

**Cancer Care Ontario**

**Action Cancer Ontario**

# **It's Time to Take Smoking Cessation in Cancer Patients Seriously**

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# Overview

- Brief review of some smoking stats
- Commonly used “excuses” for not intervening to get cancer patients to stop smoking
- Health benefits of smoking cessation in cancer patients
- Strategies to engage busy oncologists

# Smoking : A Major Public Health Problem

- Tobacco is the #1 cause of preventable death in Canada. Approximately 40,000 Canadians have premature deaths as result of smoking each year.

Health and Welfare Canada, 2000

- Smoking accounts for 30% of all cancer deaths
- Results in a large health-related economic cost each year estimated at \$3.5 billion (does not include cost of lost productivity)

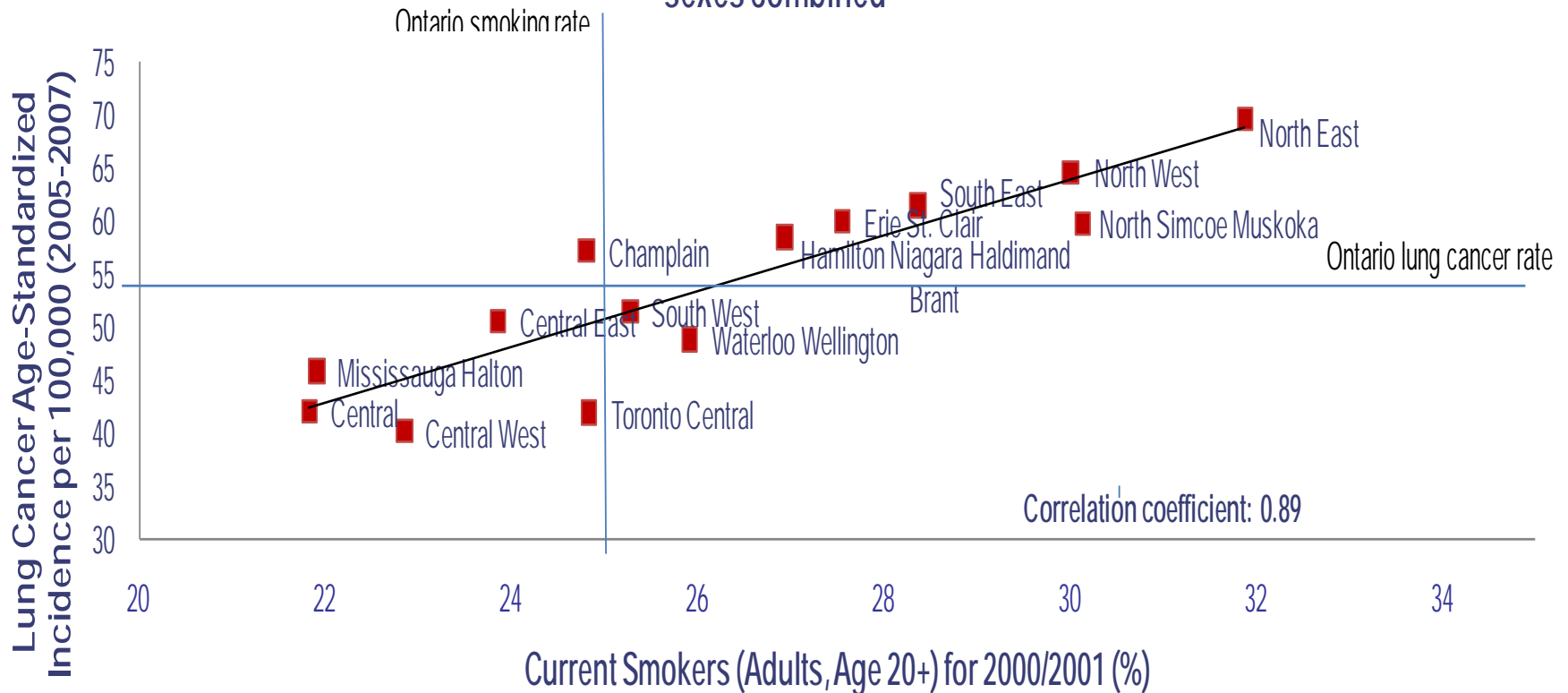
# Smoking : A Major Public Health Problem

- Smoking rates have declined in Ontario since the 1950s, but are still high (20%) and have not declined significantly in the last several years
- Greater burden of smoking in certain population subgroups: lower social economic status and educational attainment; history of mental illness and/or substance abuse, military personnel

- High smoking rates in many LHINs particularly NE, NW, HNHB, North Simcoe Muskoka, Erie St Clair
- High lung cancer rates in LHINs with high smoking rates

# Smoking strongly correlated with lung cancer incidence

Lung Cancer Incidence Rates (2005-2007) and Current Adult Smokers (2000/2001), both sexes combined



# Cigarette Smoke

- Largest single contributor to cancer risk
- Over 7,000 constituents in cigarette smoke; 250 known to be harmful, such as hydrogen cyanide, carbon monoxide, ammonia
- 69 known carcinogens in cigarette smoke, including

