

Potpourri of Hematology Oncology

Jasmine Nabi, M.D.

Oncology Associates

Hall-Perrine Cancer Center at Mercy

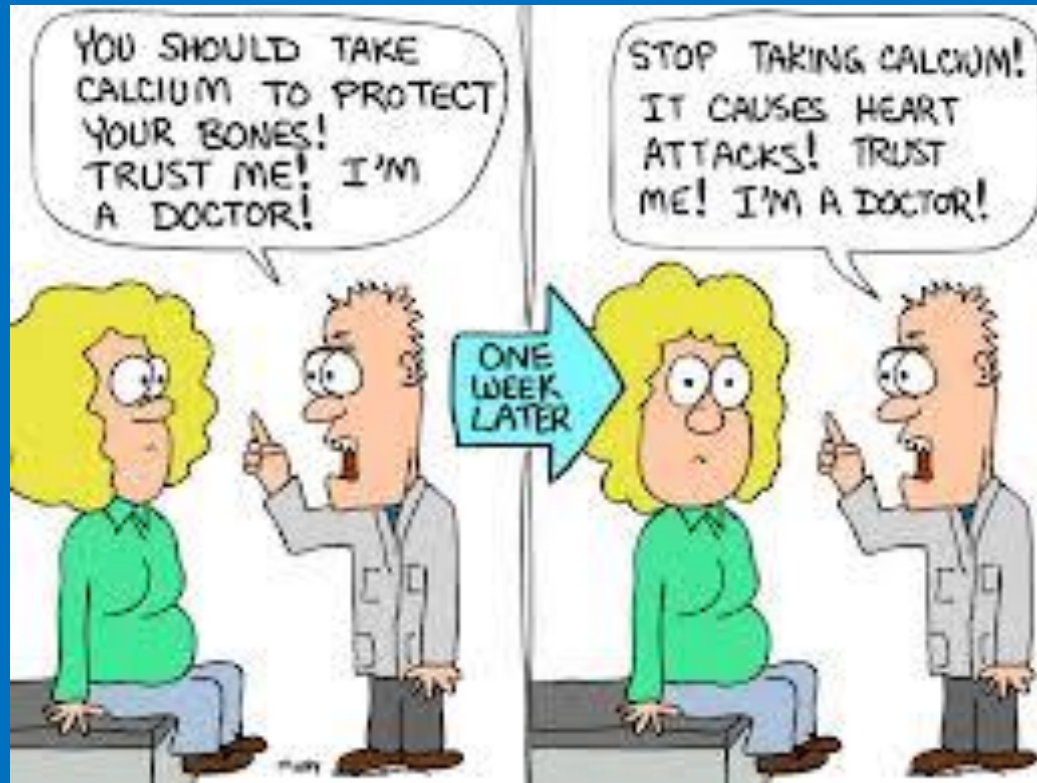
Lifestyle Modifications to Decrease the Risk of Colorectal Cancer

Estimates for 2018

American Cancer Society Data

Colorectal cancer	Men	Women
New cases	75,610	64,640
Deaths (8% of all cancer deaths)	27,390	23,240

- The incidence of colorectal cancer varies geographically.
- The incidence is higher in Western countries.
- There is a rapid increase in the rates of colon cancer among migrants from low-risk areas to high-risk areas.
- Geographic differences appear to be related to diet, environmental exposures, and genetic susceptibility.
- Physical inactivity, unhealthy diet, obesity, and smoking are thought to be contributing factors.



Many studies report conflicting results...

Red Meat

- Long-term consumption of red meat or processed meats appears to be associated with an increased risk of colorectal cancer.
- NEJM published a study in 1990 where female nurses (30 to 55 years of age) completed a questionnaire every 2 years.
- By 1986, during 512,488 person-years of follow-up, 150 incident cases of colon cancer had been documented.
- The prospective study showed increased risk of colon cancer in woman who consumed more red meat.
- No relationship was noted between fiber intake and the risk of colon cancer.

Vitamin D

- Vitamin D inhibits cell proliferation and angiogenesis.
- Vitamin D induces cell differentiation and apoptosis.
- Vitamin D has anti-inflammatory effects.
- Observational studies have revealed a link between poor vitamin D status and the risk of many cancers, including colorectal cancer.

