A211401- Reducing surgical complications in newly diagnosed lung cancer patients who smoke cigarettes

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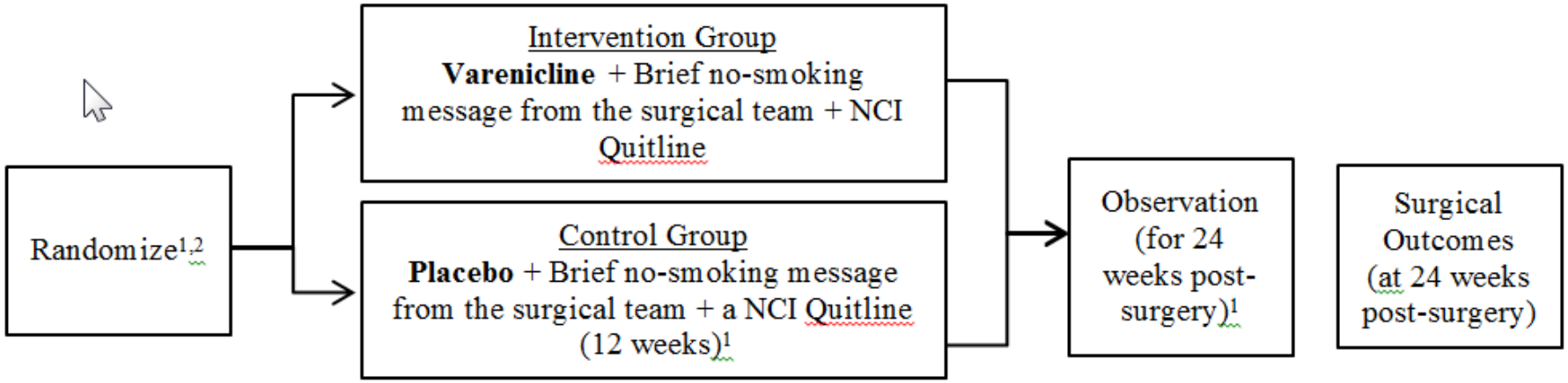
Study Schema



1 Tobacco use will be assessed prior to registration, at randomization, and every six weeks during treatment and observation until 24 weeks after surgery.

2 **Please note**: Baseline is at the time the surgical message is discussed with the cancer patient. Surgery must occur after the target quit date (TQD) defined at baseline and can be performed no sooner than 10 days after randomization and no more than twelve weeks after randomization.

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Rationale

- Can surgical teams capitalize on a *teachable moment* regarding the harmful effects of smoking that will reduce surgical complications among lung cancer patients who smoke?

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Overall Objective

To assess the effect of smoking cessation treatment on **surgical complications**, **QOL**, and **post-operative care**.

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Specific Aims:

Primary

- To determine if varenicline, when added to a behavioral intervention consisting of a brief clinician-delivered intervention with tobacco quitline follow-up, **decreases postsurgical complications through 24 weeks after surgery** in lung cancer patients who undergo surgery and are motivated to stop smoking.

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Correlative Science Objectives

- To evaluate the predictive role of the nicotinic receptor gene cluster (*CHRNA5-CHRNA3-CHRNB4*) and *CYP2A6* genotypes in smoking cessation among lung cancer patients undergoing surgery.
- To evaluate the potential moderating effect of these cessation-relevant genotypes on smoking cessation treatment between the intervention and control groups.

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Considerations for subject enrollment

- Diagnosis of Lung Cancer
- Surgical consult
- Daily smoker for 6 months prior
- No Psychiatric illness which would prevent the patient from giving informed consent.
- No Medical condition such as uncontrolled infection (including HIV), uncontrolled diabetes mellitus or cardiac disease which, in the opinion of the treating physician, would make this protocol unreasonably hazardous for the patient.
- Patients who cannot swallow oral formulations of the agent.
- Women and men of reproductive potential should agree to use an appropriate method of birth control throughout their participation in this study due to the teratogenic potential of the therapy utilized in this trial. Appropriate methods of birth control include abstinence, oral contraceptives, implantable hormonal contraceptives or double barrier method (diaphragm plus condom).

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Accrual

- **Consent and screen 783** lung cancer patients who smoke and are expected to undergo surgery –
  - Of these, a minimum of **626 participants** are expected to undergo surgery.