Arsenic

Benzene

Metals (beryllium, cadmium, nickel, chromium, polonium-210)

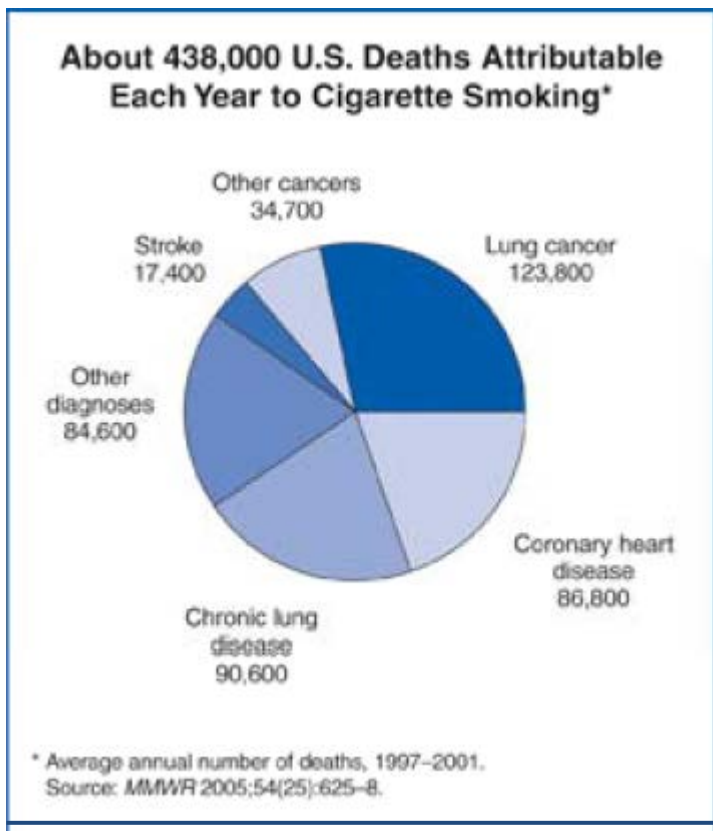
Ethylene oxide

Nitrosamines

Vinyl chloride

Polycyclic aromatic hydrocarbons

# Deaths Attributable to Cigarette Smoking



Lung Cancer 28%  
Coronary Heart Disease 19.8%  
Chronic Lung Disease 20.6%  
Stroke 3.9%  
Other Cancers 7.9%  
Other Diagnoses 19.3%



- Smoking accounts for approximately 80% of ***lung cancer*** deaths
- Sufficient scientific evidence to link tobacco causally to ***over a dozen other cancers***: mouth, nose, sinuses, pharynx, larynx, esophagus, liver, stomach, pancreas, cervix, kidney, bladder, bowel, acute myeloid leukemia

So why don't oncology care providers  
make a greater effort to help their  
patients stop smoking?

# The Usual “Excuses”

- Too late
- It's one of the patient's few pleasures
- Too busy in clinic, not enough time to talk about smoking cessation
- Need to focus on treating the cancer
- Don't know how to discuss smoking cessation

# Reality

- Health benefits of cessation are not generally known
- Considerable new information on smoking cessation in cancer patients emerging
- Most health care providers are not trained in smoking cessation pharmacotherapy or counselling

## **Adverse Health Outcomes in Cancer Patients and Survivors**

1. In cancer patients and survivors, the evidence is sufficient to infer a causal relationship between cigarette smoking and adverse health outcomes. Quitting smoking improves the prognosis of cancer patients.
2. In cancer patients and survivors, the evidence is sufficient to infer a causal relationship between cigarette smoking and increased all-cause mortality and cancer-specific mortality.
3. In cancer patients and survivors, the evidence is sufficient to infer a causal relationship between cigarette smoking and increased risk for second primary cancers known to be caused by cigarette smoking, such as lung cancer.
4. In cancer patients and survivors, the evidence is suggestive but not sufficient to infer a causal relationship between cigarette smoking and (1) the risk of recurrence, (2) poorer response to treatment, and (3) increased treatment-related toxicity.

# **Smoking Cessation Benefits to Cancer Patients**

# Benefits of Smoking Cessation

- General health benefits
- Improved outcomes with cancer therapy
  - Surgery
  - Radiation therapy
  - Systemic therapy
- Reduced toxicity
- Reduced late effects: recurrence, second malignancies, PFS, OS

# General Smoking Cessation Benefits

## Immediate benefits of smoking cessation

- Lower blood pressure, improved oxygen transportation, improvements in smell, taste, circulation, breathing, increased energy and heightened immune response
- Improvements in cognitive function and psychological well-being leading to an overall improvement in quality of life

Garces et al., Chest 2004; 126: 1733-1741



# General Smoking Cessation Benefits

- Lung cancer patients who stop smoking report less fatigue, shortness of breath and increased activity levels, improved appetite, sleep and mood

Cataldo JK et al. Oncology 2010; 78: 289-301

# Non-cancer Related Causes of Mortality

- Smoking increases mortality due to vascular disease, heart disease, cerebrovascular disease, chronic obstructive pulmonary disease, smoking-related cancers and non-smoking-related cancers

