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Personalised Lung Cancer Screening (PLuS) study to assess the importance of coexisting chronic conditions to clinical practice and policy: protocol for a multicentre observational study

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ABSTRACT

Introduction Lung cancer is the leading cause of cancer death in the USA and worldwide, and lung cancer screening (LCS) with low-dose CT (LDCT) has the potential to improve lung cancer outcomes. A critical question is whether the ratio of potential benefits to harms found in prior LCS trials applies to an older and potentially sicker population. The Personalised Lung Cancer Screening (PLuS) study will help close this knowledge gap by leveraging real-world data to fully characterise LCS recipients. The principal goal of the PLuS study is to characterise the comorbidity burden of individuals undergoing LCS and quantify the benefits and harms of LCS to enable informed decision-making.

Methods and analysis PLuS is a multicentre observational study designed to assemble an LCS cohort from the electronic health records of ~40 000 individuals undergoing annual LCS with LDCT from 2016 to 2022. Data will be integrated into a unified repository to (1) examine the burden of multimorbidity by race/ethnicity, socioeconomic status and age; (2) quantify potential benefits and harms; and (3) use the observational data with validated simulation models in the Cancer Intervention and Surveillance Modeling Network (CISNET) to provide LCS outcomes in the real-world US population. We will fit a multivariable logistic regression model to estimate the adjusted ORs of comorbidity, functional limitations and impaired pulmonary function adjusted for relevant covariates. We will also estimate the cumulative risk of LCS outcomes using discrete-time survival models. To our knowledge, this is the first study to combine observational data and simulation models to estimate the long-term impact of LCS with LDCT.

Ethics and dissemination The study was approved by the Kaiser Permanente Southern California Institutional Review Board and VA Portland Health Care System. The results will be disseminated through publications and presentations at national and international conferences. Safety considerations include protection of patient confidentiality.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Use of observational data from real-world diverse settings with an established simulation model to estimate long-term harms and benefits of lung cancer screening (LCS) to compare screened versus non-screened populations.
⇒ Diverse population (racial/ethnic, socioeconomic and geographic diversity) from four healthcare systems will increase the generalisability of the study.
⇒ Evaluation of LCS utilisation patterns and outcomes in individuals undergoing lung cancer screening by varying levels of comorbidities, functional limitations and pulmonary function.
⇒ Use of electronic health records data offers important advantages by including large numbers of patients who receive real-world care.
⇒ Inability to make causal inferences.

INTRODUCTION

Lung cancer is the leading cause of cancer-related deaths in the USA and worldwide,[1] largely because most patients have advanced, incurable disease at the time of diagnosis.[2] In 2022, it is estimated that there will be 236 740 newly diagnosed cases and 130 180 deaths attributed to lung cancer in the USA, accounting for 12.3% of all incident cancers and 21.4% of all cancer deaths.[1] Lung cancer screening (LCS) with low-dose CT (LDCT) has the potential to revolutionise lung cancer outcomes through early detection and is therefore recommended in high-risk groups to reduce lung cancer mortality.[3–9] In 2011, the National Lung Screening Trial (NLST) reported that three rounds of annual LCS with LDCT reduced the risk of lung cancer death by 20% compared with annual chest radiography.[4] In 2013, the Nederlands-Leuvens

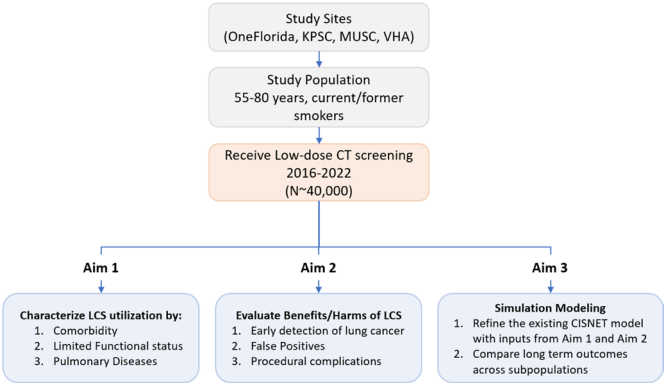

Figure 1 Schematic representation of the PLuS study design aims. CISNET, Cancer Intervention and Surveillance Modelling Network; KPSC, Kaiser Permanente Southern California; LCS, Lung Cancer Screening; MUSC, Medical University of South Carolina; OneFlorida, OneFlorida Clinical Consortium; PLuS, Personalised Lung Cancer Screening; VHA, Veterans Health Administration.

