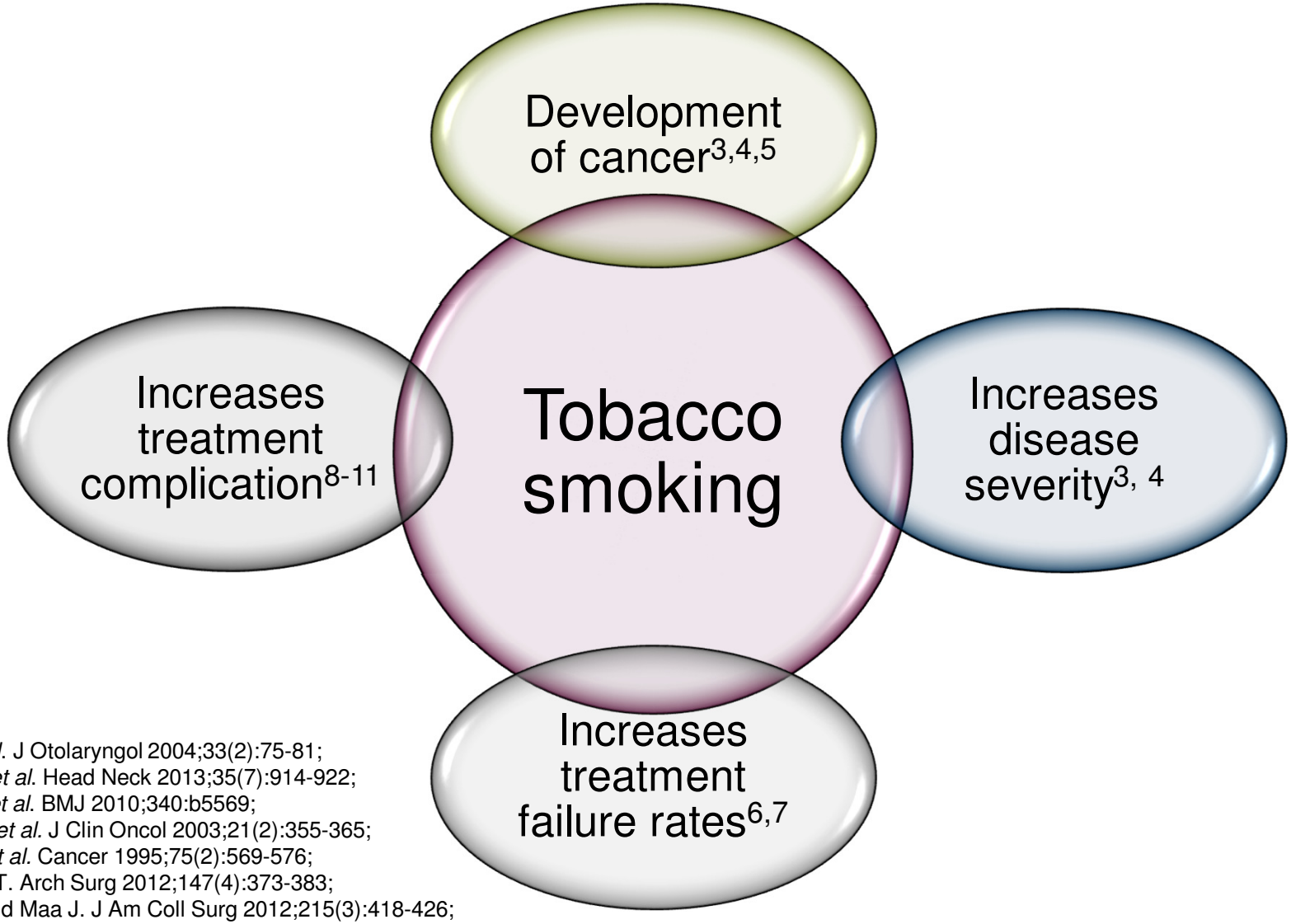
Tobacco smoking and cancer



[3] Chan Y *et al*. J Otolaryngol 2004;33(2):75-81;
[4] Hashibe M *et al*. Head Neck 2013;35(7):914-922;
[5] Parsons A *et al*. BMJ 2010;340:b5569;
[6] Schnoll RA *et al*. J Clin Oncol 2003;21(2):355-365;
[7] Ostroff JS *et al*. Cancer 1995;75(2):569-576;
[8] Sørensen LT. Arch Surg 2012;147(4):373-383;
[9] Khullar D and Maa J. J Am Coll Surg 2012;215(3):418-426;
[10] Des Rochers C *et al*. Clin Oncol (R Coll Radiol) 1992;4(4):214-216;
[11] ASA guidelines http://www.asahq.org/For-Members/Standards-Guidelines-and-Statements.aspx

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The effect of tobacco on the pharmacokinetics of anticancer drugs[12]

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 **UGTIA**l in the **liver**

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

[12] Petros WP *et al.* Pharmacotherapy 2012:32(10):920-931

Tobacco and cancer treatment

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

Smoking in **lung cancer** patients[13-16]

- 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[17]

- 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)

[13] Hamilton M *et al.* Clin Cancer Res 2006;12(7 Pt 1):2166-2171;
[14] Lu JF *et al.* Clin Pharmacol Ther 2006;80(2):136-145;
[15] Lilenbaum R *et al.* J Clin Oncol 2008;26(6):863-869;
[16] Fortin A *et al.* Int J Radiat Oncol Biol Phys 2009;74(4):1062-1069;
[17] Gritz ER *et al.* Head Neck 1999;21(5):420-427

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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

[3] Chan Y *et al*. J Otolaryngol 2004;33(2):75-81;
[5] Parsons A *et al*. BMJ 2010;340:b5569;
[17] Gritz ER *et al*. Head Neck 1999;21(5):420-427;
[18] Spitz MR *et al*. J Cancer Educ 1990;5(2):109-113

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[19-21]

- Gritz *et al*. emphasise the importance of this opportunity as **"the teachable moment"**[22]

- The ideal health care setting[23]