**But we're here to treat cancer**

# Impact of Non-cancer Related Causes of Death

- 1,334 prostate cancer patients treated with brachytherapy, only 8.7% of total deaths attributed to prostate cancer
- Current smoking increased the risk of death from cardiovascular disease (RR 3.05), cancers other than prostate cancer (RR 4.09) deaths from other causes (RR 5.52)
- ***Smoking in prostate cancer patients may play a bigger role in survival than the prostate cancer itself***

Bittner et al. Int J Radiat Oncol Phys 2008; 72:, 433 – 440

# Complications following Surgery (any type)

- Smoking impairs wound healing following surgery - inhibition of epithelization, causes vasoconstriction and induces cellular hypoxia temporarily

Gritz ER et al. Nicotine Addiction: Principles and Management 1993

- Inflammatory healing response attenuated by reduced inflammatory cell chemotactic responsiveness, migratory function and oxidative bactericidal mechanisms
- Proliferative response impaired by reduced fibroblast migration and proliferation and down-regulated collagen synthesis and deposition
- Inflammatory response restored in part within 4 weeks, but proliferative response remains impaired longer

Sorensen LT Ann Surg 2012; 255: 1069-79

# Post-operative Outcomes in Colorectal Cancer

- Database of American College of Surgeons National Surgical Quality Improvement Program
- Risk adjusted 30 day outcomes assessed for never smokers, ex-smokers and current smokers
- 47,574 patients – 26,333 colorectal cancers, 14,019 diverticular disease, 7,222 inflammatory bowel disease
- > 60% never smokers, 20.4% current smokers; 19.2% were ex-smokers
- ***Significant increase in postoperative morbidity for current smokers (OR 1.3; CI to 1.21 – 1.40 and mortality (OR, 1.5; 95% CI, 1.11 – 1.94) after colorectal surgery***
- ***Findings consistent for both malignant and benign disease; significant dose-dependent effect when stratified by pack years of smoking***

Sharma A et al., Ann Surg Oct 10, 2012

# Smoking and Surgery

- Richards et al, United Kingdom
- 423 stage I – III colorectal cancer patients treated by surgery
- Current smoking increased risk for postoperative complications (HR 1.32)
- ***Smoking decreased disease-free survival ( HR 1.25) and overall survival ( HR 1.30) with increased risk of systemic recurrence (p = .014)***

Richards CH et al. Ann Surg 2011; 254:83 – 89

# Impact of Smoking Cessation Before Resection of Lung Cancer: A Society of Thoracic Surgeons General Thoracic Surgery Database Study

David P. Mason, MD, Sreekumar Subramanian, MD, Edward R. Nowicki, MD, MS, Joshua D. Grab, MS, Sudish C. Murthy, MD, PhD, Thomas W. Rice, MD, and Eugene H. Blackstone, MD

- 7990 primary resections for lung cancer studied
- Risk of in-hospital death and respiratory complications assessed according to the timing of smoking cessation

Ann Thorac Surg 2009; 88: 362-371



# Results

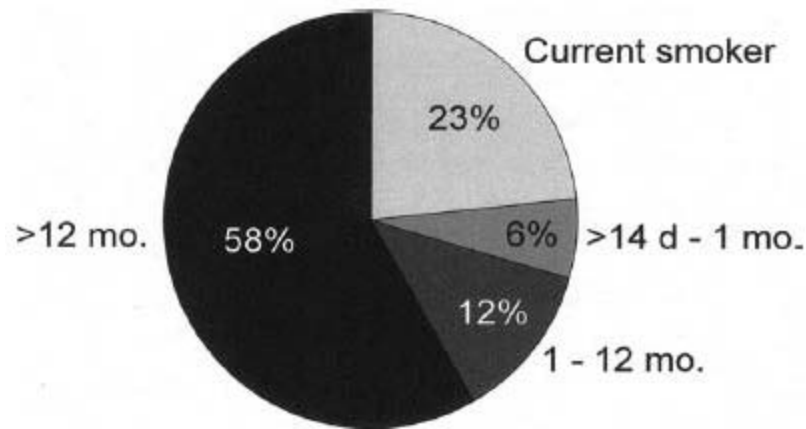


Fig 1. Interval of smoking cessation before resection for lung cancer among 6941 patients with a history of smoking.

Table 2. Outcome After Resection for Lung Cancer According to Smoking Status

Category	Overall	Hospital Mortality	Overall	Pulmonary Complications
	No. (% of 7990)	No. (%)	No. (% of 7965) <sup>a</sup>	No. (%)
Current smoker	1595 (20)	24 (1.5)	1590 (20)	110 (6.9)
Pre-op smoking cessation interval				
>14 d-1 mo	404 (5.1)	7 (1.7)	402 (5.0)	25 (6.2)
1-12 mo	940 (12)	12 (1.3)	938 (12)	60 (6.4)
>12 mo	4026 (50)	62 (1.5)	4011 (50)	234 (5.8)
Never smoked <sup>b</sup>	1025 (13)	4 (0.39)	1024 (13)	27 (2.6)
Total	7990 (100)	109 (1.4)	7965 (100)	456 (5.7)

<sup>a</sup> Excludes 25 patients who died on the day of operation.

