AGENDA
Kentucky Lung Cancer Research Program
Governance Board

Council on Postsecondary Education
Wednesday, February 26, 2014
3:00 PM
Conference Room A

Kentucky Lung Cancer Research Program
Governance Board Meeting
November 21, 2013
Via LYNC, teleconferencing

Present: Jim Roach (MAL & Chair), Joe Graviss (MAL), Travis Powell (CPE General Counsel), Linda Linville (CPE) – at CPE offices; Tim Mullett (UK), Nathan Vanderford (UK), Kris Damron (UK, KCTN), Beth Yost (UK) – at UK; John Eaton (UofL), Dianne Konzen (UofL) at UofL; Amdullah Khan, MAL – in Somerset.

Absent: Mark Evers (UK), Don Miller (UofL), Dan Flanagan (CPE), Dr. Rajan Joshi (MAL)

At 1:05 PM the KLCRP Governance Board meeting was called to order by chair, Dr. Jim Roach.

Motion made by Dr. Mullett, seconded by Dr. Eaton to approve GM meeting minutes from 9/18/13. Motion passed.

The SciMed contractual agreement for the KLCRP review was discussed with Travis Powell delineating process to date, with RFP extended on two occasions with one proposal received, reviewed for competency and recommended for approval. Mr. Graviss motioned for approval with Dr. Mullett seconding, motion passed. Expecting completion of the study is June 30, 2013, with a possible extension dependent upon schedule of GB for final face to face report. SciMed consultants will determine additional documents once their initial team meets and determines additional sources needed.

The annual report from Markey was reviewed at the September meeting. The Brown Cancer Center report was included in the November packet of information. Both were recommended for approval, with motion to approve made by Dr. Eaton, and seconded by Dr. Mullett. Motion passed.

Kris Damron provided information for a continuation of Cycle 12 study being conducted by Studts and Valentino requesting $90,000 form their grant funding. The study has new providers at University of Louisville, and Pikeville participating. This study will optimize head and neck and lung cancer accrual to quality trails and perhaps improve smoking cessation related work in this area. Dr. Eaton motioned to approve this continuation grant with Dr. Mullett seconding. Motion passed.

Dr. Roach presented the recommendation made by Brown Cancer Center to utilize 50% of their carry-forward funds in the II grant category be moved to the NCI designation budget. Nathan Vanderford explained the idea that this transfer of designated budget could still be utilized for funding grants, but for other areas as well. Clarification of this recommendation was needed which neither Ms. Konzen, nor Dr. Eaton were familiar, so the recommendation was tabled for future discussion and clarification.

Travis Powell explained the current litigation regarding the Master Tobacco Settlement Agreement with Kentucky and a number of other states. The impact of diminished funds for the KLCRP are not known at this time and may not be known for months or even years with on-going review by the Attorney General and tobacco companies. Travis will continue to monitor this development with the Attorney General's office and the state budget office. In recent budget approval by CPE, the pass-through funds were approved at $4,367,000/year for FY 14-16.

There being no further business, the meeting was adjourned at 1:40 PM.

Submitted as DRAFT 11/21/13
Linda Linville, Ph.D.

The Kentucky Lung Cancer Research Program:

A Review

Interim Report – February 22, 2014

Catherine Rahilly-Tierney MD MPH

Bernard Fuemmeler PhD MPH

Eric Grogan MD MPH

Peter Mazzone MD MPH

Pierre Massion MD

Kenneth Lieberman PhD

INTRODUCTION

The incidence of lung cancer in Kentucky has historically been the highest in the U.S., with 121.7 persons per 100,000 diagnosed with invasive lung or bronchus cancer in 2010 (most recent year available from http://apps.nccd.cdc.gov/uscs/cancersrankedbystate.aspx). The Kentucky Lung Cancer Research Program (KLCRP) was established in 2001 as a collaborative endeavor between the University of Kentucky (UK) and the University of Louisville(U of L) with the overarching objective to reduce the mortality and morbidity of Kentuckians from lung cancer. This 20-year initiative is now in its 14th year. The KLCRP is governed by a Board (GB) consisting of 9 members including 2 from each of the participating institutions, 2 from the Office of Continuing Professional Education (CPE) in Kentucky, and 3 members-at-large. The purpose of this review is determine the degree to which the KLCRP has met or is on track to meet its objectives as delineated in the program's Strategic Plan.

METHODS

To facilitate each panelist's review, we have prepared customized focus questions based on our initial reviews of the 2001 Strategic Plan and its updates in 2006, 2010, and 2012. Focus questions were prepared for each of 5 areas of priority defined by the Strategic Plans, including Prevention, Epidemiology, Early Detection and Treatment, Clinical Trials Network (CTN)/National Cancer Institute (NCI) Designation, and Investigator-Initiated (II) Grants/Translational research. These questionnaires are included in an addendum to this report. Each expert on our 5-person panel is assigned one priority area on which to focus their review, generally in an area in which they have research experience.

Members of Team Science

The panel includes expertise in research ranging from tobacco cessation to clinical trials in oncology. **Kenneth W. Lieberman PhD** is a toxicologist with faculty positions in the departments of Psychiatry, Pediatrics, and Pathology at New Jersey Medical School/Rutgers University. **Catherine Rahilly-Tierney MD MPH** is faculty at Harvard Medical School and the Division of Aging at Brigham and Women's Hospital, and is a staff physician in Primary care in the Boston Veterans Affairs System. KWL and CRT are facilitating the entire review, while Catherine is additionally serving as Team Science's epidemiologist. **Bernard Fuemmeler PhD MPH** is faculty in the Department of Community and Family Medicine at Duke University School of Medicine and is serving as the panel's expert in smoking cessation research. **Eric Grogan MD MPH** is a cardiothoracic surgeon at Vanderbilt University Medical Center and is reviewing the CTN/NCI designation priority area of the KLCRP. **Pierre Massion MD** is faculty in the Department of Allergy, Pulmonary and Critical Care Medicine at Vanderbilt University Medical Center

and is reviewing the II Grants and Translational Research priority area of the KLCRP. **Peter Mazzone MD MPH** is faculty in the Department of Pulmonary Medicine at Cleveland Clinic and is reviewing the Early Detection priority area of the KLCRP.

Process of the Review

The review will consist of 3 phases. During **Phase I**, each of the 5 members of Team Science will independently review documents provided to us by the CPE, including the original legislation establishing the KLCRP; the 2001 Strategic Plan for the program and updates in 2006, 2010, and 2012; Annual Reports and Expenditure reports from each of the 2 institutions that received monies from the program; and lists of II Grant awardees; and comprehensive lists of publications sponsored by the program from each of the 2 institutions. Each panelist will also review the websites for the KLCRP and for each of the 2 institutions. In parallel with document review phase, KWL and CRT will conduct interviews with selected administrators at each of the institutions to supplement the expert's review by identifying staff with whom the expert panelists should speak, and by eliciting opinions regarding whether or not the program is meeting its original objectives. At the conclusion of Phase I of the review, each expert will have prepared lists of selected staff at each of the 2 institutions with whom they would like to speak.

Phase II will consist of interviews between each of the panelists and selected staff members at each of the institutions. Some of these interviews will occur in-person during site visits by the panelists to each of the institutions. During **Phase III**, each panelist will prepare a report describing their findings. The panelists have been instructed to focus their report on whether or not the original KLCRP objectives in their assigned Priority Area have been met or are on track to be met, using the prepared questions as a guide. The individual reports will be summarized into a final report to be delivered to CPE.

PROGRESS TO DATE

At this time, our experts are completing their review of the documents provided to us by CPE, and that review should be completed by approximately March 12 2014. KWL and CRT have also completed interviews with several key individuals associated with the KLCRP including: Donald Miller, MD PhD, director of the James G Brown Cancer Center (JGBCC); Mark Evers MD, director of the Markey Cancer Center (MCC); Milton Pierson, Senior Associate Director at JGBCC; Nathan Vanderford PhD MBA, Assistant Director of Research at MCC; Elizabeth Yost, Assistant Director of Finance at MCC; James Roach MD, GB chairman; Joseph Graviss, GB member-at-large; Harold Carloss MD, former GB chairman; and Alan Dougherty PhD, Associate Dean for Research at MCC. We plan to schedule interviews between

panelists and chosen staff members at each of the institutions beginning early March, and project site visits to be scheduled for April.

ADDENDA

Following are each of 5 questionnaires, one for each of the 5 priority areas of the KLCRP which we identified upon our review of the original and updated Strategic Plans. We are asking our expert panel to focus their reviews and their reports on issues raised in these questionnaires.

TO: Bernard Fuemmeler PhD MPH

FROM: Sci Med Consulting, LLC

DATE: January 1, 2014

RE: **Kentucky Lung Cancer Research Program: Prevention of lung cancer**

Dear Bernard

Thank you for participating in this important project. Given your research background, we would like you to review Kentucky's Lung Cancer Research Program (KLCRP) focusing on the priority area of **Prevention** of lung cancer.

I. **Materials for your review**. To complete your review, you will be provided with the following documents:

1.Original legislation establishing the KLCRP and the Governance Board (GB) that oversees it

2.Original Strategic Plan (SP) for the KLCRP as developed by the GB in 2001, with updates in 2006, 2010, and 2012

3.Annual reports prepared by GB and the office of Continuing Postsecondary Education (CPE) about the program, from 2006 through 2013

4.Financial reports prepared by staff at University of Kentucky (UK) and University of Louisville (U of L) spanning years from 2007 through 2013

5.Lists of grant awardees at UK and U of L.

In addition to these resources, we expect you to examine the medical literature, and review the following websites:

http://kentuckylungcancer.org/ (main site for the KLCRP)

http://kentuckylungcancer.org/contact_us.html (universities' contact information for the program)

http://www.research.uky.edu/aspnet/vsprojects/spifi/search.aspx (list of UK investigator-initiated (II) awardees/grants)

In addition to these web resources, we expect you to do your own searching/investigation to find evidence/answers to the questions below.

II. **Content of your review.** We would like you to think about the following specific questions as you review these sources.

I. The lung cancer research program was originally intended to be a collaboration between UK and U of L. Is there evidence of collaborations between researchers at each of these institutions?