  - Hospital based
  - Community based
  - Individual based

[19] Vander Ark W *et al*. Laryngoscope 1997;107(7):888-892;
[20] Wewers ME *et al*. Heart Lung 1994;23(2):151-156;
[21] Wakefield M *et al*. Nurs Res 2004;53(6):396-405;
[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

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Smoking cessation interventions[3,23-26]

Pharmacological

- Nicotine replacement therapy (NRT)
- Buproprion (norepinephrine-dopamine reuptake inhibitor and nicotinic acetylcholine receptor antagonist)
- Varenicline (nicotine receptor partial agonist)
- Champix/Chantix

Non-pharmacological

- Cognitive behavioral therapy/counseling
- The 5As (ask, assess, advise, assist, arrange)
- The "Ask-Advise-Connect"
- Information pamphlets
- Telephone help-line

Combination of both

[3] Chan Y *et al.* J Otolaryngol 2004;33(2):75-81;
[23] Gritz ER *et al.* Cancer Epidemiol Biomarkers Prev 1993;2(3):261-270;
[24] Schwartz JL. Washington, DC: US Department of Health and Human Services Public Health Service, National Institutes of Health; 1987;
[25] Fiore MC *et al.* Rockville, MD: US Department of Health and Human Services, Public Health Service; 2008;
[26] Vidrine JI *et al.* JAMA Intern Med 2013:173(6):458-464

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Nicotine Replacement Therapy (NRT)

- Stead *et al.*[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

[27] Stead LF *et al.* Cochrane Database Syst Rev 2012;11:CD000146

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Varenicline

- In a recent **Cochrane systematic review**, Cahill *et al*.[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)[29,30]

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

[28] Cahill K *et al*. Cochrane Database Syst Rev 2012;4:CD006103;
[29] Food and Drug Administration. 2011 www.fda.gov/Drugs/DrugSafety/ucm259161.htm
[30] Food and Drug Administration. 2011 www.fda.gov/Drugs/DrugSafety/ucm276737.htm