<sup>b</sup> Includes patients who smoked fewer than 100 cigarettes in their lifetime.

# Toxicity of Radiation can be Greater in Smokers

- Advanced head and neck cancer patients treated with radiation therapy had a longer duration of mucositis if they continued smoking (23.4 wks) vs those who quit at start of radiation and remained abstinent (13.6 wks)

Rugg T et al. Br J Radio 63: 554-6, 1990

- Smokers less likely to regain satisfactory voice quality following radiation therapy for laryngeal cancer

Karim AB et al Cancer 51: 47-9, 1983

- Lung cancer patients: 20% greater chance of radiation pneumonitis

# Smoking and Radiation Treatment

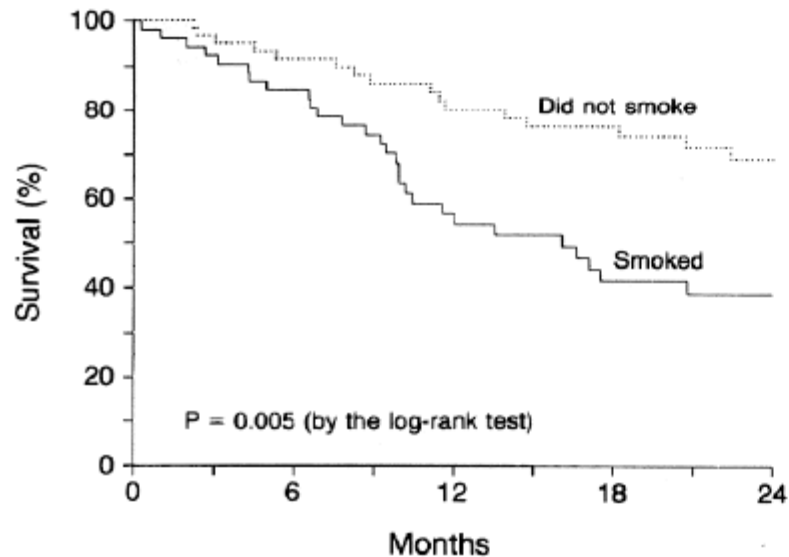
- Smokers who continue to smoke during XRT have a ***significantly lower rate of complete response to radiation therapy (45% vs 74%) and 2-year survival (39% vs 66%)***
- Recent quitters were more similar to long-term quitters than to continued smokers in survival likelihood at 18 months

Browman GP et al. NEJM 1993

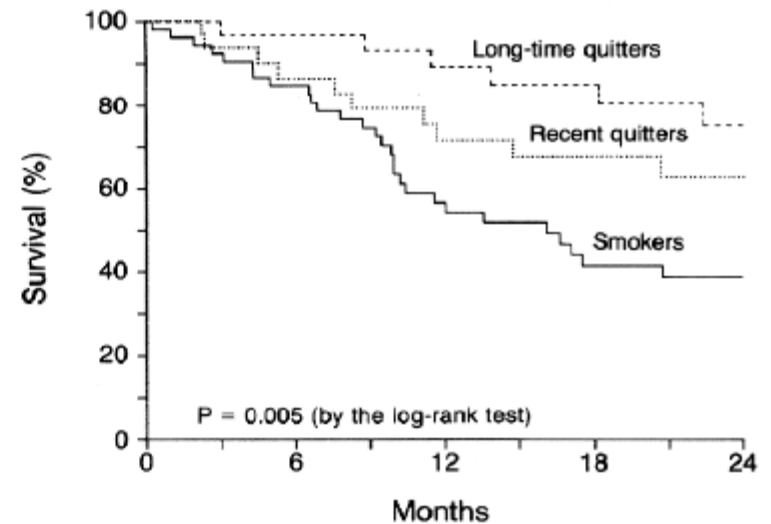
- RTOG trials 9003 and 0129 in ***oropharyngeal cancer smoking during RT decreased overall survival (HR 2.33) and progression free survival (HR 2.19)***
- ***Risk of progression or death increased by 1% per pack-year smoked*** (for both HR, 1.01; 95% CI, 1.00-1.01; p<.002) or 2% per year smoking (for both HR 1.02; 95% CI 1.01-1.03; p<.001) in both trials.

Gillison ML J Clin Oncol 2012, 30(17)