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Study Visits

- 12 weeks of treatment – beginning as little as 10 days prior to surgery and up to 12 weeks prior to surgery
- TQD – 8 days after starting medication
- Follow up to 6 months post surgery

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Study Calendar

	Consent /screen*	Baseline	Day of Surgery**	Week 6	Week 12	Week 18	Week 24
Visit Type	In person	In person	In person	In Person	Phone/in person	Phone/In person	In person
Med Hx/PE	X	X					
Screen/registration	X						
AE/Con Meds		X**	X**	X**	X**	X**	X**
Quit Message		X					
Quitline		X					
Study Med		X	X	X			
PHQ-9		X		X	X		X
Tobacco Use Assessment		X	X	X	X	X	X
SEQ-12		X		X	X		X
LASA		X	X	X	X		X
Saliva		X	X	X	X*	X*	X*
Blood		X					

* - visit can be completed over the phone, but the patient must return to the site for a salivary cotinine sample (physician visit not required)

** - can be collected as self report or record abstraction

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Treatment Assignments and Blinding

- 1:1 Randomization
  - **Stratified** by type of resection performed:
    - Minimally invasive (such as Lobectomy or Robotic surgery)
    - Other (such as bi-lobectomy or pneumonectomy)
  - **Randomization** Groups:
    - Intervention Group:
      - **varenicline**
      - a brief no-smoking message from the surgical team
      - behavioral support provided by a telephone smoking quitline (NCI's 1-877-44U-QUIT) for 12 weeks.
    - Control Group:
      - **placebo**
      - a brief no-smoking message from the surgical team
      - behavioral support provided by a telephone smoking quitline (NCI's 1-877-44U-QUIT) for 12 weeks.

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Teachable Moment Training

- Surgeons and designated members of the surgeon's team will be trained and educated in the basics of smoking cessation counseling and delivery of the No-Smoking message to the surgical oncology patient.
- Study subjects will be provided with a folded **flyer** which will re-inforce the surgical team message as well as the quitline phone number
- All **training will be documented** and each site must have this training prior to study start up – for consistency.

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Objectives

- Learn about the risks of smoking around the time of cancer surgery
- Learn about the benefits to quitting smoking around the time of cancer surgery
- Learn what tobacco quitlines are and how they can help patients obtain and maintain abstinence
- Learn how to introduce a patient to the quitline
- Learn how to perform a warm handoff of a patient to the quitline

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Teachable Moment Training

- Surgical Team Message

- Study Coordinator Team Message
  - example

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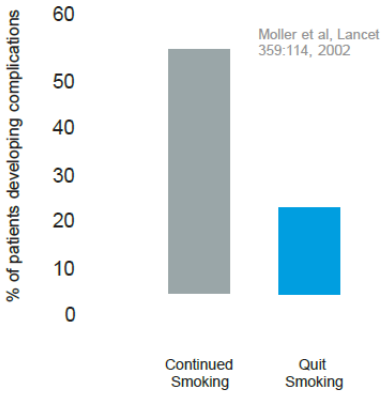
Quitting smoking now will help you to have the best possible results after your surgery.

Heart and lung function starts improving within 12 hours of quitting as levels of toxins such as carbon monoxide in your body decrease, improving blood flow and reducing your chances of problems such as a heart attack.

Quitting smoking also helps the healing process and reduces the chances that your wound will become infected after surgery.



This study shows that quitting smoking dramatically decrease the rate of complications after surgery.

There are many other advantages to quitting smoking before your surgery.

Advantage 1: Quitting smoking increases the chances that your cancer treatment will be successful and that you will live longer.

Advantage 2: You may have tried to quit before, but your chances of successfully quitting are greater if you try to quit before surgery compared with other times.

Advantage 3: Quitting has many other health benefits, lowering the chances that you will suffer from emphysema, heart disease, and many other smoking-related diseases. It also eliminates your loved ones' exposure to second-hand smoke.

Quitting can be tough, but you don't have to do this alone; free help is available. Trained specialists are now conveniently available by telephone through a Tobacco Quitline; calls are free and confidential. Using the Quitline will increase the chances that stop-smoking medications will work.

NCITobacco Quitline 1-877-44U-QUIT

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Tobacco Quitline Hours

Monday-Friday
8 a.m.-8 p.m. ET

NCI Quitline:

1-877-44U-QUIT
(1-877-448-7848)

You may see other numbers advertised elsewhere, but please call the number below, which gives special help to smokers with cancer.

1-877-44U-QUIT
(1-877-448-7848)

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200 First Street SW
Rochester, Minnesota 55905
www.mayoclinic.org

MC2892-xx

Be Smoke-Free for Surgery

Why you should quit smoking for your surgery –

Tobacco Quitline 1-877-44U-QUIT – A free service to help you quit

Tobacco Quitlines are free and use a toll-free number

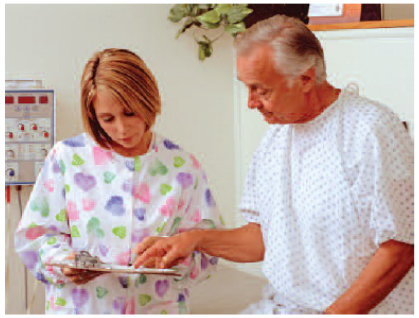
No matter how often you use them, they are always free of charge.