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Summary of cessation interventions: pharmacological[25,31]

Method of therapy	Advantages	Disadvantages
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)
Buproprion 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 Buproprion 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

[25] Fiore MC *et al*. Rockville, MD: US Department of Health and Human Services, Public Health Service; 2008;
[31] VHA Tobacco Use Cessation Guidance. http://www.publichealth.va.gov/docs/smoking/cessationguidelinepart3_508.pdf

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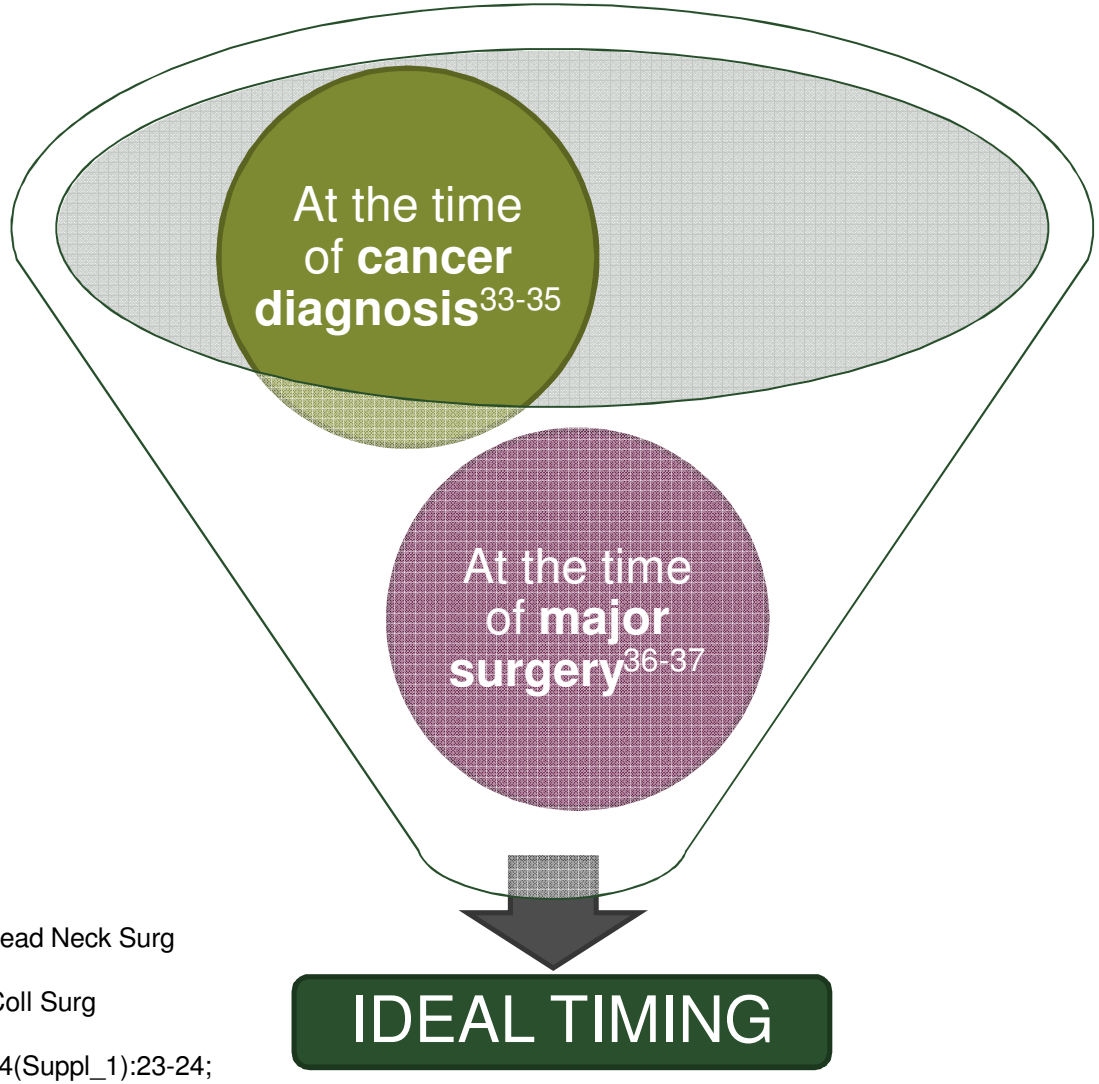
Timing of cessation intervention[32]