# Smoking and Head/Neck Cancer Treatment



GROUP	0	6	12	18	24
Smoked	53	49	43	36	24
Did not smoke	62	58	51	44	40

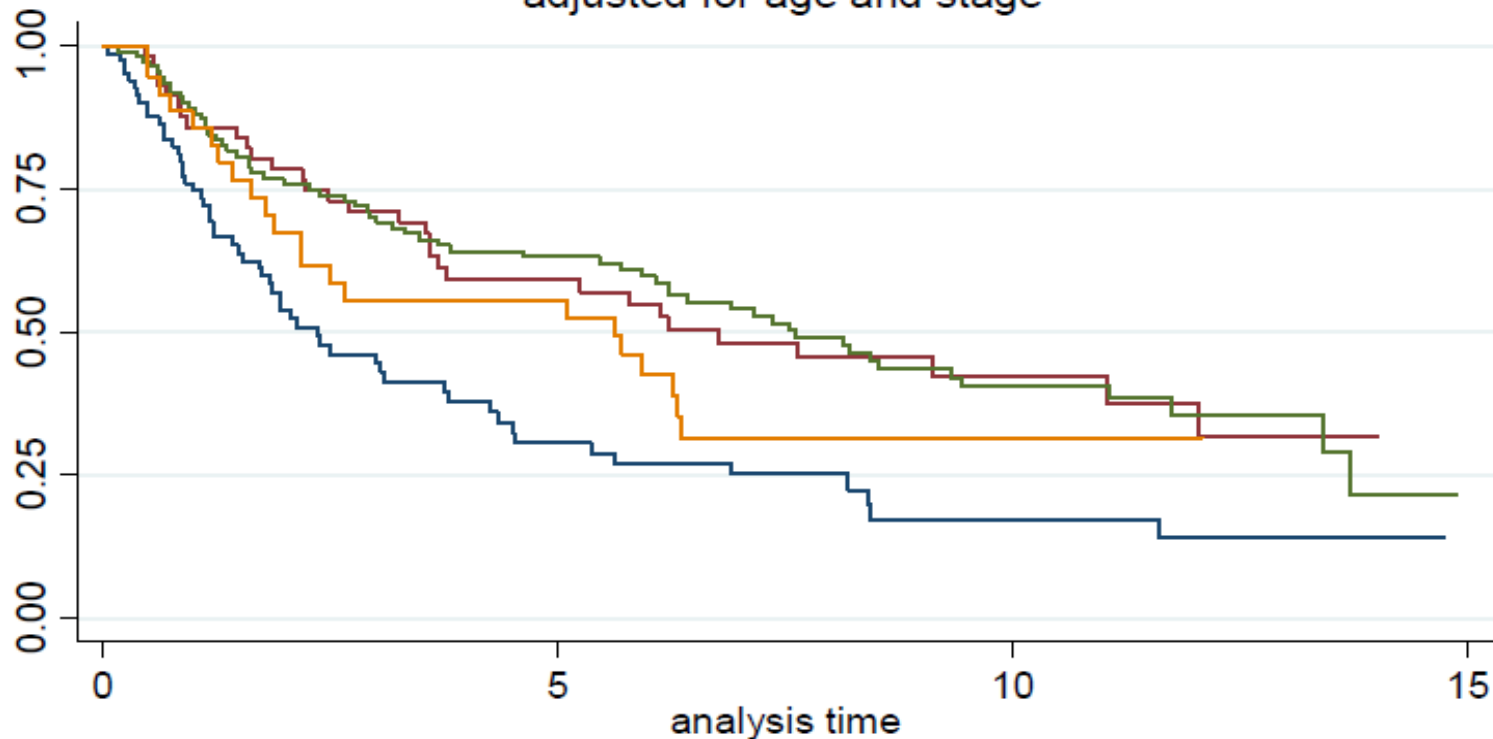


GROUP	0	6	12	18	24
Smokers	53	49	43	36	24
Recent quitters	32	28	24	20	18
Long-time quitters	30	30	27	24	22

- 115 Stage III-IV SCCA of H/N treated with XRT +/- fluorouracil
- 41% decrease in 2-year OS in patients who smoked during XRT
  - No difference based upon fluorouracil vs. placebo
  - No difference in toxicity (smokers during XRT vs. nonsmokers)

# Roswell Park Experience

Overall Survival: Head & Neck, Men  
adjusted for age and stage



— Current — Recently Quit  
— Former — Never

Test for homogeneity of survival curves:  $p < .01$

Graham Warren Department of Radiation Medicine and Department of Pharmacology and Therapeutics

[http://www.roswellpark.edu/sites/default/files/Nicotine%202011-5-10%20retreat-published\\_0.pdf](http://www.roswellpark.edu/sites/default/files/Nicotine%202011-5-10%20retreat-published_0.pdf)