Aspirin

- A substantial body of evidence suggests that aspirin and other NSAIDs protect against the development of colonic adenomas and cancer.
- Regular use of aspirin and other NSAIDs is associated with a 20-40% reduction in the risk of colonic adenomas and colorectal cancer in individuals at average risk.
- Low and high doses of aspirin are protective.

United States Preventative Services Task Force Recommendations

Adults ages 50 to 59 years	The USPSTF recommends low-dose aspirin use for the primary prevention of cardiovascular disease (CVD) and colorectal cancer in adults ages 50 to 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years.	B
Adults ages 60 to 69 years	The decision to use low-dose aspirin to prevent CVD and colorectal cancer in adults ages 60 to 69 years who have a greater than 10% 10-year CVD risk should be an individual one. Persons who are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years are more likely to benefit. Persons who place a higher value on the potential benefits than the potential harms may choose to use low-dose aspirin.	C
Adults younger than age 50 years	The current evidence is insufficient to assess the balance of benefits and harms of aspirin use to prevent CVD and colorectal cancer in adults younger than age 50 years.	I
Adults age 70 years and older	The current evidence is insufficient to assess the balance of benefits and harms of aspirin use to prevent CVD and colorectal cancer in adults age 70 years and older.	I

Proportion of colon cancer risk that might be preventable in a cohort of middle-aged US men.

Platz EA¹, Willett WC, Colditz GA, Rimm EB, Spiegelman D, Giovannucci E.

⊕ Author information

Abstract

OBJECTIVE: Diet and lifestyle likely play major roles in colon cancer incidence; however, the proportion of colon cancer risk that might be preventable is unknown. Thus, we estimated the proportion of colon cancer risk among men in the prospective Health Professionals Follow-up Study that might be attributable to a constellation of modifiable risk factors, and thus might be preventable.

METHODS: We included 47,927 men aged 40-75 years in 1986, among whom we confirmed 411 colon cancer cases from 1986 to 1996. Risk factors considered were obesity, physical inactivity, alcohol consumption, early adulthood cigarette smoking, red meat consumption, and low intake of folic acid from supplements. We calculated a risk score that was the sum across the six risk factors of the values of 1 (better exposure) to 5 (worse exposure) corresponding to the exposure category. We entered the risk score into a logistic regression model and estimated the population attributable risk percent (PAR%) using the method of Bruzzi et al.

RESULTS: After adjusting for age and family history of colorectal cancer and comparing the risk score for the combined six modifiable colon cancer risk factors at or above the approximate 20th, 10th, or 5th percentiles vs. below, the PAR% increased from 39% (95% confidence interval (CI) = 23-58%), to 48% (95% CI = 25-71%), to 55% (95% CI = 27-80%), respectively. Using a second method in which we used cut-points consistent with general-good health behaviors for each risk factor, comparing men with at least one risk factor to men without any risk factors (3.1% of the men), the PAR% was 71% (95% CI = 33-92%).

CONCLUSION: The findings from this analysis suggest that, if all the members of this cohort of middle-aged US men had a modifiable exposure distribution comparable to the men with low risk scores, a large proportion of colon cancer risk might be avoidable. Additional study is required to determine whether making changes in these six risk factors now would reduce the risk of colorectal neoplasia, or whether the proportion of colon neoplasia that might be avoidable would be similar in populations with different characteristics.

Screening for Lung Cancer

Estimated Deaths (2018)

Male

Lung & bronchus	83,550	26%
Prostate	29,430	9%
Colon & rectum	27,390	8%
Pancreas	23,020	7%
Liver & intrahepatic bile duct	20,540	6%
Leukemia	14,270	4%
Esophagus	12,850	4%
Urinary bladder	12,520	4%
Non-Hodgkin lymphoma	11,510	4%
Kidney & renal pelvis	10,010	3%
All sites	323,630	100%



Estimated Deaths (2018)