II. Is there evidence of a trend of increasing number of publications each year coming out of UK and U of L? Specifically, the 2006 updated SP calls for a 300% increase in publications between 2000 and 2008. Did this take place?

III. The original SP called for improvement and expansion of smoking cessation/prevention initiatives targeting schools. Is there any evidence that extant programs were expanded or new ones initiated?

IV. The original SP called for "clinical implementation of smoking cessation" – interpretation of this might be the initiation or augmentation of clinics that specifically work with patients toward smoking cessation. Is there any evidence that such clinics were set up at one or both of the cancer centers?

V. The original SP called for the development of behavior studies on smoking cessation and tobacco abuse.
   a. Can you find evidence of such studies being initiated and published?
   b. Can you find evidence that advances in smoking cessation (one example might be availability of support for safe use of varenicline) being incorporated into any clinical programs focused on smoking cessation?

VI. The 5-year section of the original SP called for the development of a website where Kentuckians could read about the risks of tobacco use including lung cancer.
   a. Does such a website exist?
   b. Is there any evidence for more active programs targeting smoking prevention and cessation, such as phone outreach programs or informational brochures made available through schools/mailing campaigns etc?

VII. The long-term section of the original SP called for updates provided to Kentuckians regarding innovations in lung cancer treatment and prevention. Presumably such updates would be available through mass media (articles in the lay press) or on the aforementioned website. Can you find evidence that such updates were made available at any time to the lay public?

VIII. The Assessment of Success section of the original SP called for assessments of trends in knowledge of Kentuckians related to risks of tobacco use and related to therapies of lung cancer.
   a. Have there been any studies looking at trends in knowledge of the population in Kentucky?
   b. Is there evidence of public activism (non-for-profit organizations focused on prevention and cessation, etc)?

IX. Are there any publications that demonstrate trends in smoking rates in adults and adolescents in Kentucky? If so, is a decrease in such rates over time demonstrated?

X. The 2010 updated SP calls for development of lung cancer prevention methodologies without being specific. Can you find any evidence that any KLCRP funding went toward lung cancer prevention programs?

III. Interviews and site visits with selected staff from UK and U of L.

In the process of reviewing the documents and websites we provide, the medical literature, and any other sources you might discover, we expect you to identify key staff people at these institutions with whom you would like to speak. We will facilitate conference calls and site visits, to take place starting approximately early March.

KLCRP Epidemiology of Lung Cancer in Kentucky: pertinent questions

1. Have new projects been initiated/funded that "increase understanding of lung cancer in commonwealth of Kentucky"?
    a. Is there evidence of studies that describe the epidemiology of lung cancer in Kentucky, through year 5 after the KLCRP was established?
2. The lung cancer research program was originally intended to be a collaboration between UK and U of L (see KLCRP 1st Strategic Plan 2001 page 3). Is their evidence of collaborations between researchers at each of these institutions?
3. Is there evidence of a trend of increasing number of publications each year coming out of UK and U of L?
    XI. Specifically, the 2006 updated Strategic Plan calls for a 300% increase in publications between 2000 and 2008. Did this take place?
4. Starting with the 2006 updated Strategic plan, there is a call for expanding the LCRP to include support for research related to cancers other than lung, that are associated with smoking. Is there evidence for support of research on non-lung, smoking –related cancers at these 2 institutions?
5. Original SP called for baseline demographics, tx and outcome of lung cancer cases be published by "Area Development Districts" using Kentucky Cancer Registry. Did this happen?
    a. Original SP also called for expansion of the KCR to include other variables. Did this happen?
        a. As part of this, they wanted the KCR to be expanded to include molecular biomarkers, did this happen?
    b. Was a data coordinator to manage research projects out of this database hired?
    c. Was software making the data accessible to docs who want to add to it OR researchers who want to use it, developed?
    d. One goal listed in the 5-year development section of the original SP was "rapid case ascertainment." Can you determine the length of time between diagnosis of an incident case and the date the case's data is entered into the KCR?
6. Original SP called for development of a family registry of lung cancer cases.
    a. Did this happen?
    b. The 5-year development section of the original SP called for this registry to ultimately have tissue and blood banked. Did this happen?
7. Original SP called for information re: lung cancer epidemiology be dispersed to the population quarterly. Did/does this happen?
8. For EG/PM: Is there evidence of published information on the 2 most affected "ADDs" in Kentucky in the first 2-5 years of the program? If so, which areas are these?
9. The long-range section of the original Strategic Plan called for studies to identify genetic mutations associated with increased risk of lung cancer.
    a. Did/do any such studies take place?
    b. Did a screening program for genetic factors associated with increased risk of lung cancer get underway?

10. Have there been publications reporting trends in incident lung cancer in Kentucky? Publications reporting trends in mortality/survival of incident cases in Kentucky?
11. Has there been an improvement in OS of lung cancer cases in Kentucky?
12. Have there been publications describing a study in which the relationship between emphysema and lung cancer is studied using Kentucky data?
13. 2010 SP calls for studies that refine methodologies for risk factor delineation – did this happen?

TO: Peter Mazzone MD MPH

FROM: Sci Med Consulting, LLC

DATE: January 1, 2014

RE: **Kentucky Lung Cancer Research Program: Early detection and treatment of lung cancer**

Dear Peter

Thank you for participating in this important project. Given your research backgrounds, we would like you to review Kentucky's Lung Cancer Research Program (KLCRP) focusing on the priority area of **early detection and treatment** of lung cancer.

I. **Materials for your review**. To complete your review, you will be provided with the following documents:

1.Original legislation establishing the KLCRP and the Governance Board (GB) that oversees it

2.Original Strategic Plan (SP) for the KLCRP as developed by the GB in 2001, with updates in 2006, 2010, and 2012

3.Annual reports prepared by GB and the office of Continuing Postsecondary Education (CPE) about the program, from 2006 through 2013

4.Financial reports prepared by staff at University of Kentucky (UK) and University of Louisville (U of L) spanning years from 2007 through 2013

5.Lists of grant awardees at UK and U of L.

In addition to these resources, we expect you to examine the medical literature, and review the following websites:

http://kentuckylungcancer.org/ (main site for the KLCRP)

http://kentuckylungcancer.org/contact_us.html (universities' contact information for the program)

http://www.research.uky.edu/aspnet/vsprojects/spifi/search.aspx (list of UK investigator-initiated (II) awardees/grants)

In addition to these web resources, we expect you to do your own searching/investigation to find evidence/answers to the questions below.

II. **Content of your review.** We would like you to think about the following specific questions as you review these sources.

I. The lung cancer research program was originally intended to be a collaboration between UK and U of L (see KLCRP 1st Strategic Plan 2001 page 3). Is there evidence of collaborations between researchers at each of these institutions?

II. Is there evidence of a trend of increasing number of publications each year coming out of UK and U of L? Specifically, the 2006 updated SP calls for a 300% increase in publications between 2000 and 2008. Did this take place?

III. The original SP foresaw a CT scan screening program developed and implemented between year 1 and Year 10 of the program. Did this occur?
   a. As part of this, the original SP called for a mobile CT scan network to service underserved areas of Kentucky. Can you find evidence that such a program was set up?
   b. As part of this, the original SP called for a CT scanning program to be developed in the 2 areas of highest lung cancer incidence (they call these "Area Development Districts").
      i. Is there evidence that epidemiology data was published naming these areas? When was that published? (Coordinate with CRT on this!)
      ii. Is there evidence that CT scanning program was made available in these areas?
      iii. By the 2006 updated SP, the GB names active early detection programs in each ADD as an endpoint of interest by 2008. Can you find evidence that each ADD in Kentucky has such screening taking place, either coordinated locally or from a remote center?
   c. Can you identify one or more centralized programs where screening modalities (PET/CT/facilities for bronchoscopy/facilities for CT surgery) are organized in one place?
      i. The 5-year section of the original SP called for augmentation of screening program(s) using novel/advance modalities of detection (molecular markers, other assays beyond imaging). If you can identify such a screening program, was that program limited to imaging or were additional testing modalities added?
      ii. If such facility(s) exist, do they have organized core labs for banking specimens that can be used for research purposes? Is there evidence that research taking advantage of such a resource is taking place?
      iii. If such facility(s) exist, is there evidence of resources/funding from the LCRP to support such a facility(s)?
      iv. Is there evidence of outreach from a centralized screening program to regional/local hospitals to ensure patients remote from the larger centers still have access to lung cancer screening, if warranted?

IV. In the long-range section of the original SP, a goal of publishing data from the screening program (screening rates, rates of incident lung cancer diagnosed, etc).
   a. Can you find evidence of any such publications (reporting numbers of patients screened, or trends over time in numbers screened) in the lay press and/or the

medical literature? Is there evidence of studies validating an evidence-based algorithm for lung cancer risk assessment?

b. Is there evidence/publications reporting improvement in detection of lung cancer at earlier stages?
c. Is there evidence that data from Kentucky has been included in papers addressing rates of screening and early detection for lung cancer at the national level?
d. Is there evidence of investigator-initiated studies related to early lung cancer detection, biomarkers associated with lung cancer, etc?

V. In the 2006 updated SP, there is a call for adoption of national screening recommendations for the detection of lung cancer.
   a. Have there been any studies looking at compliance with such guidelines in Kentucky?
   b. Is there evidence of CME programs available to Kentucky primary care physicians in which updated guidelines related to lung cancer surveillance are imparted?

VI. Is there evidence that community physicians are satisfied with the resources available to them?
   a. Is there evidence that input from community physicians related to accessibility of lung cancer screening programs is procured in efforts to improve any lung cancer screening programs (s) that exist?
   b. Is there evidence that community physicians are satisfied with the availability of lung cancer screening modalities for their patients? Is there evidence that community physicians are satisfied with the availability of programs to which they can refer patients with lung nodules/masses for early diagnosis and treatment?

III. Interviews and site visits with selected staff from UK and U of L.

In the process of reviewing the documents and websites we provide, the medical literature, and any other sources you might discover, we expect you to identify key staff people at these institutions with whom you would like to speak. We will facilitate conference calls and site visits, to take place starting approximately early March.

TO: Eric Grogan MD MPH

FROM: Sci Med Consulting, LLC

DATE: January 1, 2014

RE: Kentucky Lung Cancer Research Program: Clinical Trials Network and National Cancer Institute designation

Thank you for participating in this important project. Given your research background, we would like you to review Kentucky's Lung Cancer Research Program (KLCRP) focusing on the priority area of **establishing a clinical trials network and National Cancer Institute designation**.