[32] Nayan S *et al*. Otolaryngol Head Neck Surg 2013:149(2):200-211;
[33] Khullar D and Maa J. J Am Coll Surg 2012;215(3):418-426;
[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;
[37] Warren GW *et al*. J Oncol Pract 2013;9(5):258-262

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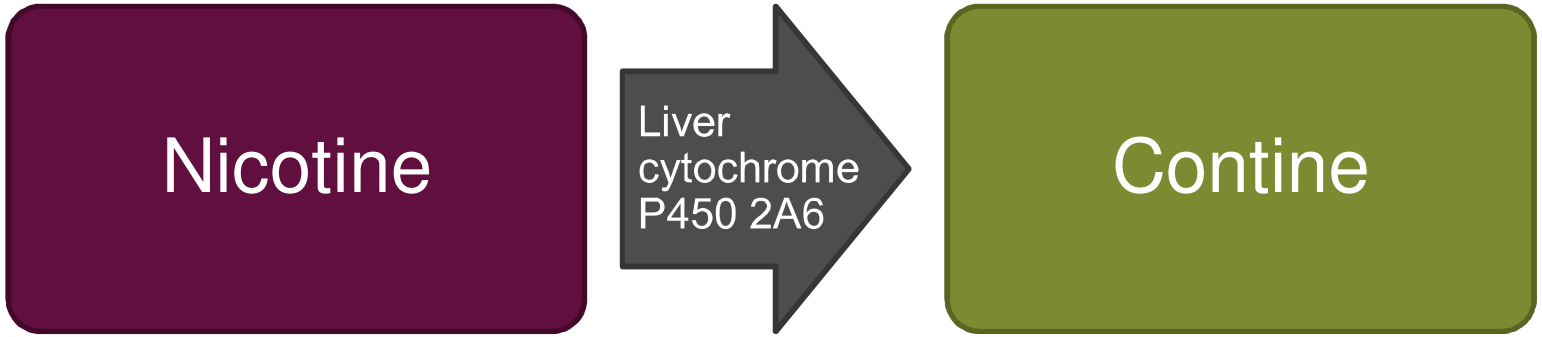
Methods to verify smoking cessation[38]