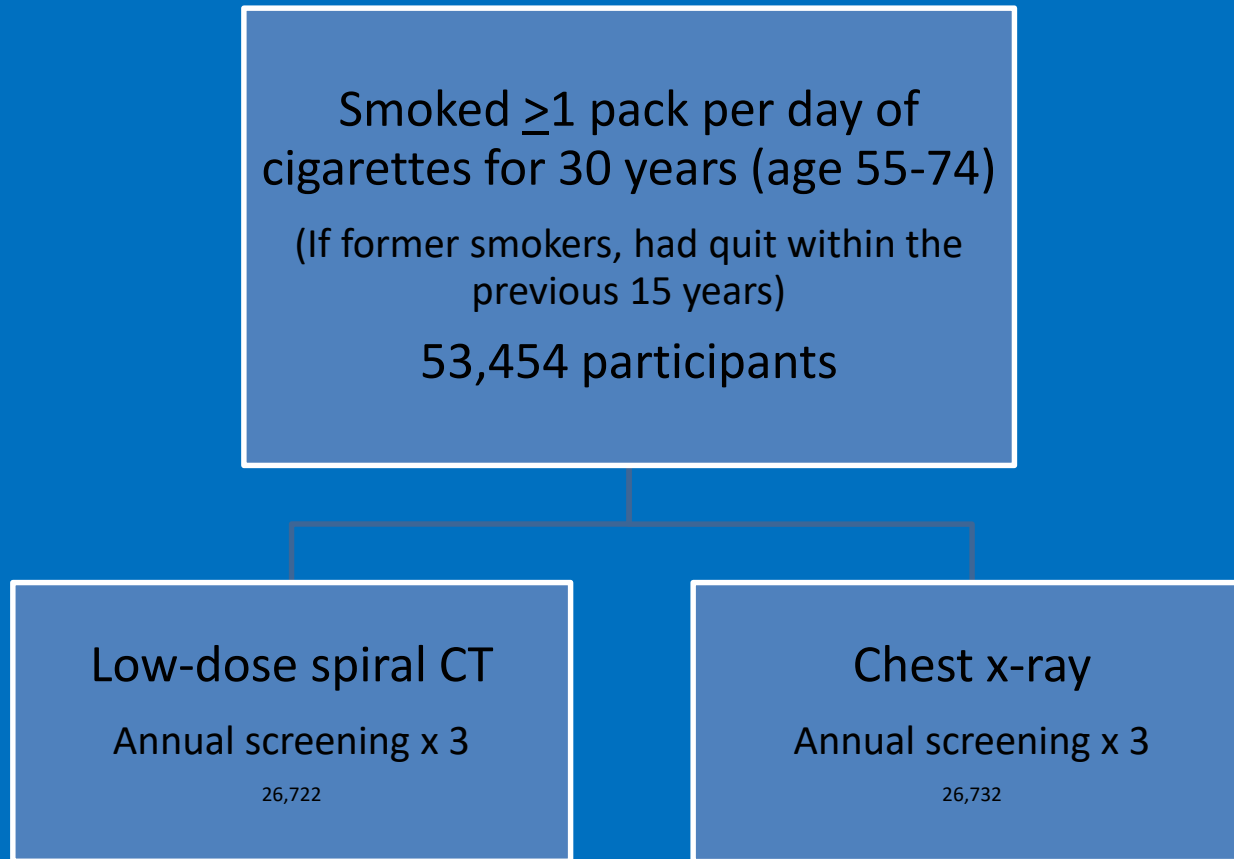
Female



Lung & bronchus	70,500	25%
Breast	40,920	14%
Colon & rectum	23,240	8%
Pancreas	21,310	7%
Ovary	14,070	5%
Uterine corpus	11,350	4%
Leukemia	10,100	4%
Liver & intrahepatic bile duct	9,660	3%
Non-Hodgkin lymphoma	8,400	3%
Brain & other nervous system	7,340	3%
All sites	286,010	100%