I. **Materials for your review**. To complete your review, you will be provided with the following documents:

1.Original legislation establishing the KLCRP and the Governance Board (GB) that oversees it

2.Original Strategic Plan (SP) for the KLCRP as developed by the GB in 2001, with updates in 2006, 2010, and 2012

3.Annual reports prepared by GB and the office of Continuing Postsecondary Education (CPE) about the program, from 2006 through 2013

4.Financial reports prepared by staff at University of Kentucky (UK) and University of Louisville (U of L) spanning years from 2007 through 2013

5.Lists of grant awardees at UK and U of L.

In addition to these resources, we expect you to examine the medical literature, and review the following websites:

http://kentuckylungcancer.org/ (main site for the KLCRP)

http://kentuckylungcancer.org/contact_us.html (universities' contact information for the program)

http://www.research.uky.edu/aspnet/vsprojects/spifi/search.aspx (list of UK investigator-initiated (II) awardees/grants)

In addition to these web resources, we expect you to do your own searching/investigation to find evidence/answers to the questions below.

II. **Content of your review.** We would like you to think about the following specific questions as you review these sources.

I. The lung cancer research program was originally intended to be a collaboration between UK and U of L. Is there evidence of collaborations between researchers at each of these institutions?

II. Is there evidence of a trend of increasing number of publications each year coming out of UK and U of L? Specifically, the 2006 updated SP calls for a 300% increase in publications between 2000 and 2008. Did this take place?

III. The original SP foresees the Clinical Trials Network (CTN) developing between year 2 and 20 of the program.
   a. A Task Force was to be developed to set up a CTN. Can you identify such a task force?
   b. The Task Force was supposed to make assessments of what impediments might have existed to patient enrollment in clinical trials in KY. Is there any evidence of such reports or assessments?
   c. Was a state-based IRB set up?
   d. The original SP called for a pilot program to assess the feasibility of remote, web-based enrollment of patients into clinical trials. Is there evidence that such a pilot was attempted? Was it successful? Does a program to enroll patients in remote areas in clinical trials exist today?
   e. How many sites are available now for recruitment into clinical trials? How long has each of these been in operation?

IV. Is there evidence of a central Network Operations Office(s) from which multi-site clinical trials can be coordinated?
   a. Is there evidence of coordinated efforts to develop training materials and train staff and investigators at multiple clinical sites for patient recruitment and monitoring in clinical trials?
   b. Is there evidence that such an Office additionally involves itself in organizing committees/task forces to develop novel methods in clinical trials implementation? Does the Office interact with committees at regional sites to improve clinical trial implementation?

V. Is there evidence of administrative body(s) through which industry-sponsored clinical trials can be funded and coordinated? Is there evidence that over time, an increasing number of industry-sponsored trials take place either wholly or partially in Kentucky (ie Kentuckians have access to them)?

VI. The 2006 updated SP mentions that one objective of the Clinical Trials facet of the KLCRP is that there is an increase in the number of active clinical trials in Kentucky.
   a. Is there evidence of an increasing number of clinical trials of any kind in Kentucky?
   b. Is there evidence of participation in national or international cooperative group studies/trials?

c. Is there evidence that the number of Kentuckians enrolled in clinical trials is increasing over time?

VII. The original SP called for the CTN to be "augmented with new technologies" starting around year 4 of the program. Examples might be additional laboratory facilities for banking blood; pharmacy facilities for preparing new therapeutics; new imaging equipment to monitor enrolled patients, etc. Can you find any evidence that CTN sites expanded in any of these ways?

VIII. The 5-year section of the original SP called for statewide telemedicine conferences including all physicians enrolling patients into clinical trials, in which dialogue regarding obstacles to enrollment, findings for trials already underway or completed, etc could take place. Is there evidence that such meeting(s) take place?

IX. All of the SPs call for NCI designation of one or both cancer centers. This has occurred for the Markey Center in Spring of 2013.

a. Is it likely that U of L will additionally be so designated?
b. Is there evidence that U of L has submitted documents required for NCI designation? Where is the U of L in the submission process?
c. Is there evidence of interactions with the NCI Centers Branch Director? Were there recommendations received from such a Director?
d. The 2010 updated SP calls for 3-5 NCI-designable cancer research programs at each institution.
    i. Can you identify such programs?
    ii. The 2010 updated SP calls for NCI funding to each institution in the range of $12-15 million. Is there evidence that such funding has come/is coming into the institutions to support aforementioned programs?
e. Is there evidence of preparation of P30 application for NCI designation?

X. Is there evidence that community physicians referring cases of lung cancer are satisfied with the resources (oncologists, treatment centers, access to clinical trials, etc) available to them?

a. Is there evidence that lung cancer patients have access to multi-disciplinary clinics that manage all aspects of their disease (ie with social workers, mental health workers, etc)
b. Is there evidence that Kentucky physicians in the community are satisfied with resources available to them to facilitate referring patients with lung cancer for clinical trial enrollment? Is information about available clinical trials reaching the public, either through mass media (websites, lay press) or by educating community physicians about them?

XI. Starting with the 2006 updated SP, there is a call for expanding the LCRP to include support for research related to cancers other than lung, that are associated with smoking. Is there evidence for support of research on non-lung, smoking –related cancers at these 2 institutions?

III. Interviews and site visits with selected staff from UK and U of L.

In the process of reviewing the documents and websites we provide, the medical literature, and any other sources you might discover, we expect you to identify key staff people at these institutions with whom you would like to speak. We will facilitate conference calls and site visits, to take place starting approximately early March.

TO: Pierre Massion MD

FROM: Sci Med Consulting, LLC

DATE: January 1, 2014

RE: Kentucky Lung Cancer Research Program: Translational Research and Investigator-Initiated Grants

Dear Pierre

Thank you for participating in this important project. Given your research background, we would like you to review Kentucky's Lung Cancer Research Program (KLCRP) focusing on the priority area of **translational research and investigator-initiated grants**.

I. Materials for your review. To complete your review, you will be provided with the following documents:

1.Original legislation establishing the KLCRP and the Governance Board (GB) that oversees it

2.Original Strategic Plan (SP) for the KLCRP as developed by the GB in 2001, with updates in 2006, 2010, and 2012

3.Annual reports prepared by GB and the office of Continuing Postsecondary Education (CPE) about the program, from 2006 through 2013

4.Financial reports prepared by staff at University of Kentucky (UK) and University of Louisville (U of L) spanning years from 2007 through 2013

5.Lists of grant awardees at UK and U of L.

In addition to these resources, we expect you to examine the medical literature, and review the following websites:

http://kentuckylungcancer.org/ (main site for the KLCRP)

http://kentuckylungcancer.org/contact_us.html (universities' contact information for the program)

http://www.research.uky.edu/aspnet/vsprojects/spifi/search.aspx (list of UK investigator-initiated (II) awardees/grants)

In addition to these web resources, we expect you to do your own searching/investigation to find evidence/answers to the questions below.

II. Content of your review. We would like you to think about the following specific questions as you review these sources.

I. The lung cancer research program was originally intended to be a collaboration between UK and U of L . Is there evidence of collaborations between researchers at each of these institutions?

II. Is there evidence of a trend of increasing number of publications each year coming out of UK and U of L? Specifically, the 2006 updated SP calls for a 300% increase in publications between 2000 and 2008. Did this take place?

III. What is the process for grant review for investigator-initiated projects?
   a. The original SP called for the selection by the GB of an External Advisory Committee to evaluate new proposals within the first 2 years of the program. Was such a Committee established?
   b. Is there adequate internal review (ie by the GB) of internal grant proposals prior to funding such projects? What criteria does the GB use to evaluate investigator initiated proposals?

IV. The original SP foresees Investigator Initiated projects funded starting during year 2 of the LCRP. Did this take place?
   a. Can you determine when the initial RFPs for the first funded projects were made available? Have additional RFPs been made available each year for Kentucky researchers?
   b. The original RFPs from the GB were supposed to be in the areas of both basic and translational research. Can you identify evidence that projects in these areas are funded?
   c. The original SP also called for funding of investigator-initiated projects/studies related to improving radiation therapy techniques and better chemotherapy regimens, including new drug development and immunotherapy, for lung cancer patients. Is there evidence that such studies were/are funded in Kentucky?

V. The original Strategic Plan called for annual workshops open to investigators of varying disciplines and importantly from both institutions. Can you find evidence that such workshops take place?

VI. The original SP called for recruitment of a molecular epidemiologist within the first 2 years of the program.
   a. Was such a researcher recruited? Who?
   b. The 2006 updated SP called for the ongoing recruitment of additional scientists into both the cancer centers. Can you find evidence that both young investigators and established investigators are continuously being recruited to either of the cancer centers?
   c. In addition to recruitment of new faculty, the 2010 updated SP called for existing faculty at the 2 institutions to direct some of their focus to lung cancer. Is there evidence that tenured faculty at either institution instigated new projects related to lung cancer?

VII. The original SP called for a Task Force to set up a state-wide system for acquiring and banking tissue, harnessing the expertise of UK and U of L pathologists and molecular biologists. Was such a program initiated? Is it operational today?

VIII. The 2006 updated SP called for identification of molecular abnormalities for lung cancer susceptibility. Can you find any studies or publications that describe novel biomarkers/genetic factors from investigators at UK and/or U of L?

IX. The 2006 updated SP calls for an increase over time in NIH, DOD, and NCI Program Project investigator-initiated research.
   a. Is there evidence that of increasing numbers of funded projects from these sources?
   b. Is there evidence of NCI multi-project grants, SPORE grants, and or NCI cooperative grants?

X. The 2006 updated SP calls for expansion of the available space for bench research. Is there evidence of expansions/new facilities being built at either cancer center?

XI. The 2010 updated SP called for mentorship/development of early stage investigators in the area of lung cancer. Is there evidence of an environment that fosters such mentorship/growth of young investigators at these 2 institutions?

XII. Starting with the 2006 updated SP, there is a call for expanding the LCRP to include support for research related to cancers other than lung, that are associated with smoking. Is there evidence for support of research on non-lung, smoking –related cancers at these 2 institutions?