Longkanker Screenings Onderzoek (NELSON) trial found 24% fewer lung cancer deaths in a cohort screened with four rounds of LDCT compared with regular care.[10] Based on the findings from the NLST, annual LCS with LDCT is recommended in the USA for persons aged 55–80 years who have a 30-pack-year smoking history at a minimum and either currently smoke or have quit within the past 15 years.[11] In 2021, the US Preventive Services Task Force (USPSTF) and the American Cancer Society modified their recommendations to include adults 50–80 years old with a history of smoking for ≥20 pack-years and either currently smoke or have quit within the past 15 years to undergo LDCT.[12 13] These modified recommendations issued in 2021 will lead to a larger number of adults undergoing LDCT.

However, as LCS is implemented more widely in real-world populations and more diverse settings, the ratio of benefits to harms may well differ from that observed in the highly controlled environment and the relatively young, generally healthy participants of the NLST (only 25% of NLST participants were age ≥65, and none were >74 years).[4] A post hoc analysis of data from the NLST observed that older participants had a higher risk of false-positive results and complications from invasive procedures after screening.[14] Older individuals with a prolonged history of smoking have an increased risk of lung cancer death and also have a higher risk of morbidity and mortality from significant comorbidities such as chronic obstructive pulmonary disease (COPD) and cardiovascular diseases.[15–18] US adults eligible for LCS are likely to be older and are substantially more likely to have a history of current smoking, a higher comorbidity burden[18 19] and lower average life expectancy than NLST participants.[18] Our prior study using the US Behavioural Risk Factor Surveillance System data found that comorbid conditions were associated with a higher likelihood of undergoing LCS with LDCT.[20] These comorbidity-related differences, along with sociodemographic differences noted by others, raise questions about the generalisability of the NLST results to the full screening-eligible US population.[21–23]

Currently, there is little evidence to guide the selection of LCS among individuals with coexisting comorbid conditions. Therefore, the purpose of the Personalised Lung Cancer Screening (PLuS) study is to address the following gaps by (1) comprehensively and precisely characterising the patient population undergoing LCS in real-world settings with regard to the burden of multimorbidity (defined as chronic coexisting conditions, functional limitations and/or impaired pulmonary function), and examining this burden by race/ethnicity, socioeconomic status and age; (2) quantifying potential harms (eg, false-positive results, procedure-related complications) and benefits (eg, early-stage disease at diagnosis) of LCS among persons with diverse levels of multimorbidity; and (3) comparing the effectiveness of LCS in relation to long-term outcomes (both benefits and harms) across subpopulations with diverse levels of multimorbidity using validated Cancer Intervention and Surveillance Modeling Network (CISNET) simulation models and refined model input parameters based on real-world data. The conceptual framework for the PLuS study is presented in figure 1. This study will precisely characterise vulnerable subpopulations with multimorbidities, quantifying potential benefits and harms of LCS to enable more informed decision-making by health providers and patients contemplating LCS.

METHOD AND ANALYSIS

Study design and setting

The PLuS study will be conducted using real-world data on patients screened with LDCT from four diverse healthcare systems identified in Florida, California, South Carolina and the Veterans Health Administration.

Study population

The target population includes all adults who have undergone LCS with LDCT, including screened individuals who did not meet former or current eligibility criteria, and who have had one or more primary care visits at one of the four participating healthcare systems. The data will be extracted from electronic health records (EHR) and Medicare claims from 2016 to 2022. Individuals with a history of lung cancer within the 5 years prior to the LDCT scan or individuals with scans performed for diagnostic purposes will be excluded.

Each of the four participating healthcare systems is community-based and provides comprehensive services, including primary and specialty care, to large and diverse populations. In addition, each healthcare system has implemented LCS since at least November 2015. The geographic diversity and varied care delivery models of these four healthcare systems enhance our study's ability to characterise the burden of multimorbidity and evaluate the outcomes of LCS in real-world settings.