National Lung Screening Trial

August 2002 through April 2004

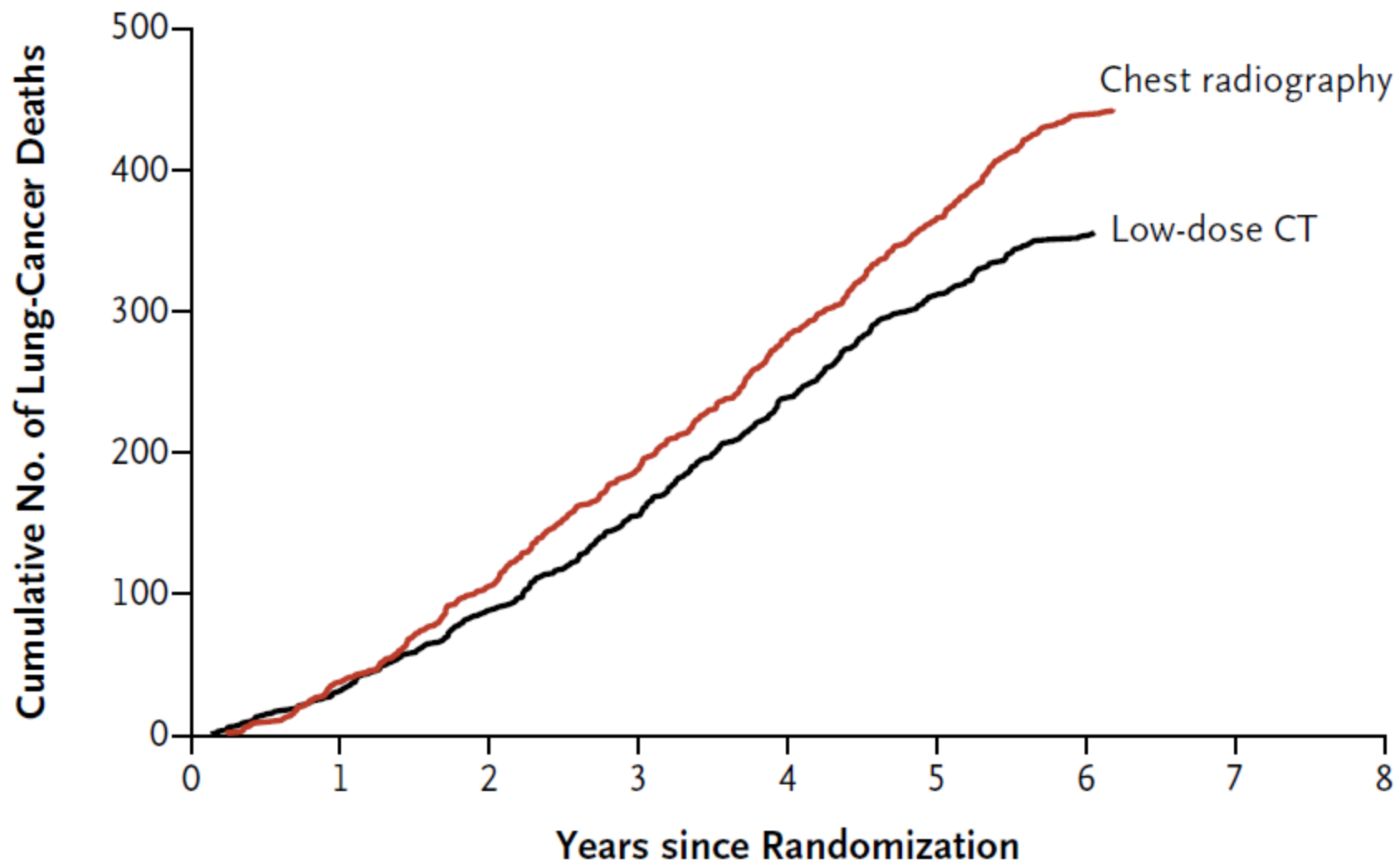


Results

Imaging	Positive test	Incidence of lung cancer per 100,000 person-years	Death from lung cancer per 100,000 person-years
Low-dose CT	24.2%	645 (1060 cancers)	247
Chest x-ray	6.9%	572 (941 cancers)	309

A relative reduction in mortality from lung cancer with low-dose CT screening of 20%.