III. Interviews and site visits with selected staff from UK and U of L.

In the process of reviewing the documents and websites we provide, the medical literature, and any other sources you might discover, we expect you to identify key staff people at these institutions with whom you would like to speak. We will facilitate conference calls and site visits, to take place starting approximately early March.

Pierre Massion, MD, is the Ingram Professor of Cancer Research. He is Professor of Medicine in the Division of Allergy, Pulmonary and Critical Care Medicine and Professor of Cancer Biology at Vanderbilt Medical Center. Dr. Massion has worked in the field of lung cancer biology, early detection and therapeutics for 16 years. He is the director of the Thoracic Program at the Vanderbilt Ingram Cancer Center and thereby overseeing and fostering a rich environment to translate science from the program to trials in the cooperative groups. He has over 80 publications in the areas of lung cancer development, role of oncogenes in the progression of lung tumor cells and innovative strategies towards the development of molecular biomarkers for early detection of lung cancer and intermediate endpoint biomarkers of response to chemoprevention. He served as Chief of the Pulmonary and Critical Care Medicine section at the Nashville VA Medical Center between 2007-2012. He is certified by the American Board of Internal Medicine in Internal Medicine and in Pulmonary and Critical Care Medicine. He is the principal investigator of the Vanderbilt SPORE in lung cancer and of the Vanderbilt Clinical Validation Center sponsored by the EDRN to validate candidate biomarkers of lung cancer. He is also co-PI of two DOD grants, one of which offers lung cancer screening across 12 VA and military hospitals to validate candidate biomarkers of risk and of diagnosis for lung cancer. Dr. Massion has mentored over 19 postdoctoral fellows, 11 graduate students and 20 undergraduate students. He is committed to pursuing innovative strategies to deepen the understanding of lung cancer development and progression. His laboratory applies novel genomic and proteomic technologies to biological specimens to address questions related to the identification and validation of molecular determinants of disease diagnosis, progression, prognosis, and intermediate endpoint biomarkers of response to chemo-preventive strategies. He is the PI of 6 active clinical studies - http://www.clinicaltrials.gov. He is the Chair of the Lung Cancer Cooperative group in the EDRN and the Chair of the Scientific Advisory Board of the largest non-profit lung cancer foundation LUNGevity. He is a contributing member to the National Comprehensive Cancer Network related Non-Small Cell Lung Cancer Guidelines committee.
http://www.vicc.org/dd/display.php?person=pierre.massion

Eric Grogan, MD, MPH, was born in Charlottesville, Virginia and raised in Paducah, Kentucky. He attended Lipscomb University in Nashville, TN and graduated summa cum laude in 1995. In 1999, he received his medical degree with honors from Vanderbilt University. After completing a general surgery internship and residency at Vanderbilt, Dr. Grogan continued his cardiothoracic surgery training at the University of Virginia where he also was the minimally invasive thoracic fellow. During his surgical training, he also obtained a Master's in Public Health from Vanderbilt University focusing on surgical outcomes research and quality improvement.

Dr. Grogan's current research focuses on the early detection and optimal therapy for patients with lung cancer. He holds a secondary appointment with the Department of Medicine and the Institute for Medicine and Public Health.
Dr. Grogan joined the Vanderbilt University faculty in 2008. He serves as the chief of Thoracic Surgery at Nashville VA Hospital.

Dr. Grogan's clinical practice includes all areas of general thoracic surgery. He has experience in the treatment of lung and esophageal cancer, lung failure surgery, lung transplantation, mediastinal tumors, and tracheal and bronchoplastic procedures. Dr. Grogan's clinical interests have focused on minimally

invasive thoracic surgery for treatment of lung cancer and benign esophageal diseases. He performs VATS lobectomies, radiotracer guided excision of small pulmonary nodules, and laparoscopic and thoracoscopic esophageal surgical procedures. http://www.vicc.org/dd/display.php?person=eric.l.grogan

Peter Mazzone, MD, MPH, is Staff and Director of Education at Cleveland Clinic's Respiratory Institute. In addition, he is Director of the Lung Cancer Program for the Respiratory Institute and Director of the Pulmonary Rehabilitation Program.

Dr. Mazzone is board-certified in internal medicine, pulmonary medicine and critical care medicine.

Treatment interests include lung nodules, lung cancer and intensive care unit medicine. Research interests focus on breath analysis, lung cancer diagnostics, lung nodule evaluation, lung physiology assessment and lung cancer screening.
http://my.clevelandclinic.org/staff_directory/staff_display.aspx?DoctorID=4280

Michael Maitland, MD, PhD, focuses on caring for patients with metastatic lung cancer, and patients with different types of advanced solid tumors who are interested in experimental treatment.

He is a broadly trained physician-scientist who leads a research program in translational medicine and cancer therapeutics. The goal of translational medicine is to improve patient care by quickly and effectively applying recent advances in laboratory research. The program currently concentrates on kinase inhibitors, a large and promising class of new cancer drugs.

Dr. Maitland applies his expertise in human genetics, clinical pharmacology, molecular biology, and clinical investigation to develop new methods to tailor the selection and dosing of medical treatment to each patient's specific circumstances. Personalized treatment aims to make cancer care more effective, but with fewer side effects and complications. http://www.uchospitals.edu/physicians/michael-maitland.html

Bernard Frank Fuemmeler, PhD, MPH, MS
Department / Division
Community and Family Medicine / CFM - Research and Education

Research Interests:
Unhealthy lifestyle factors, such as alcohol and tobacco use, poor dietary intake, lack of physical activity, and high body mass index are the leading causes of cancer and chronic disease. The prevention of such diseases will be advanced through a more thorough understanding of the complex determinants of these lifestyle factors and the development of novel interventions that help change individual behavior for the better. Dr. Fuemmeler's program of research takes a lifespan epidemiologic approach toward understanding the determinants contributing to child and adolescent health behaviors, and ultimately to adult chronic disease, as well as seeks to develop innovative intervention strategies to promote health in children, adolescents and their families.

Dr. Fuemmeler also has strong interests in the use of mobile health (mHealth) for improving patient self-management and adherence and is co-director of the mHealth@duke colloquium series. This is an interdisciplinary group sponsored by the School of Medicine designed to bring together mHealth researchers at Duke and the Durham Community.
http://cfm.mc.duke.edu/modules/faculty_dh/viewDetails.php?uid=0380453

Catherine Rahilly-Tierney, MD, MPH
Dr. Rahilly-Tierney obtained her M.D. from the University of Rochester School of Medicine and Dentistry, followed by residency training in Internal Medicine at the Mount Sinai Medical Center in New York City. She then moved to Boston where she completed the Harvard Program in General Internal Medicine. She earned her M.P.H at the Harvard School of Public Health, focusing on biostatistics and epidemiology. Her background in academics has provided her with a deep understanding of how to design studies and interpret data, expertise in SAS programming, and a well-honed ability to write compelling scientific manuscripts and reports. Currently she is an Instructor in Medicine at Harvard Medical School and an Associate Epidemiologist at Brigham & Women's Hospital. American Board of Internal Medicine-certified and holding an active medical license in Massachusetts, she is also a Staff Physician at the Boston VA.

Dr. Rahilly-Tierney has selected a team of professionals whose combined experience includes regulatory affairs, pharma co-epidemiology, database building and maintaining, observational database mining, and SAS programming. These individuals represent the very best that their diverse fields have to offer. Dr. Rahilly-Tierney and her team have produced academic papers, pharma co-vigilance reports, literature reviews, and more and look forward to applying their synergism to your project.
http://www.crtepiconsulting.com/our-people.html

Kenneth Lieberman, PhD
Dr. Lieberman, is leading the Sci-Med Consulting group. He is a toxicologist with faculty positions in the departments of Psychiatry, Pediatrics, and Pathology at New Jersey medical School/Rutgers University. Sci-Med associate company's goal is to meet the needs of clients by the application of scientific information and data in obtaining the best solution to their environmental requirements in an efficient and consistent manner, offering clients top quality services delivered in a timely and economical way, while guiding them through complex and difficult scientific and technical matters. The firm provides services core competencies ranging from risk assessment, clinical and basic research, occupational and environmental health to sophisticated epidemiological investigations.

University of Kentucky Markey Cancer Center
Investigator-Initiated Grant Proposal Recommendations
KLCRP - Governance Board
February 26, 2014

Investigator	Application Title	FY 14-15	FY 15-16
Suzanne Arnold	A randomized phase II trial of induction chemotherapy and low-dose fractionated radiation in head and neck cancer with correlative evaluation of DNA repair.	$ 75,000	$ 75,000
Tadahide Izumi	Establishment of Buccal Cell Biomarkers for Carcinogenesis Related to Tobacco Product Consumption	$ 75,000	$ 75,000
Jeremiah Martin	A Singleparm, Phase II study of thoracoscopic lung cancer staging with the use of intraoperative ultrasound at the time of definitive resectin.	$ 75,000	$ 75,000
Jamie Studts	Disseminating LCS through Shared Decision Making: A Web-based CE Intervention for Primary Care Providers	$ 75,000	$ 75,000

Screening for Lung Cancer

U.S. Preventive Services Task Force Recommendation Statement

The U.S. Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

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Contents

Summary of Recommendation and Evidence

The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) 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. (B recommendation)

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Rationale

Importance

Lung cancer is the third most common cancer and the leading cause of cancer death in the United States (1). The most important

risk factor for lung cancer is smoking, which results in approximately 85% of all U.S. lung cancer cases (2). Although the prevalence of smoking has decreased, approximately 37% of U.S. adults are current or former smokers (2). The incidence of lung cancer increases with age and occurs most commonly in persons aged 55 years or older. Increasing age and cumulative exposure to tobacco smoke are the 2 most common risk factors for lung cancer.

Lung cancer has a poor prognosis, and nearly 90% of persons with lung cancer die of the disease. However, early-stage non–small cell lung cancer (NSCLC) has a better prognosis and can be treated with surgical resection.

Detection

Most lung cancer cases are NSCLC, and most screening programs focus on the detection and treatment of early-stage NSCLC. Although chest radiography and sputum cytologic evaluation have been used to screen for lung cancer, LDCT has greater sensitivity for detecting early-stage cancer (3).