Tobacco Quitlines let you talk with experienced specialists who can help you quit smoking

The Tobacco Quitline uses trained specialists or coaches (real people, not recordings). They are trained to help you quit smoking in a caring, respectful, non- judgmental and supportive way. They will take the time to understand your situation, and work with you to devise a plan that is right for you. For example, they will talk with you about what you have tried in the past. If you are having difficulty quitting, your tobacco specialist will keep working with you to get you back on track in a caring and supportive way no matter what happens. They will be there for you when you need them.

Calls are at times that are most convenient for you

Calls to the Tobacco Quitline can be made Monday thru Friday from 8:00 a.m. to 8:00 p.m. ET. At the first call, the Quitline will get some information about you, then work with you to find the best time to talk. They can call you back at the number and time that you provide. If you want to talk to a specialist right away, the Quitline usually has several available to take you call.



Tobacco Quitlines have helped many people quit smoking

Many studies show that Tobacco Quitlines actually work to help smokers quit. Quitlines can more than double your chances of success. Working with the quitline will increase the chances that stop-smoking medication will work.

If you have thought about quitting smoking, there is no better time than now that you are having surgery. Most smokers try to quit several times, but most smokers also eventually succeed – you can do it!

Just like you should NOT EAT the morning of surgery, you also should NOT SMOKE the morning of surgery.

Your privacy is always protected

No one else will have access to any information you share with the Tobacco Quitline specialist. For example, insurance companies will not have access to your information. In addition, the specialists will not have access to information in your medical record.

Quitting smoking will help you have the best possible results after surgery and will increase your chances of recovering from cancer.

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Dosing

Agent	Dose	Route	Day	
Varenicline/Placebo	0.5 mg	Oral	Days 1-3	1 pill per day
Varenicline/Placebo	0.5 mg	Oral	Days 4-7	2 pills per day – Minimum of 8 hours apart
Varenicline/Placebo	1.0 mg	Oral	Days 8-84	2 pills per day – Minimum of 8 hours apart

- Recommendations:
  - Dosing should occur with 240 mL of water
  - Eat prior to dosing to decrease gastric upset.
  - There should be at least 8 hours between the morning and evening dosing.
  - If a dose is missed, the patient should take it as soon as s/he remembers.
  - If it is almost time for the next dose (within 6 hours), the patient should skip the missed dose and take the next one as scheduled.
  - Patients should not take a double dose of varenicline/placebo.

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Dose Modification

Dose Level 0	**1.0 mg twice daily**
Dose Level -1	1.0 mg once daily
Temporary discontinuation	

- All missed doses should be considered as skipped and not delayed. That is, the duration of treatment must not continue past the original 12-week stop date.
- If treatment is skipped for more than four weeks due to toxicity, permanently discontinue varenicline/placebo.

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Surgical Adverse Events – primary endpoint

- 30-day mortality
- 30-day re-hospitalization
- 1-year mortality
- Anastomotic failure
- Anesthesia-related respiratory complications
- Bleeding (transfusions > 5 U)
- Coma (> 24 hours)
- Deep venous thrombosis/ thrombophlebitis
- Failure to wean from the ventilator
- ICU readmission
- Impaired bone healing
- Implant loss (breast reconstruction)
- Increased postoperative pain
- Renal insufficiency/failure
- Return to operating room
- Sepsis/septic shock
- Stroke/cerebral accident
- Surgical infection (organ space)
- Surgical site infections
- Urinary tract infections
- Increased postoperative surgical stay
- Increased scarring and asymmetry
- Intubation (unplanned)/re-intubation
- Lower rates of successful digital replantation (microsurgery)
- Myocardial infarction
- Pneumonia
- Prolonged intubation
- Prolonged ventilator support
- Pulmonary complications
- Pulmonary embolism
- Reduced skin flap survival
- Vascular complications
- Vein graft failure
- Venous thromboembolism
- Ventilator (> 48 hours)
- Wound healing (delayed)
- Wound infection (sternal)
- Wound infections (superficial and deep)

These complications were identified as being sufficiently numerous from an investigation of the national surgical database (ACS-NSQIP). They will be defined using the General Thoracic Surgery Database (GTSD) for study purposes.

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Questions and Answers?

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