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

[38] Griebel B *et al*. Oncol Nurs Forum 1998;25(5):897-902

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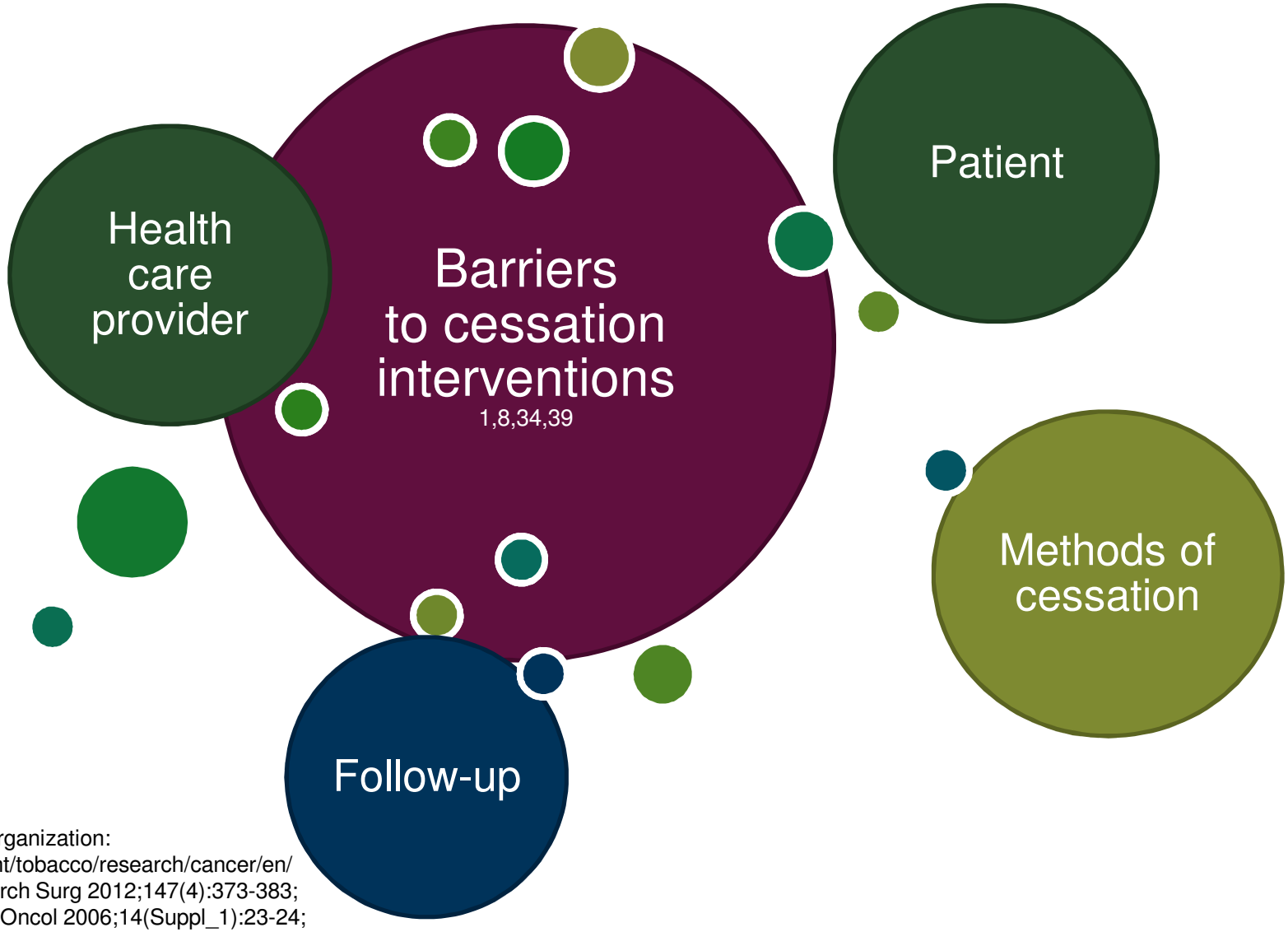

[1] World Health Organization: http://www.who.int/tobacco/research/cancer/en/
[8] Sørensen LT. Arch Surg 2012;147(4):373-383;
[34] Krstev S. Arch Oncol 2006;14(Suppl_1):23-24;
[39] Gritz ER *et al*. Cancer Epidemiol Biomarkers Prev 1993;2(3):261-270

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Follow-up

- **Regular** follow-up is a critical component of cessation interventions[1,24]
- **Longer** follow-up more accurately reflects the success or failure of an intervention by Fiore *et al.*[25]

[1] World Health Organization: http://www.who.int/tobacco/research/cancer/en/
[24] Schwartz JL. Washington, DC: US Department of Health and Human Services Public Health Service, National Institutes of Health; 1987;
[25] Fiore MC *et al.* Rockville, MD: US Department of Health and Human Services, Public Health Service; 2008