Study sites

The OneFlorida Clinical Consortium (OneFlorida) provides care for 15 million patients across all 67 counties in Florida, of which 45.9% are white.[24 25] OneFlorida consists of 12 healthcare organisations including academic health centres, private health systems and community clinics. The consortium was recently designated as one of the nation's 13 clinical data research networks by the National Patient-Centred Clinical Research Network (PCORnet), which was created to conduct comparative effectiveness research and to accelerate the translation of promising research findings into improved patient care.[24 25]

Kaiser Permanente Southern California (KPSC) is a fully integrated healthcare system that serves over 4.6 million members.[26] The system currently includes over 7600 physicians and 26 000 nurses, who provide care at 15 hospitals and 231 medical office buildings.[26] The KPSC membership is racially/ethnically and socioeconomically diverse, reflecting the population of the Southern California region from which it is drawn.[27] In March 2019, the total membership (including children) was 43% Hispanic, 35% non-Hispanic white, 9% black and 12% Asian/Pacific Islander.[27]

The Medical University of South Carolina (MUSC) serves approximately 1.5 million individuals from a diverse population, of which 30% are black. The MUSC Health comprises ~2000 beds, more than 100 outreach sites, the MUSC College of Medicine, the physicians' practice plan and nearly 275 telehealth locations. At the end of 2015, the MUSC launched its LCS Programme at the NCI-designated Hollings Cancer Centre.

The Veterans Health Administration (VHA) serves 9 million veterans annually.[28] It was estimated that 900 000 VHA-enrolled veterans met the 2013 USPSTF eligibility criteria,[29] and as the CISNET models underlying the 2021 criteria reported, the number of eligible patients may almost double; ~2 million Veterans may now be eligible.[12] As of 2019, almost 72 000 Veterans had at least one LDCT for LCS in 96 of 139 (69.1%) facilities in 44 states.[30]

The utilisation of a multicentre study design aims to provide racial/ethnic, geographic and socioeconomic status (SES) diversity, and the four participating healthcare systems extend the spectrum of US healthcare delivery models. In addition to the data extraction from the EHRs via the International Classification of Diseases (ICD) and Current Procedural Terminology codes, a computable phenotype (CP) algorithm will be employed to extract data from the unstructured clinical narratives from the EHRs through natural language processing (NLP). The NLP procedure substantially improves the accuracy and coverage of CP algorithms and enables the extraction of the necessary variables that may be missing in the structured EHRs for downstream data analyses.[31]

Comorbidity

Comorbidity will be assessed by two traditional comorbidity indices, the Charlson Comorbidity Index (CCI) and/or the Elixhauser Index, as well as by newer CPs. The modified CCI score is a summary measure of 17 comorbidities that are weighted based on severity.[32–34] The Elixhauser system was developed to predict hospital charges, length of stay and in-hospital mortality by identifying comorbidities that are relevant to hospitalisation (but not the primary reason for hospitalisation) along with the severity of the condition that prompted hospitalisation.[35 36] The Charlson/Elixhauser score will be calculated from EHR during the 12 months prior to each LCS[33–35 37] and will be categorised as 0=best health, 1=average health and 2=worst health. We have chosen to use the Charlson/Elixhauser combined comorbidity score as it has been shown to offer improvements in comorbidity summarisation over other existing scores.[37] In addition to using count-based measures of comorbidity, we will use novel methods to identify distinct comorbidity profiles.[38]

Pulmonary function

History of COPD will be identified through the EHR data and categorised as yes versus no. However, in a subset of our study participants (KPSC and OneFlorida), we will capture the severity of COPD[39] by using the previously validated structured data on spirometry. COPD severity will be classified using the new Global Initiative for Obstructive Lung Disease (GOLD) classification system; categories A, B, C and D will be based on spirometry indicators.[40] We will also evaluate forced expiratory volume (FEV) and ejection fraction (EF) data for patients with heart failure.[41] Additionally, impaired pulmonary function will be defined as FEV1/FVC <70%, where FEV1 is FEV in one second and FVC is forced vital capacity.[39]

Functional limitations

Consistent with our prior studies,[42 43] patient indicators of functional limitations will be derived from claims and EHR data in a subset of study participants. As with comorbidity, functional limitations will be ascertained during the 12 months prior to the baseline LDCT. Detailed Function Related Indicators (FRI) algorithms have been described previously.[44 45] The 16 indicators will be coded as binary variables, and individuals will receive a score for each aspect of functional limitations with the average score generating the FRI score (online supplemental table 1). We will categorise FRI as being in best health if patients have an FRI score of 0, average health if they have an FRI score of 1 and worst health if they have an FRI score of ≥2.