Benefits of Detection and Early Treatment

Although lung cancer screening is not an alternative to smoking cessation, the USPSTF found adequate evidence that annual screening for lung cancer with LDCT in a defined population of high-risk persons can prevent a substantial number of lung cancer–related deaths. Direct evidence from a large, well-conducted, randomized, controlled trial (RCT) provides moderate certainty of the benefit of lung cancer screening with LDCT in this population (4). The magnitude of benefit to the person depends on that person's risk for lung cancer because those who are at highest risk are most likely to benefit. Screening cannot prevent most lung cancer–related deaths, and smoking cessation remains essential.

Harms of Detection and Early Intervention and Treatment

The harms associated with LDCT screening include false-negative and false-positive results, incidental findings, overdiagnosis, and radiation exposure. False-positive LDCT results occur in a substantial proportion of screened persons; 95% of all positive results do not lead to a diagnosis of cancer. In a high-quality screening program, further imaging can resolve most false-positive results; however, some patients may require invasive procedures.

The USPSTF found insufficient evidence on the harms associated with incidental findings. Overdiagnosis of lung cancer occurs, but its precise magnitude is uncertain. A modeling study performed for the USPSTF estimated that 10% to 12% of screen-detected cancer cases are overdiagnosed—that is, they would not have been detected in the patient's lifetime without screening. Radiation harms, including cancer resulting from cumulative exposure to radiation, vary depending on the age at the start of screening; the number of scans received; and the person's exposure to other sources of radiation, particularly other medical imaging.

USPSTF Assessment

The USPSTF concludes with moderate certainty that annual screening for lung cancer with LDCT is of moderate net benefit in asymptomatic persons who are at high risk for lung cancer based on age, total cumulative exposure to tobacco smoke, and years since quitting smoking. The moderate net benefit of screening depends on limiting screening to persons who are at high risk, the accuracy of image interpretation being similar to that found in the NLST (National Lung Screening Trial), and the resolution of most false-positive results without invasive procedures (4).

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Clinical Considerations

Patient Population Under Consideration

The risk for lung cancer increases with age and cumulative exposure to tobacco smoke and decreases with time since quitting smoking. The best evidence for the benefit of screening comes from the NLST, which enrolled adults aged 55 to 74 years who had at least a 30 pack-year smoking history and were current smokers or had quit within the past 15 years. As with all screening trials, the NLST tested a specific intervention over a finite period. Because initial eligibility extended through age 74 years and participants received 3 annual screening computed tomographic scans, the oldest participants in the trial were aged 77 years.

The USPSTF used modeling studies to predict the benefits and harms of screening programs that use different screening intervals, age ranges, smoking histories, and times since quitting. A program that annually screens 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 is projected to have a reasonable balance of benefits and harms. The model assumes that persons who achieve 15 years of smoking cessation during the screening program discontinue screening. This model predicts the outcomes of continuing the screening program used in the NLST through age 80 years.

Screening may not be appropriate for patients with substantial comorbid conditions, particularly those who are in the upper end of the screening age range. The NLST excluded persons who were unlikely to complete curative lung cancer surgery and those with medical conditions that posed a substantial risk for death during the 8-year trial. The baseline characteristics of the NLST showed a relatively healthy sample, and fewer than 10% of enrolled participants were older than 70 years (5). Persons with serious comorbid conditions may experience net harm, no net benefit, or at least substantially less net benefit. Similarly, persons who are unwilling to have curative lung surgery are unlikely to benefit from a screening program.

Assessment of Risk

Age, total exposure to tobacco smoke, and years since quitting smoking are important risk factors for lung cancer and were used to determine eligibility in the NLST. Other risk factors include specific occupational exposures, radon exposure, family history, and history of pulmonary fibrosis or chronic obstructive lung disease. The incidence of lung cancer is relatively low in persons younger than 50 years but increases with age, especially after age 60 years. In current and former smokers, age-specific incidence rates increase with age and cumulative exposure to tobacco smoke.

Smoking cessation substantially reduces a person's risk for developing and dying of lung cancer. Among persons enrolled in the NLST, those who were at highest risk because of additional risk factors or a greater cumulative exposure to tobacco smoke experienced most of the benefit (6). A validated multivariate model showed that persons in the highest 60% of risk accounted for 88% of all deaths preventable by screening.

Screening Tests

Low-dose computed tomography has shown high sensitivity and acceptable specificity for the detection of lung cancer in high-risk persons. Chest radiography and sputum cytologic evaluation have not shown adequate sensitivity or specificity as screening tests. Therefore, LDCT is currently the only recommended screening test for lung cancer.

Treatment

Surgical resection is the current standard of care for localized NSCLC. This type of cancer is treated with surgical resection when possible and also with radiation and chemotherapy. Annual LDCT screening may not be useful for patients with life-limiting comorbid conditions or poor functional status who may not be candidates for surgery.

Other Approaches to Prevention

Smoking cessation is the most important intervention to prevent NSCLC. Advising smokers to stop smoking and preventing nonsmokers from being exposed to tobacco smoke are the most effective ways to decrease the morbidity and mortality associated with lung cancer. Current smokers should be informed of their continuing risk for lung cancer and offered cessation treatments. Screening with LDCT should be viewed as an adjunct to tobacco cessation interventions.

Useful Resources

Clinicians have many resources to help patients stop smoking. The Centers for Disease Control and Prevention has developed a Web site with many such resources, including information on tobacco quit lines, available in several languages (www.cdc.gov/tobacco/campaign/tips). Quit lines provide telephone-based behavioral counseling and support to tobacco users who want to quit smoking. Counseling is provided by trained cessation specialists who follow standardized protocols that may include several sessions and are generally provided at no cost to users. The content has been adapted for specific populations and can be tailored for individual clients. Strong evidence shows that quit lines can expand the use of evidence-based tobacco cessation treatments in populations that may have limited access to treatment options.

Combination therapy with counseling and medications is more effective at increasing cessation rates than either component alone. The U.S. Food and Drug Administration has approved several forms of nicotine replacement therapy (gum, lozenge, transdermal patch, inhaler, and nasal spray), as well as bupropion and varenicline. More information on the treatment of tobacco dependence can be found in the U.S. Public Health Service Reference Guide “Treating Tobacco Use and Dependence: 2008 Update” (available at www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/clinicians/reference/tobaqrg.pdf). The National Cancer Institute has developed a patient and physician guide for shared decision making for lung cancer screening based on the NLST (available at www.cancer.gov/newscenter/qa/2002/NLSTstudyGuidePatientsPhysicians). This 1-page resource may be a useful communication tool for providers and patients.

In addition, the National Comprehensive Cancer Network has developed guidelines for the follow-up of lung nodules (7). The appropriate follow-up and management of abnormalities found on LDCT scans are important given the high rates of false-positive results and the potential for harms. Lung cancer screening with LDCT should be implemented as part of a program of care, as outlined in the next section.

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Other Considerations

Implementation of a Lung Cancer Screening Program

Screening Eligibility, Screening Intervals, and Starting and Stopping Ages

The NLST, the largest RCT to date with more than 50,000 patients, enrolled participants aged 55 to 74 years at the time of randomization who had a tobacco use history of at least 30 pack-years and were current smokers or had quit within the past 15 years (4). The USPSTF recommends extending the program used in the NLST through age 80 years. Screening should be discontinued once the person has not smoked for 15 years.

The NLST enrolled generally healthy persons, and the findings may not accurately reflect the balance of benefits and harms in those with comorbid conditions. The USPSTF recommends discontinuing screening if a person develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

Clinicians will encounter patients who are interested in screening but do not meet the criteria of high risk for lung cancer as described previously. The balance of benefits and harms of screening may be unfavorable in these lower-risk patients. Current evidence is lacking on the net benefit of expanding LDCT screening to include lower-risk patients. It is important that persons who are at lower risk for lung cancer be aware of the potential harms of screening. Future improvements in risk assessment tools will help clinicians better individualize patients' risks (6).

Smoking Cessation Counseling

All persons enrolled in a screening program should receive smoking cessation interventions. To be consistent with the USPSTF recommendation on counseling and interventions to prevent tobacco use and tobacco-caused disease, persons who are referred to a lung cancer screening program through primary care should receive these interventions before referral. Because many persons may enter screening through pathways besides referral from primary care, the USPSTF encourages incorporating such interventions into the screening program.

Shared Decision Making

Shared decision making is important for persons within the population for whom screening is recommended. The benefit of screening varies with risk because persons who are at higher risk because of smoking history or other risk factors are more likely to benefit. Screening cannot prevent most lung cancer deaths, and smoking cessation remains essential. Lung cancer screening has substantial harms, most notably the risk for false-positive results and incidental findings that lead to a cascade of testing and treatment that may result in more harms, including the anxiety of living with a lesion that may be cancer. Overdiagnosis of lung cancer and the risks of radiation are real harms, although their magnitude is uncertain. The decision to begin screening should be the result of a thorough discussion of the possible benefits, limitations, and known and uncertain harms.

Standardization of LDCT Screening and Follow-Up of Abnormal Findings

The evidence for the effectiveness of screening for lung cancer with LDCT comes from RCTs done in large academic medical centers with expertise in using LDCT and diagnosing and managing abnormal lung lesions. Clinical settings that have high rates of diagnostic accuracy using LDCT, appropriate follow-up protocols for positive results, and clear criteria for doing invasive procedures are more likely to duplicate the results found in trials. The USPSTF supports adherence to quality standards for LDCT (8) and establishing protocols to follow up abnormal results, such as those proposed by the National Comprehensive Cancer Network (7). A mechanism should be implemented to ensure adherence to these standards.

In the context of substantial uncertainty about how best to manage individual lesions, as well as the magnitude of some of the harms of screening, the USPSTF encourages the development of a registry to ensure that appropriate data are collected from screening programs to foster continuous improvement over time. The registry should also compile data on incidental findings and the testing and interventions that occur as a result of these findings.

Research Needs and Gaps

Smoking prevalence and lung cancer incidence are higher among socioeconomically disadvantaged populations, and more research is needed in these groups. In addition, if lung cancer screening with LDCT is implemented more widely in diverse community settings, it is important to evaluate whether variability in follow-up protocols of positive results on LDCT scans results in a different balance of benefits and harms than that observed in RCTs.