B Death from Lung Cancer

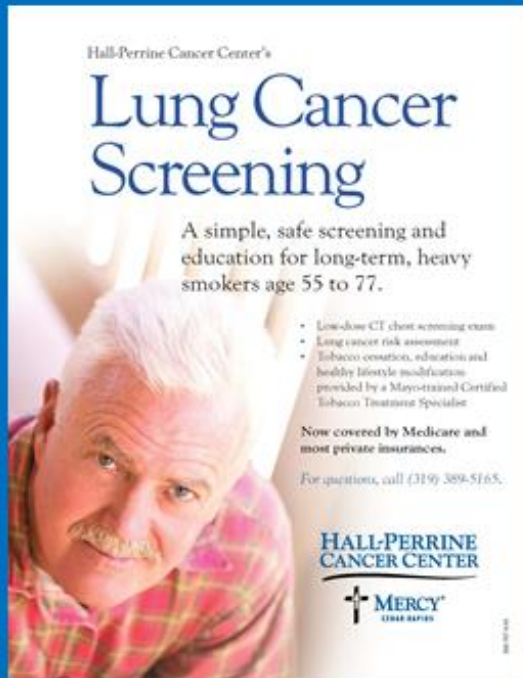


Things to consider...

- CT scans used today are technologically more advanced than those that were used in the trial.
- The reduction in the rate of death from lung cancer associated with an ongoing low-dose CT screening program was not estimated in the trial. (The trial only had 3 rounds of screening.)

- The USPSTF recommends annual screening for lung cancer with low dose CT in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.
- Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

- In 2015, the centers for Medicare and Medicaid services (CMS) issued a national coverage determination. (Medicare coverage of lung cancer screening with low dose CT if certain eligibility requirements are met.)



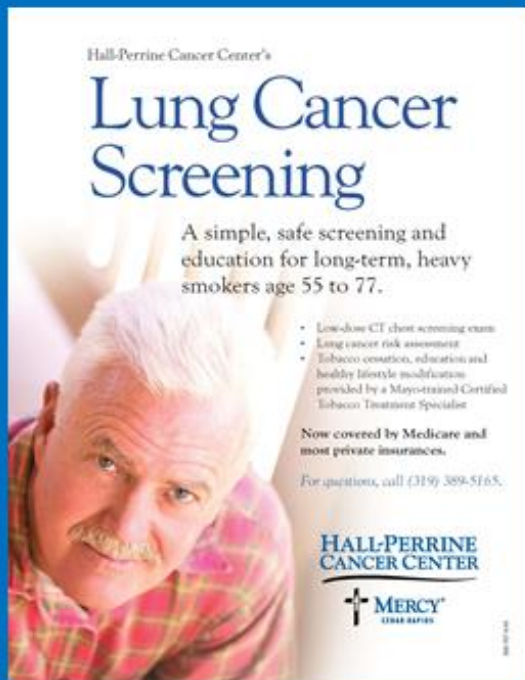
Medicare requires data be entered into a national registry (previously entered manually)

Data from Epic will now auto-populate information

A Best Practice Assessment pop-up in Epic will state if a patient meets criteria for low-dose CT screening

Medicare requires some sort of tobacco counseling along with the low-dose CT

The low-dose CT is scheduled with an assessment by Tobacco Treatment Specialist (Dawn Sabin)



The patient will receive a letter with the results

If necessary, the coordinator will contact the provider for a referral to pulmonary

Epic “glitch” with scheduling has been corrected (should be able to obtain scans in a timely manner)

The program is gearing up to perform low-dose CT scans 3 days a week (previously just once a week)

The low-dose CT scan may be costly for patients who have a high deductible (no more pay for service exams)

CAR T-cell Therapy

Categories of Drugs Used to Treat Cancer

- **Traditional chemotherapy** (affects cancer cells + healthy cells)
- **Targeted therapy** (target and disable genes or proteins found in cancer cells)
- **Hormone therapy** (breast and prostate cancers)
- **Immunotherapy** (helps your immune system fight cancer)