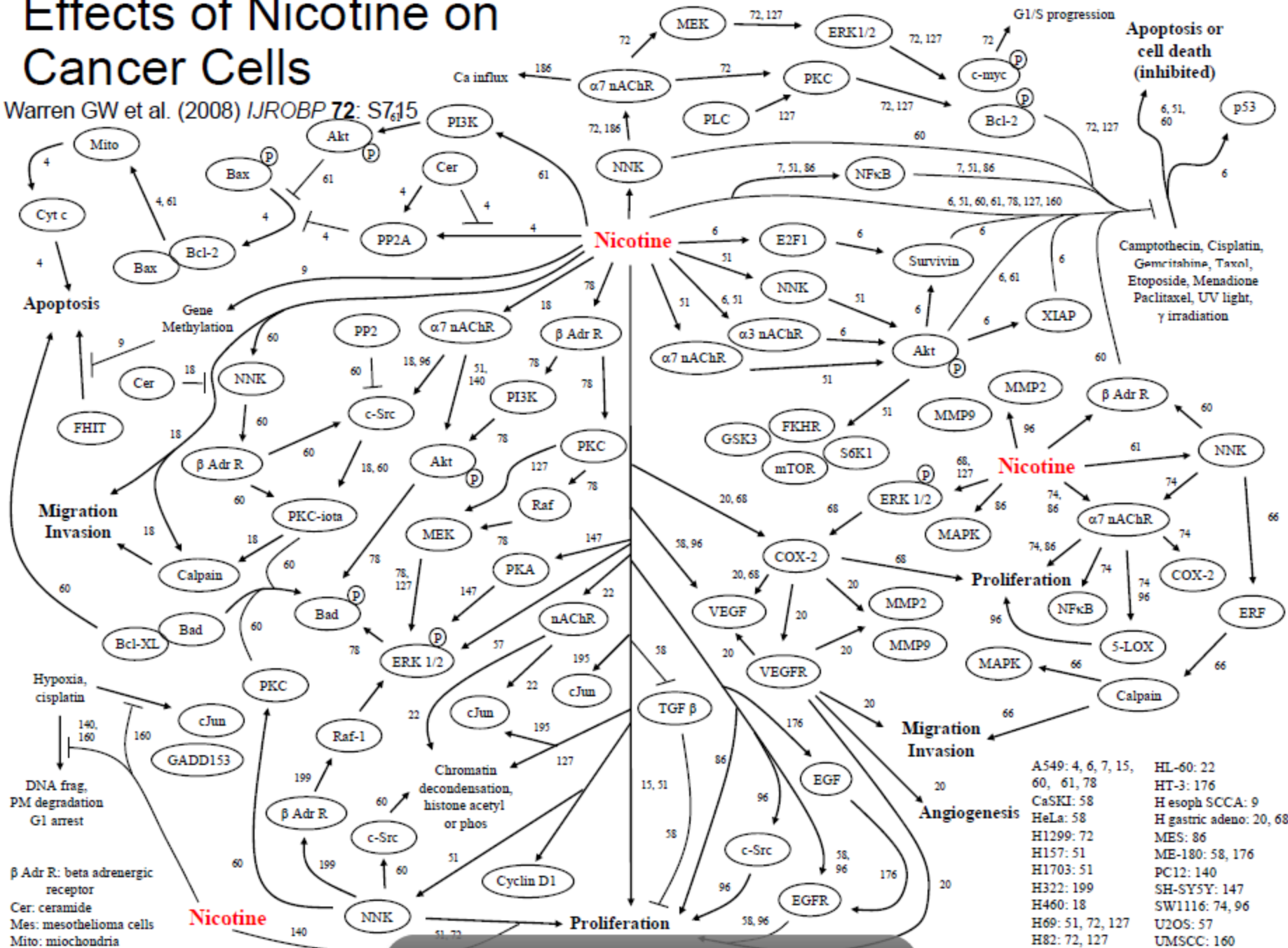
# Smoking and Chemotherapy

- Multiple mechanisms by which smoking (nicotine) can have detrimental effect on treatment with systemic therapy
- Nicotine:
  - increases metabolism of multiple drugs by inducing hepatic enzymes
  - can inhibit the apoptotic potential of several drugs including cisplatin
  - can induce tumour cell proliferation and angiogenesis

Zhang J et al Am J Respir Cell Mol Biol 2009; 40: 135-46

# Effects of Nicotine on Cancer Cells

Warren GW et al. (2008) *IJROBP* 72: S715



# Smoking and Chemotherapy

## Irinotecan

- Lowered dose-normalized area under plasma concentration-time curve in smokers (median, 3.9 vs 28.7 ng h/ml/mg;  $p = .001$ ) compared to non-smokers;
- Grade 3 to 4 treatment-induced neutropenia: 6% smokers, 30% non-smokers (OR and 0.10; 95% 0.02 to 0.43;  $p < .001$ )

Van der Bol et al. J Clin Oncol 2007; 25: 2719- 2726

## Erlotinib

- Lower overall response in smokers vs never smokers ( 3.9 vs 24.7%;  $p, 0.001$ ); twice the normal dose required to produce needed circulating levels in smokers versus non-smokers

Shepherd FA et al NEJM 2005; 353: 123-132



# Effect of Smoking on Molecular Targeted Therapies

- 278 metastatic Renal Cell Cancers treated with sunitinib:
  - 59 active smokers,
- Median progression free survival – 9 months; overall survival – 22 months
- After adjustment for known outcome associated factors, patients actively smoking had significantly lower PFS by 7 months (4 months versus 11,  $p < .0001$ ) and overall survival by 15 months ( 11 months versus 26,  $p < .0001$ )
- Active smoking associated with less clinical benefit (response plus stable disease in 54% versus 88%)

# **Impacts of Smoking on Recurrence and Survival**

# Continued Smoking, Non-small Cell Lung Cancer\* vs. Cessation after Diagnosis

- All cause mortality (HR 2.94, 95% CI, 1.15 – 7.54)
- Second primary (HR 2.29, 95% CI, 0.50 – 10.58)
- Recurrence (HR 1.86, 95% CI, 1.01 – 3.41)
- ***Five-year survival (life table modeling), for those at 65yr who continue to smoke is 33%; 70% for those who quit***