More research is also needed on the use of biomarkers to focus LDCT efforts in persons who are at highest risk for lung cancer. The role of biomarkers in accurately discriminating between benign and malignant nodules and in identifying more aggressive disease

needs to be determined.

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Discussion

Burden of Disease

Lung cancer is the third most common cancer in the United States. Age-adjusted incidence rates per 100,000 persons are higher in men and vary according to the duration of and exposure to tobacco smoke. The most important risk factor for lung cancer is smoking, which results in approximately 85% of all lung cancer cases in the United States. Although the prevalence of smoking has decreased, approximately 37% of U.S. adults are current or former smokers. In 2008, an estimated 7 million U.S. adults aged 55 to 75 years had a 30 pack-year or more smoking history (2).

The incidence of lung cancer increases with age, occurring most commonly in adults aged 55 years or older. Lung cancer is the leading cause of cancer-related death in the United States, accounting for approximately 28% of all deaths from cancer. Death from lung cancer is often related to the initial stage of diagnosis. The average 5-year survival rate for lung cancer is among the lowest (17%) of all types of cancer but is higher when the disease is diagnosed at an early stage (52%). However, only 15% of lung cancer cases are diagnosed at such a stage (2).

Scope of Review

To update the 2004 recommendation, the USPSTF commissioned a systematic evidence review to assess the efficacy of LDCT, chest radiography, and sputum cytologic evaluation for lung cancer screening in asymptomatic persons who are at average or high risk for lung cancer (current or former smokers) (3). The review focused on new evidence from RCTs to determine the effectiveness of these screening tests in improving health outcomes. Information about the harms associated with these screening tests was obtained from RCTs and cohort studies. The benefits and harms associated with surgical resection of early-stage NSCLC were also examined.

In addition to the evidence review, the USPSTF commissioned modeling studies from the Cancer Intervention and Surveillance Modeling Network (CISNET) to provide information about the optimum age at which to begin and end screening, the optimum screening interval, and the relative benefits and harms of different screening strategies (9, 10). The modeling studies complement the evidence that the systematic review provides.

Accuracy of Screening Tests

The sensitivity of chest radiography for detecting lung cancer varies depending on the size and location of the lesion, image quality of the scan, and skill of the radiologist who interprets the scan. Low-dose computed tomography has emerged as a test with higher sensitivity and specificity for lung cancer than chest radiography. In 2004, the USPSTF found inadequate evidence to recommend for or against screening for lung cancer with LDCT, chest radiography, sputum cytologic evaluation, or a combination of these tests (I statement). Since then, many RCTs have been done and published, resulting in more data on the benefits and harms of screening. Recent data from the NLST showed a sensitivity of 93.8% and specificity of 73.4% for LDCT and a sensitivity of 73.5% and specificity of 91.3% for chest radiography (11). Sputum cytologic evaluation is now rarely used for lung cancer screening, and no studies reported on the test characteristics of this screening method.

Effectiveness of Early Detection and Treatment

Four RCTs reported the effectiveness of LDCT for lung cancer screening. The largest trial, the NLST, showed a reduction in lung cancer mortality of 16% (95% CI, 5.0% to 25.0%) (12) and a reduction in all-cause mortality of 6.7% (95% CI, 1.2% to 13.6%) (4). This trial included more than 50,000 asymptomatic adults aged 55 to 74 years who had at least a 30 pack-year smoking history.

Participants were current or former smokers and were randomly assigned to LDCT or chest radiography. They received annual testing at baseline and years 1 and 2 and were followed for a median of 6.5 years. After 6 to 7 years of follow-up, 2.06% of patients in the chest radiography group and 1.75% of those in the LDCT group had died of lung cancer, for an absolute difference of 0.31% and a number needed to screen of about 320 (4). The number needed to screen is based on 3 annual screenings; screening the same sample over a longer period will result in a much lower estimate.

In contrast to the NLST, 3 small European trials showed potential harm or no benefit of screening. Two small fair-quality trials, the DANTE (Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays) trial and the DLCST (Danish Lung Cancer Screening Trial), showed no benefit associated with LDCT compared with no LDCT (13–15). However, these were smaller trials (n = 2472 and 4104, respectively) that may have had limited power to detect a true benefit.

Of note, the inclusion criteria in the DLCST resulted in younger and healthier participants than in other trials. The relative risk for

all-cause mortality in the DLCST was 1.46 (95% CI, 0.99 to 2.15). This finding raises the possibility of potential harm of screening a young, healthy population. Follow-up in the DLCST was 4.7 years (15). Combined data from the DLCST and the NELSON (Dutch–Belgian Randomised Lung Cancer Screening) trial will be reported soon (2).

When these 3 fair- or good-quality trials were combined in a meta-analysis, the relative risk for lung cancer mortality was 0.81 (95% CI, 0.72 to 0.91) (2). Another European trial, the MILD (Multicentric Italian Lung Detection) study, was rated as poor quality because of concerns about the adequacy of randomization; its results were not included in the final meta-analysis (16).

Two fair- to good-quality trials found no benefits associated with chest radiography screening (2). The larger of these trials, the PLCO (Prostate, Lung, Colorectal, and Ovarian) Cancer Screening Trial, evaluated more than 150,000 participants from the general population and found no benefits of this type of screening in this group or in a subgroup that had tobacco smoke exposure (17).

Smaller RCTs from Europe had different eligibility criteria and have not yet duplicated the findings of the NLST; therefore, only moderate certainty exists about the magnitude of benefit from screening (3). As with all screening trials, these studies were done over a limited time frame, with the NLST evaluating the effect of 3 annual screenings. Modeling is required to estimate the effect of screening beyond that evaluated in a clinical trial. Estimates of the results of different screening intervals, ages at which to start and stop screening, and thresholds for smoking history come from modeling studies that CISNET conducted for the USPSTF.

Annual screening with LDCT provides the greatest benefit in decreasing lung cancer mortality compared with biennial or triennial screening (9, 10). The Table shows the results of annual screening strategies between the ages of 55 and 80 years that had a better balance of benefits and harms than other strategies in this age range. Focusing screening efforts on the highest-risk persons, those with at least a 40 pack-year smoking history, results in the lowest number of screening scans per death averted and, therefore, the least harm to patients in terms of risk for overdiagnosis and consequences of false-positive results.

Screening progressively larger proportions of the population by lowering the screening threshold increases the number of deaths averted but with a progressively higher number of screening scans per death averted, therefore increasing harm. The Table shows that increasing the proportion of the population screened from 13% to 36% increases the number of deaths averted by 75% but increases the number of screening scans by 327%, greatly increasing the probability of an untoward event after the evaluation of a false-positive result and the number of radiation-induced cancer deaths. The highlighted program—screening current or former smokers aged 55 to 80 years who have at least a 30 pack-year smoking history and discontinuing (or not starting) screening after 15 years of smoking abstinence—most closely resembles the strategy applied to participants in the NLST and offers a reasonable balance of benefits and harms.

The CISNET modeling studies show similar life-years gained per death averted and proportion of cancer cases detected at an early stage across the screening strategies. The modeling studies estimate that 9.5% to 11.9% of screen-detected cancer cases are overdiagnosed—that is, they would not have been detected in the patient's lifetime without screening (9, 10).

Table. Screening Scenarios From CISNET Models*

Screening Scenario†				Benefit		Harm‡			CT Screens per Lung Cancer Death Averted, *n*
Minimum Pack-Years at Screening, *n*	Minimum Age at Which to Begin Screening, *y*	Time Since Last Cigarette, *y*	Population Ever Screened, %	Lung Cancer Deaths Averted, %	Lung Cancer Deaths Averted, *n*	Total CT Screens, *n*	Radiation-Induced Lung Cancer Deaths, *n*	Overdiagnosis, %§	
40	60	25	13.0	11.0	410	171,924	17	11.2	437
40	55	25	13.9	12.3	458	221,606	21	11.1	506
30	60	25	18.8	13.3	495	253,095	21	11.9	534
30	**55**	**15**	**19.3**	**14.0**	**521**	**286,813**	**24**	**9.9**	**577**
20	60	25	24.8	15.4	573	327,024	25	9.8	597
30	55	25	20.4	15.8	588	342,880	25	10.0	609
20	55	25	27.4	17.9	664	455,381	31	10.4	719
10	55	25	36.0	19.4	721	561,744	35	9.5	819

Abbreviation: CISNET=Cancer Intervention and Surveillance Modeling Network; CT=computed tomography.
Note: Bolded row highlights the screening scenario with a reasonable balance of benefits and harms and that is recommended by the USPSTF.

* All scenarios model the results of following a cohort of 100,000 persons from age 45 to 90 years or until death from any cause, with a varying number of smokers and former smokers screened on the basis of smoking history, age, and years since stopping smoking.
† For all scenarios, screening is continued through age 80 years.
‡Number of CT screenings is a measure of harm because it relates to the number of patients who will have risk for overdiagnosis and potential consequences from false-positive results.
§ Percentage of screen-detected cancer that is overdiagnosis; that is, cancer that would not have been diagnosed in the patient's lifetime without screening.

Potential Harms of Screening and Treatment

Harms associated with LDCT screening include false-negative and false-positive results, incidental findings, overdiagnosis, radiation exposure, and psychological distress. The sensitivity of LDCT ranged from 80% to 100%, suggesting a false-negative rate of 0% to 20%. The specificity of LDCT ranged from 28% to 100%.

The positive predictive value for lung cancer of an abnormal test result ranged from 2% to 42% . As mentioned previously, the NLST is the largest trial of lung cancer screening to date, and recent results showed a sensitivity of 93.8% and specificity of 73.4% for LDCT. In the NLST, the positive predictive value for a positive finding of a pulmonary nodule measuring 4 mm or larger was 3.8% (11).

Over the 3 rounds of screening in the NLST, 24.2% of screening test results were positive; 96.4% of these were false-positives. Most positive test results were followed by additional imaging. Approximately 2.5% of positive test results required additional invasive diagnostic procedures, such as bronchoscopy, needle biopsy, or thoracoscopy. Of the 17,053 positive test results evaluated, there were approximately 61 complications and 6 deaths after a diagnostic procedure. Recently published data from the first round of screening in the NLST showed an average of 1 follow-up scan per positive screening test result. Approximately 1.9% of NLST participants had a biopsy (11).