2018 Nobel Prize in Medicine Awarded to 2 Cancer Immunotherapy Researchers



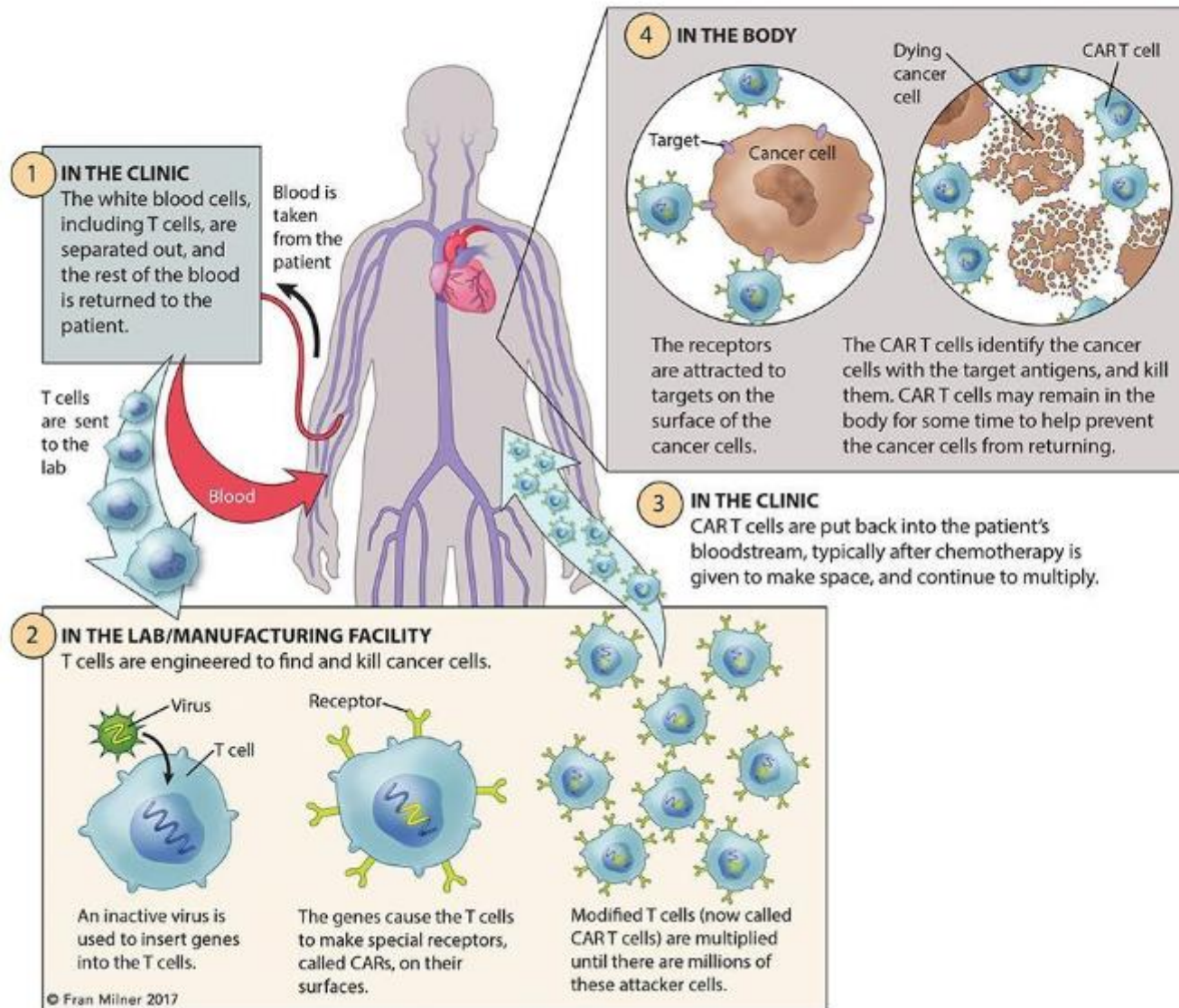
The Nobel Prize for Physiology and Medicine was awarded to James P. Allison, left, and Tasuku Honjo on Monday for their work on cancer research. Jonathan Nackstrand/Agence France-Presse — Getty Images

Chimeric antigen receptor (CAR) T cells

Genetically Modified T cells

- Step 1: T cells are collected from the patient via apheresis
- Step 2: T cell are re-engineered in the laboratory (DNA introduced to produce chimeric antigen receptors on the surface of cells- allows the T cells to recognize an antigen on targeted tumor cells)
- Step 3: The re-engineered CAR T cells are multiplied and frozen
- Step 4: The CAR T cells are sent back to the treatment center and infused into the patient

Chimeric Antigen Receptor T-Cell Therapy: How it Works



Hypercoagulable Workup

Possible Tests

- Protein C (\$45)
- Protein S (\$50)
- Antithrombin III (\$39)
- Factor V Leiden (\$78)
- Prothrombin gene mutation (\$93)
- Lupus anticoagulant (\$45)
- Antiphospholipid antibodies (~\$20)
- Beta-2 glycoprotein 1 antibodies (\$20)
- MTHFR mutation (\$126)

- No general consensus exists on who should undergo thrombophilia testing.
- Evidence-based guidelines recommend against routine thrombophilia testing because identification of inherited abnormalities does not alter the duration of recommended anticoagulation or reliably predict the risk of recurrence.