\*early-stage lung cancer

Parsons A et al., BMJ 2010; 340: b5569

# Continued Smoking, Small Cell Lung Cancer\* vs. Cessation after Diagnosis

- All cause mortality (HR 1.86, 95% CI, 1.33 – 2.59)
- Second primary (HR 4.31, 95% CI, 1.09 – 16.98)
- Recurrence (HR 1.26, 95% CI, 1.06 – 1.50)
- ***Estimated five-year survival (life table modeling) in continuing smokers 29% vs. 63% of those who quit***

\*limited stage;

Parsons A et al., BMJ 2010; 340: b5569

# Prostate Cancer

- A number of studies show an association between **continued smoking and earlier recurrence**
- **Radical prostatectomy** N = 1,416: 34.2% of current smokers vs 14.8% of former smokers and 12.1% of never smokers recurred after a mean of 7.3 years

Joshua CE et al. JAMA 305: 2548-55, 2011

- A prospective observational study of 5,366 men, prostate cancer-specific death rates were 15.3 per 1000 person-years for current smokers versus 9.6 per 1000 person years in never smokers

Kenfield SA et al JAMA 305: 2548-55, 2011

# Synergistic interaction between smoking and cytotoxic treatments

- Travis et al. 2002
- 222 Hodgkin's disease patients with lung cancer matched to 444 HD patients without lung cancer
- **Current smoking at diagnosis of HD increased risk of lung cancer** (RR 21.2) with lesser risks in former smokers (RR 4.0)
- In current smokers with at least one pack per day habit, current smoking increased risk of lung cancer in a **synergistic** manner when **combined with cytotoxic treatments**:
  - RR 20.2 smoking combined with RT
  - RR 16.8 when smoking combined with alkylating agents
  - RR 49.1 smoking combined with RT + alkylating agents

# Smoking as a Risk Factor for Second Malignancy

- Persons presenting with both smoking-related and non-smoking related malignancy face increased risk of a second malignancy at the same site or another site if they continue to smoke

Gritz ER et al. Cancer Causes Control 2: 105 – 12, 1991

- When prognosis is more favorable for the initial cancer, the evidence is even stronger that continued smoking increases the risk of a new primary cancers for up to 20 years after the original diagnosis
- In two studies of **survivors of SCLC**, **risk of a second cancer (mostly NSCLC) was 3.5 fold to 4.4 fold higher** than the general population; the risk was even higher after chest radiation (RR = 21.0) and alkylating agents (RR = 19.0)

Richardson GE et al. Ann Int Med 119: 383-90, 1993

Tucker MA et al. J Natl Cancer Inst 89: 1782-8, 1997

# Smoking as a Risk Factor for Second Malignancy

- The ***risk of developing lung cancer*** in **breast cancer survivors** treated with radiation therapy is negligible in non-smokers but **high in smokers** (adjusted odds ratio = 5.6) and **even higher in smokers receiving XRT** (adjusted odds ratio = 8.6)
- Patients with **oral and pharyngeal cancers** who smoke have a very high rate of second primary cancers; the risk of a second cancer increased with continued smoking up to almost 5 times (OR = 4.7) for all aerodigestive cancers among long-term heavy smokers even after controlling for alcohol



# Summary of Cessation Benefits: Surgical Outcomes

Reduced risk of:

- Wound healing problems
- Infection
- Pulmonary complications
- Total complications

# Summary of Cessation Benefits: Treatment

- Improves response to anti-cancer therapy (radiation, systemic) in a variety of cancer types
- Anti-cancer therapy likely to produce fewer complications among nonsmokers
- Metabolism of cytotoxic and molecular targeted drugs can be affected by smoking, and reduce their effect

# Summary of Cessation Benefits: Survival

- Increased survival time demonstrated for a number of tumour types
- Probably decreases chance of recurrence following treatment
- Lessens risk of developing a second primary cancer

# A Paradigm Shift is Needed in Cancer Centres

From:

- Primary focus on treating the cancer
- Viewing tobacco use as a “bad habit” rather than an addiction

To:

- Smoking cessation is a part of quality cancer care
- The best cancer treatment outcomes will only be achieved if smoking cessation incorporated into the care of patients

# Lack of accountability for assessing tobacco use in patients and providing associated cessation treatment

- In the US, recent survey of National Cancer Institute designated cancer centers found only 62% of centers routinely provided tobacco education materials
- Just over half reported effective identification of patient tobacco use
- 20% had no cessation services
- Less than half of cancer centers had personnel designated to provide tobacco cessation treatment

Goldstein AO et al. Nicotine Tob Res 2013; 15:52 – 58

# So how to make it possible for physicians to support smoking cessation?

- Inform physicians on how smoking cessation benefits their patients (repeatedly)
- Make it easy for them to communicate to their patients
  - Script the “ask and offer”
  - Script a sentence or two on the benefits in cancer patients
  - Use other providers to support the smoking cessation message
  - Make referral easy; on site access to smoking cessation “experts”
  - Handouts/ posters for patients on benefits
- Report data on physician and RCC performance by centre
- Use CCO’s performance management cycle to drive improvement
- If physicians want to prescribe, provide easy to use, cheat sheet (OHI)