The most common incidental findings on LDCT were emphysema and coronary artery calcifications. Other pulmonary findings included bronchiectasis, pulmonary fibrosis, carcinoid tumors, and hamartomas. The NLST reported 7.5% clinically significant LDCT abnormalities that were not lung cancer. None of the studies reported data on the evaluations that may have occurred in response to the incidental findings. Therefore, the harms and benefits associated with incidental findings cannot currently be determined (2).

Overdiagnosis was not formally reported in any study. The NLST found 119 more lung cancer cases in approximately 26,000 participants in the LDCT group than in the chest radiography group after 6.5 years of follow-up, which suggests some overdiagnosis. Recent data from the Italian Continuing Observation of Smoking Subjects cohort study of approximately 5000 participants showed that of the 120 incident cancer cases, 25% were slow-growing or indolent (based on volume-doubling time), thus possibly indicating some overdiagnosis with LDCT (18).

Radiation exposure associated with LDCT ranged from 0.61 to 1.5 mSv per scan. To provide context, annual background radiation exposure in the United States averages 2.4 mSv, radiation exposure from mammography is 0.7 mSv, and radiation exposure from head computed tomography is 1.7 mSv. The risk for radiation-induced lung cancer depends on the age at which a person begins screening and the amount of cumulative radiation received. On the basis of modeling studies, starting annual LDCT screening before age 50 years may result in more radiation-related lung cancer deaths than starting annual screening after age 50 years (9, 10).

Overall, LDCT screening did not seem to result in substantial long-term psychological distress, although assessment has been limited. No studies reported long-term differences in anxiety or distress levels associated with LDCT in participants.

No RCTs compared treatment of stage IA or IB lung cancer with surgical resection versus no treatment. Surgical resection is the standard of care in the United States for early-stage NSCLC. Studies of symptomatic and unselected patients reported 5-year survival rates associated with surgical resection of 71% to 90% for stage IA cancer and 42% to 75% for stage IB cancer. No RCTs of LDCT screening evaluated the harms associated with screen-detected cancer. Studies that reported the harms of surgical resection were done in patients who were identified in clinical practice and had comorbid conditions (3).

Estimate of Magnitude of Net Benefit

On the basis of data from the systematic evidence review and modeling studies, the USPSTF determined with moderate certainty that annual LDCT screening provides substantial net benefit in persons aged 55 to 80 years at high risk for lung cancer. Evidence from the NLST supports this recommendation because participants in that trial were in this age range and had a similar degree of lung cancer risk from cumulative tobacco exposure. Persons who do not meet the minimum eligibility criteria for the NLST may have less net benefit and more harms from screening (persons aged 55 to 74 years at enrollment who have a ≥30 pack-year smoking history and are current smokers or have quit in the past 15 years). For these persons, the absolute benefit of screening is strongly associated with their age and smoking history.

Modeling studies conducted by CISNET investigators for the USPSTF showed that annual LDCT screening yielded the greatest net benefit (compared with biennial or triennial screening) (9, 10). Benefits were measured as percentage of early-stage detection of

lung cancer, percentage and absolute number of lung cancer deaths averted, and number of life-years gained. Harms were measured as number of total LDCT screenings per 100,000 persons and per person, number of cases of overdiagnosed lung cancer, and number of radiation-induced lung cancer deaths. The microsimulation models used standardized data on smoking history and non–lung cancer mortality to simulate the effects of various screening programs on the mortality rate of a U.S. cohort born in 1950. This cohort was chosen because these persons reach age 63 years (approximate midrange of participants' ages in the NLST) in 2013.

Modeling evidence suggests that an annual screening program starting at age 55 years and ending after age 80 years (in persons who have a 30 pack-year smoking history and currently smoke or have quit in the past 15 years) resulted in approximately 50% of lung cancer cases detected at an early stage (9, 10). This screening protocol would result in a 14% reduction in lung cancer mortality, or an estimated 521 lung cancer deaths prevented per 100,000 persons in the population. The harms associated with this screening protocol are an estimated overdiagnosis of 10% of screen-detected cases and radiation-induced lung cancer deaths of less than 1%. As mentioned previously, a person's absolute net benefit from screening may depend not just on age but functional status and the presence of other comorbid conditions

How Does Evidence Fit With Biological Understanding?

Lung cancer is a proliferation of malignant cells arising in the tissues or airways of the lungs. In addition to age and exposure to tobacco smoke, other risk factors for lung cancer include family history; chronic obstructive pulmonary disease; pulmonary fibrosis; and exposure to indoor cooking fumes, radon, asbestos, arsenic, chromium, and coal tar. Non–small cell lung cancer is a heterogeneous category that includes adenocarcinoma, squamous cell carcinoma, large cell carcinoma, and undifferentiated carcinoma. Adenocarcinoma is the most common subtype, encompassing 36% of all lung cancer cases.

Currently, 75% of patients with lung cancer present with symptoms of advanced local or metastatic disease that result in poor prognosis (2). At the earliest stage, median 5-year survival for NSCLC is 77%. Patients with localized disease (defined as cancer limited to the lung without metastasis to other organs or lymph nodes) have a median 5-year survival of 52% compared with 25% for those with regional spread and 4% for those with distant metastasis. Thus, earlier detection and treatment of lung cancer give patients a greater chance for cure.

Response to Public Comments

A draft version of this recommendation statement was posted for public comment on the USPSTF Web site from 30 July to 26 August 2013. Most of the comments generally agreed with the recommendation statement, although some suggested restricting screening to a higher-risk group and others suggested expanding eligibility criteria beyond those used in the NLST. Many comments expressed concerns about implementation of a screening program, predicting substantially greater harm in the community setting than was found in the NLST. Some comments expressed concern about the cost of implementing a screening program and the potential paradoxical effect of enabling persons to continue smoking with the perception that medical care can mitigate the risks of smoking.

In response to these comments, the USPSTF further emphasized the importance of tobacco cessation as the primary way to prevent lung cancer and provided links to resources that clinicians can use to help their patients quit smoking. A section on implementation of a screening program was added, emphasizing the need for monitoring this implementation, quality assurance in diagnostic imaging, and appropriate follow-up to replicate the benefits observed in the NLST in the general population. The USPSTF also clarified that, in addition to age and smoking history, such risk factors as occupational exposure, family history, and history of other lung diseases are important when assessing patients' risks for lung cancer.

The USPSTF acknowledges the importance of accurately identifying persons who are at highest risk to maximize the benefits and minimize the harms of screening and calls for more research to improve risk assessment tools. The USPSTF did not incorporate the costs of a screening program or the potential savings from a reduction in treatment of advanced lung cancer into the recommendation.

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Update of Previous USPSTF Recommendation

This recommendation updates the 2004 recommendation, in which the USPSTF concluded that the evidence was insufficient to recommend for or against screening for lung cancer in asymptomatic persons with LDCT, chest radiography, sputum cytologic evaluation, or a combination of these tests. In the current recommendation, the USPSTF recommends annual screening for lung cancer with LDCT in persons who are at high risk based on age and cumulative tobacco smoke exposure.

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Recommendations of Others

In 2012, the American College of Chest Physicians, the American Society of Clinical Oncology, and the American Thoracic Society (19) recommended screening for lung cancer with LDCT primarily on the basis of results from the NLST, using eligibility criteria that closely modeled those of the NLST (persons aged 55 to 74 years who have a ≥30 pack-year smoking history and currently smoke or have quit in the past 15 years). The recommendations also stipulated that screening should be offered only in clinical settings similar to those in the trial.

The American Association for Thoracic Surgery (20) recommends annual screening with LDCT in current and former smokers aged 55 to 79 years who have a 30 pack-year smoking history. It also recommends annual screening starting at age 50 to 79 years in patients who have a 20 pack-year smoking history and additional comorbid conditions that produce a cumulative risk for cancer of at least 5% over the next 5 years. Furthermore, it recommends annual screening in long-term cancer survivors aged 55 to 79 years.

In 2013, the American Cancer Society (21) also began recommending screening for lung cancer with LDCT in high-risk patients who are in relatively good health and meet the NLST criteria (persons aged 55 to 74 years who have a ≥30 pack-year smoking history and currently smoke or have quit in the past 15 years). It recommends against the use of chest radiography and strongly suggests that all adults who receive screening enter an organized screening program that has experience in LDCT.

In addition, the National Comprehensive Cancer Network (7) recommends LDCT screening in selected patients who are at high risk for lung cancer. High risk is defined as persons aged 55 to 74 years who have at least a 30 pack-year smoking history and, if a former smoker, 15 years or less since quitting or persons aged 50 years or older who have at least a 20 pack-year smoking history and 1 additional risk factor. It does not recommend lung cancer screening in persons who are at moderate risk (aged ≥50 years and ≥20 pack-year smoking history or secondhand smoke exposure but no additional lung cancer risk factors) or low risk (younger than 50 years or smoking history of <20 pack-years).

Members of the U.S. Preventive Services Task Force

Members of the U.S. Preventive Services Task Force at the time this recommendation was finalized† are Virginia A. Moyer, MD, MPH, *Chair* (American Board of Pediatrics, Chapel Hill, North Carolina); Michael L. LeFevre, MD, MSPH, *Co-Vice Chair* (University of Missouri School of Medicine, Columbia, Missouri); Albert L. Siu, MD, MSPH, *Co-Vice Chair* (Mount Sinai School of Medicine, New York, and James J. Peters Veterans Affairs Medical Center, Bronx, New York); Linda Ciofu Baumann, PhD, RN (University of Wisconsin, Madison, Wisconsin); Kirsten Bibbins-Domingo, PhD, MD (University of California, San Francisco, San Francisco, California); Susan J. Curry, PhD (University of Iowa College of Public Health, Iowa City, Iowa); Mark Ebell, MD, MS (University of Georgia, Athens, Georgia); Glenn Flores, MD (University of Texas Southwestern, Dallas, Texas); Francisco A.R. García, MD, MPH (Pima County Department of Health, Tucson, Arizona); Adelita Gonzales Cantu, RN, PhD (University of Texas Health Science Center, San Antonio, Texas); David C. Grossman, MD, MPH (Group Health Cooperative, Seattle, Washington); Jessica Herzstein, MD, MPH (Air Products, Allentown, Pennsylvania); Wanda K. Nicholson, MD, MPH, MBA (University of North Carolina School of Medicine, Chapel Hill, North Carolina); Douglas K. Owens, MD, MS (Veterans Affairs Palo Alto Health Care System, Palo Alto, and Stanford University, Stanford, California); William R. Phillips, MD, MPH (University of Washington, Seattle, Washington); and Michael P. Pignone, MD, MPH (University of North Carolina, Chapel Hill, North Carolina).