- Hip/knee arthroplasty, cancer surgery, and abdominal/pelvic surgery are associated with a particularly high risk of venous thromboembolism.
- Approximately 40% of venous thromboembolism are associated with hospitalization.
- Approximately 20% of all venous thromboembolism occur in patients with cancer.

- Approximately 6% of patients with unprovoked venous thromboembolism have an undiagnosed cancer at the time of thrombosis.
- Approximately 10% of patients with unprovoked venous thromboembolism will be diagnosed with a cancer in the year following the thrombotic event.
- Cancer should be considered in select patients- unexplained symptoms (weight loss) or abnormal laboratory tests (anemia).

#1 Case Presentation

- The patient is a 36 year old woman who was diagnosed with a left lower extremity DVT (below the knee) in 2001.
- At the time, the patient was taking oral contraceptive pills + smoking.
- A hypercoagulable workup revealed factor V Leiden mutation (heterozygous).

#1 Case Continued...

- The patient completed 1 year of Coumadin.
- The patient was diagnosed with superficial thrombophlebitis of the left lower extremity in 2004.
- The patient was still taking oral contraceptive pills + smoking.
- It was decided to keep the patient on anticoagulation therapy.

#1 Case Continued...

- During pregnancy, the patient was treated with Lovenox and heparin.
- The patient was evaluated in the hematology clinic in 2018.
- The patient had Essure fallopian tube procedure for contraception.
- The patient was no longer smoking.
- The patient was instructed to discontinue Xarelto and take a daily aspirin.

#2 Case Presentation

- The patient is a 41 year old woman who was diagnosed with a pulmonary embolism in January 2018.
- At the time, the patient was taking oral contraceptive pills.
- The patient was prescribed Eliquis.

#2 Case Continued...

- The patient did not have prolonged immobility or history of travel.
- The patient denies pregnancy complications and spontaneous miscarriage.
- There is no family history of thrombosis.

#2 Case Continued...

- The patient states that she sometimes forgets to take Eliquis.
- The patient states that she is having unprotected sex while on anticoagulation.

#3 Case Presentation

- The patient is a 55-year-old woman with multiple comorbidities (including diabetes with neuropathy, COPD, sleep apnea, morbid obesity).
- The patient was initially diagnosed with a pulmonary embolism in 2007.
- While the patient was on warfarin, the patient was found to have low protein C and protein S levels.
- The patient completed 6 months of warfarin therapy.

#3 Case Continued...

- In 2018, the patient sought medical attention for shortness of breath.
- A CT scan of the chest showed a small pulmonary embolism.
- The patient was started on Eliquis.

Type of Thrombotic Event	Duration of Anticoagulant Therapy
Distal leg DVT <ul style="list-style-type: none"> • Provoked/unprovoked (mild symptoms) • Provoked/unprovoked (moderate-severe symptoms) 	<ul style="list-style-type: none"> • No anticoagulation suggested (serial US x 2 weeks) • 3 months
Proximal leg DVT or PE <ul style="list-style-type: none"> • Provoked (surgery/trauma/immobility) • Unprovoked • Recurrent 	<ul style="list-style-type: none"> • 3 months • Extended • Duration of therapy depends on whether the thrombotic events were provoked or unprovoked
Upper extremity DVT (proximal)	<ul style="list-style-type: none"> • At least 3 months
Cancer associated DVT or PE	<ul style="list-style-type: none"> • As long as the cancer is active or being treated. • Low molecular weight heparin is the preferred anticoagulant
Chronic thromboembolic pulmonary hypertension	<ul style="list-style-type: none"> • Extended