# Keeping it Simple

- Eliminate the assessment of the willingness to quit
- Evidence supports an “ask and offer” approach
- Cochrane review: offering assistance motivates more attempts to stop smoking than offering advice to quit on medical grounds
- Clinicians should consistently offer treatment opportunities as often as possible to motivate attempts to quit

# Scripts

- **Ask:** Do you smoke or have you smoked in the last 6 months?
- **Brief advice:** Stopping is the best thing you can do to improve your health. I understand that it can be hard to stop, but I (we) can help you
- **In oncology:** Stopping smoking will enable the cancer treatments to work better and reduce the side effects. To get the best results from the treatment that we are going to give you, I need you to stop smoking



# Scripts

## Cessation support:

- Two options:
  1. **Refer:** physicians without sufficient time or expertise should refer – most (all) oncologists (RCC smoking cessation counsellor, family physician, Public Health, Smoker's Help line)
  2. **Provide support:** can include planning for quit date, medications, counselling, follow-up



HOSPITAL LETTERHEAD

Addressograph

**Physician's Orders**

<b>Medication Allergies/Reactions</b>	<b>Substance or Food Allergies/Reactions</b>
<input type="checkbox"/> none known	<input type="checkbox"/> none known
<b>SMOKING CESSATION PHARMACOTHERAPY</b>	
<b>Init.</b>	<b>I.V. &amp; Medication (Meds, dose, frequency, route)</b>
<b>NICOTINE REPLACEMENT THERAPY (NRT)</b>	
<input type="checkbox"/>	<b>Patient smoking &lt;10 cigarettes per day:</b> Nicotine Patch 7 mg daily x 6 weeks
<input type="checkbox"/>	<b>Patient smoking 10-20 cigarettes per day:</b> Nicotine Patch 14 mg daily x 6 weeks; then Nicotine Patch 7 mg x daily x 4 weeks.
<input type="checkbox"/>	<b>Patients smoking &gt;20 cigarettes per day:</b> Nicotine Patch 21 mg daily x 6 weeks; then Nicotine Patch 14 mg daily x 2 weeks; then Nicotine Patch 7 mg daily x 2 weeks.
<input type="checkbox"/>	<b>Patients smoking &gt;30 cigarettes per day:</b> Nicotine Patch 35 mg (21 mg + 14 mg) daily or Nicotine Patch 28 mg (21 mg + 7 mg) daily (starting dose based on patient's need) x 6 weeks; then Nicotine Patch 28 mg (21 mg + 7 mg) daily x 4 weeks; then Nicotine Patch 21 mg daily x 4 weeks; then Nicotine Patch 14 mg daily x 2 weeks; then Nicotine Patch 7 mg daily x 2 weeks.
<input type="checkbox"/>	<b>Patients smoking &gt;40 cigarettes per day:</b> Nicotine Patch 42 mg (21 mg + 21 mg) daily x 6 weeks; then Nicotine Patch 35 mg (21 mg + 14 mg) daily x 2 weeks; then Nicotine Patch 28 mg (21 mg + 7 mg) daily x 2 weeks; then Nicotine Patch 21 mg daily x 2 weeks; then Nicotine Patch 14 mg daily x 2 weeks; then Nicotine Patch 7 mg daily x 2 weeks.
<input type="checkbox"/>	<b>PLUS Adjunctive Therapy:</b>
<input type="checkbox"/>	Nicotine (Nicorette <sup>®</sup> ) Gum 2 mg pieces PRN, max. _____ pieces per day
<input type="checkbox"/>	Nicotine (Nicorette <sup>®</sup> ) Inhaler PRN, max. _____ cartridges per day
	Patch may be removed at HS, if patient complains of insomnia. It may be necessary for some patients to remain on NRT longer, if patient continues to have urges to smoke, please consult smoking cessation.
<b>VARENICLINE (CHAMPX<sup>®</sup>) ONLY</b>	
<input type="checkbox"/>	0.5 mg PO daily _____ Days 0.5 mg PO twice daily _____ Days 1 mg PO twice daily _____ Weeks
	It may be necessary to have the dose lowered temporarily or permanently if patient experiences nausea or other side effects.
<b>BUPROPION (ZYBAN<sup>®</sup>) ONLY</b>	
<input type="checkbox"/>	150 mg PO daily _____ Days 150 mg PO twice daily _____ Days 150 mg PO twice daily _____ Weeks
	It may be necessary to have the dose lowered temporarily or permanently if patient experiences nausea or other side effects.
Date (****/mm/dd) :	Time : Physician : Signature :

# Why Smoking Cessation at the Cancer Centres?

- Cancer patient experience is unique
  - Frequent contact with cancer centre;
  - Bonding with care providers;
  - Opportunity for many teachable moments
- Cessation may increase patient's feelings of self-control; can 'do something' to help themselves, especially if benefits to cancer treatment explained
- Cancer diagnosis also a **teachable moment** for family members

# Progress and Next steps

- Provincial Leadership has committed to the Steering committee recommendations
- A secretariat focused on smoking cessation has been established at Cancer Care Ontario
- Regional “champions” identified
- Advisory Committee on Smoking Cessation established
- An implementation plan developed

**Questions?**