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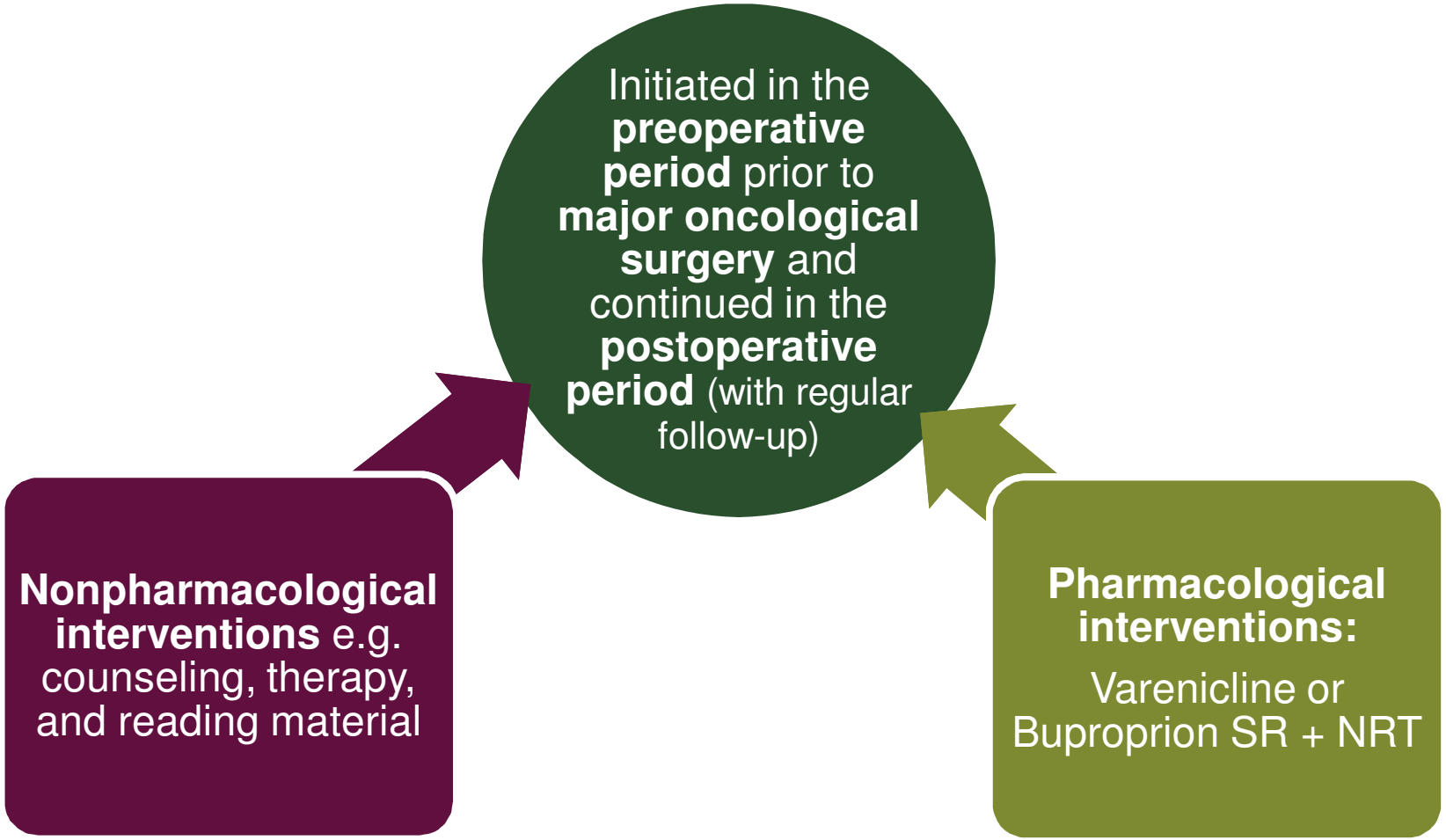
Follow-up II

- 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

[37] Warren GW *et al.* J Oncol Pract 2013;9(5):258-262

The ideal smoking cessation method

- Based on the **systematic review** published in 2013[32]:



[32] Nayan S *et al.* Otolaryngol Head Neck Surg 2013:149(2):200-211

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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

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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

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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

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Thank you!