† For a list of current Task Force members, go to www.uspreventiveservicestaskforce.org/members.htm.

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References

1. American Cancer Society. Cancer Facts & Figures 2013. Atlanta: American Cancer Society; 2013. Accessed at http://www.cancer.org/research/cancerfactsfigures/cancerfactsfigures/cancer-facts-figures-2013 on 21 November 2013.
2. Humphrey L, Deffebach M, Pappas M, Baumann C, Artis K, Priest Mitchell JP, et al. Screening for Lung Cancer: Systematic Review to Update the U.S. Preventive Services Task Force Recommendation Statement. Evidence Synthesis No. 105. AHRQ Publication No. 13-05196-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2013.
3. Humphrey LL, Deffebach M, Pappas M, Baumann C, Artis K, Priest Mitchell JP, et al. Screening for lung cancer with low-dose computed tomography: a systematic review to update the U.S. Preventive Services Task Force recommendation. *Ann Intern Med*, 2013;159:411-20.
4. Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, et al.; National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. *New Engl J Med*. 2011;365(5):395-409.
5. Aberle DR, Adams AM, Berg CD, Clapp JD, Clingan KL, Gareen IF, et al.; National Lung Screening Trial Research Team. Baseline characteristics of participants in the randomized National Lung Screening Trial. *J Natl Cancer Inst*. 2010;102(23):1771-9.
6. Kovalchik SA, Tammemagi M, Berg CD, Caporaso NE, Riley TL, Korch M, et al. Targeting of low-dose CT screening according to the risk of lung-cancer death. *New Engl J Med*. 2013;369(3):245-54.
7. National Comprehensive Cancer Network. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology: Lung Cancer Screening. Fort Washington, PA: National Comprehensive Cancer Network; 2014.
8. Medicare Improvements for Patients and Providers Act, 42 U.S.C. §101-304 (2008).
9. de Koning HJ, Plevritis S, Hazelton WD, ten Haaf K, Munshi V, Jeon J, et al. Benefits and Harms of Computed Tomography Lung

Cancer Screening Programs for High-Risk Populations. AHRQ Publication No. 13-05196-EF-2. Rockville, MD: Agency for Healthcare Research and Quality; 2013.
10. de Koning HJ, Meza R, Plevritis SK, ten Haaf K, Munshi VD, Jeon J, et al. Benefits and harms of lung cancer screening: modeling strategies for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2013.
11. Church TR, Black WC, Aberle DR, Berg CD, Clingan KL, Duan F et al.; National Lung Screening Trial Research Team. Results of initial low-dose computed tomographic screening for lung cancer. *New Engl J Med*. 2013;368(21):1980-91.
12. Pinsky PF, Church TR, Izmirlian G, Kramer BS. The National Lung Screening Trial: results stratified by demographics, smoking history, and lung cancer histology. *Cancer*. 2013.
13. Infante M, Lutman FR, Cavuto S, Brambilla G, Chiesa G, Passera E, et al; DANTE Study Group. Lung cancer screening with spiral CT: baseline results of the randomized DANTE trial. *Lung Cancer*. 2008;59(3):355-63.
14. Infante M, Cavuto S, Lutman FR, Brambilla G, Chiesa G, Ceresoli G, et al; DANTE Study Group. A randomized study of lung cancer screening with spiral computed tomography: three-year results from the DANTE trial. *Am J Respir Crit Care Med*. 2009;180(5):445-53.
15. Saghir Z, Dirksen A, Ashraf H, Bach KS, Brodersen J, Clementsen PF, et al. CT screening for lung cancer brings forward early disease. The randomised Danish Lung Cancer Screening Trial: status after five annual screening rounds with low-dose CT. *Thorax*. 2012;67(4):296-301.
16. Pastorino U, Rossi M, Rosato V, Marchianò A, Sverzellati N, Morosi C, et al. Annual or biennial CT screening versus observation in heavy smokers: 5-year results of the MILD trial. *Eur J Cancer Prev*. 2012;21(3):308-15.
17. Oken MM, Hocking WG, Kvale PA, Andriole GL, Buys SS, Church, TR, et al; PLCO Project Team. Screening by chest radiograph and lung cancer mortality: the Prostate, Lung, Colorectal, and Ovarian (PLCO) randomized trial. *JAMA*. 2011;306(17):1865-73.
18. Veronesi G, Maisonneuve P, Bellomi M, Rampinelli C, Durli I, Bertolotti R, et al. Estimating overdiagnosis in low-dose computed tomography screening for lung cancer: a cohort study. *Ann Intern Med*. 2012;157(11):776-84.
19. Bach PB, Mirkin JN, Oliver TK, Azzoli CG, Berry DA, Brawley OW, et al. Benefits and harms of CT screening for lung cancer: a systematic review. *JAMA*. 2012;307(22):2418-29.
20. Jaklitsch MT, Jacobson FL, Austin JH, Field JK, Jett JR, Keshavjee S, et al. The American Association for Thoracic Surgery guidelines for lung cancer screening using low-dose computed tomography scans for lung cancer survivors and other high-risk groups. *J Thor Cardiovas Surg.* 2012;144(1):33-8.
21. Wender R, Fontham ET, Barrera E Jr, Colditz GA, Church TR, Ettinger DS, et al. American Cancer Society lung cancer screening guidelines. *CA Cancer J Clin.* 2013;63(2):107-17.

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KLCRP Fund Balances
FY 10-11 thru 2/26/14

		Revenue	UK		UofL		BALANCE
			Grant	Program	Grant	Program	
Grant Carry-forward Prior Years			$ 764,366	$ -	$ 764,366	$ -	$ 1,528,732
FY 10-11							
Allocation from MTS		$ 3,938,788					
Grant Allocation			$ 523,344		$ 523,344		
Program Allocation				$ 1,677,418		$ 1,214,682	
	12/15/2010				$ (750,000)		
	2/16/2011		$ (150,000)				
	3//24/11		$ (300,000)				
	5/26/2011					$ (1,214,682)	
	5/26/2011			$ (1,677,418)			
BALANCE			**$ 837,710**	**$ -**	**$ 537,710**	**$ -**	**$ 1,375,419**
FY 11-12							
Carry-Forward			$ 837,710		$ 537,710		$ 1,375,420
Allocation from MTS		$ 3,962,600					
Grant Allocation		$ (35,754)	$ 732,123		$ 732,123		
Program Allocation				$ 1,428,308		$ 1,034,292	
	9/6/2011		$ (150,000)				
	9/21/2011		$ (150,000)				
	5/24/2012			$ (1,428,308)			
	6/25/2012					$ (1,034,292)	
BALANCE		**$ 3,926,846**	**$ 1,269,833**	**$ -**	**$ 1,269,833**	**$ -**	**$ 2,539,666**
FY 12-13							
Carry-Forward			$ 1,269,833	$ -	$ 1,269,833	$ -	$ 2,539,666
Allocation from MTS		$ 3,472,800					
Grant Allocation			$ 750,000		$ 750,000		
Program Allocation				$ 1,144,224		$ 828,596	
	7/16/2012		$ (473,344)				
	6/16/2012				$ (732,123)		
	11/15/2012		$ (50,000)				
	3/11/2013		$ (150,000)				
	4/15/2013		$ (300,000)				
	4/15/2013			$ (1,593,724)			
	5/2/2013					$ (1,154,076)	
	5/2/2013				$ (750,000)		
BALANCE			**$ 1,046,489**	**$ (449,500)**	**$ 537,710**	**$ (325,480)**	**$ 809,219**
FY 13-14							
Carry-Forward			$ 1,046,489	$ (449,500)	$ 537,710	$ (325,480)	$ 809,219
FY13 acctg error correction			$ (449,500)	$ 449,500	$ (325,480)	$ 325,480	
Allocation from MTS		$ 3,412,800					
Grant Allocation			$ 750,000		$ 750,000		
Program Allocation				$ 1,109,424		$ 803,376	
BALANCE to 2/26/14			**$ 1,346,989**	**$ 1,109,424**	**$ 962,230**	**$ 803,376**	**$ 4,222,019**

Kentucky Lung Cancer Research Program
FY Formula Calculations
As of 2-26-14

		FY10-FY11	FY11-12	
TBC0 settlement after ovarian deduction		3,938,787.87	3,962,600.00	
Grant allocation 50/50		(1,046,687.88)	~~(1,500,000.00)~~	see below adjustment
	Subtotal	2,892,099.99	2,462,600.00	
UK 58%		(1,677,418.00)	(1,428,308.00)	
UL 42%		(1,214,682.00)	(1,034,292.00)	

	FY11-12
35,754.00	budget reduction grants
(1,464,246.00)	**grant allocation revised**
(732,123.00)	50/50 grant allocation

*FY12 grant allocation 1.5M reduced by $35,754 budget reduction

		FY12-13		
		Incorrect calc	**Correct calc**	
		775K ovarian not subtracted		
TBCO settlement before ovarian deduction		4,247,800.00	4,247,800.00	
Ovarian deduction			(775,000.00)	
Grant allocation 50/50		(1,500,000.00)	(1,500,000.00)	
	Subtotal	2,747,800.00	1,972,800.00	**overallocation FY13**
UK 58%		(1,593,724.00)	(1,144,224.00)	(449,500.00) UK
UL 42%		(1,154,076.00)	(828,576.00)	(325,500.00) UL

		FY13 - 14
TBC0 settlement after ovarian deduction		3,412,800.00
Grant allocation 50/50		(1,500,000.00)
	Subtotal	1,912,800.00
UK 58%		(1,109,424.00)
UL 42%		(803,376.00)

Question 1: will grant allocation remain 1.5 M in FY14?

Question 2:- what will be the method to correct the FY13 overallocation?
Scenario 1: reduce grant balances by overallocation amounts respectively
Scenario 2: reduce FY14 program money by overallocation amounts respectively