Outcomes of interest

The primary outcome for Aim 1 is the prevalence of multimorbidity in the LCS cohort. The primary outcomes in Aim 2 are the events that follow LCS with LDCT, such as the outcomes of the baseline LDCT and subsequent LDCT tests including false-positive results through biopsies, lung cancer stage at diagnosis (derived from tumour registries and supplemented by pathology reports) and procedure-related complications. Other outcomes will

include LDCT results characterised based on Lung-RADS reports and lung cancer treatment. These outcome data will be derived from the EHR, claims data and tumour registries.

False-positive results

The results will be defined based on Lung-RADS categories, with a category of three or four denoting a positive screen. A Lung-RADS positive screen not followed by lung cancer diagnosis within 3 years will be defined as a false positive.[46] An invasive procedure within 1 year following a false positive will be defined as a Lung-RADS false-positive screen with an invasive procedure.[47] Each LDCT result will be classified as a true-positive, false-positive, true negative or false negative.[47]

Procedural complications

We will include complications following invasive diagnostic procedures (percutaneous cytological examination or biopsies, bronchoscopy, surgical biopsies) that lead to lung cancer diagnosis.[4] Procedures after the date of lung cancer diagnosis will be excluded. Serious complications within 7–30 days of biopsies include pneumothorax, bleeding (pulmonary haemorrhage), acute respiratory failure, acute renal failure, allergic reaction to iodinated contrast material requiring hospitalisation and acute myocardial infarction. We will evaluate procedural complications among all persons undergoing LCS; complications will be classified as minor or major according to the Society of Interventional Radiology (SIR) Guidelines.[48]

Lung cancer stage at diagnosis

Stage will be ascertained using respective institutional cancer registries (using ICD 9/10 codes) and supplemented by the patient's pathology reports obtained through EHR. The key variables will include the American Joint Committee on Cancer stage, histology and the presence/absence of metastases.

LDCT results

The results of the LCS with LDCT will be extracted from the Lung-RADS reports, which is a standardised template for reporting LDCT results.[47 49] All participating healthcare systems currently use Lung-RADS for reporting. The receipt and timing of additional CT examinations will be examined based on these reports.

Lung cancer treatment will include data on treatment modalities focusing on the differences between surgery, chemotherapy and radiation therapy among patients with early-stage lung cancer. Receipt of curative radiotherapy may be a marker of overtreatment due to inappropriate LCS of patients with a high risk of other causes of mortality.[50]

The primary outcome of Aim 3 will evaluate the benefits and harms of LDCT screening for vulnerable populations with various multimorbidity levels, including lung cancer deaths averted, life-years gained, overdiagnosis, false-positive tests and radiation-related lung cancer deaths using simulation modelling. The real-world data inputs generated in Aim 1 and Aim 2 will be used to refine the University of Michigan Lung Cancer Screening model (UM-LCS).[51] The model inputs for the simulation modelling are presented in table 1. Detailed statistical methods can be found under the statistical plan.

Covariates

The following variable information will be extracted from the EHR data using previously validated methods:[52] age at each visit, race/ethnicity, history of smoking status and pack-years. Area-level SES measures will include the proportion of adults with a college education (US Census)[53] and other measures at the census block group level, including the diversity index score (a measure of the racial and ethnic diversity of a geographical area, ranging from 0 (no diversity) to 100 (complete diversity)), median disposable income, median household income, average annual health insurance expenditures,

Table 1 Model elements and data sources for simulation modelling

Model inputs	Possible data sources
Lung cancer incidence by age, sex and smoking history	NHS/HPFS, SEER
Tumour stage distribution by histology and sex	SEER, PLCO, NLST
Lung cancer-specific survival times by age, histology, stage and sex	SEER
Preclinical sojourn time in each stage	NLST, PLCO
Sensitivity and specificity of LDCT; false-positive rates	NLST/LungRADS and real-world LCSC
Adherence with Lung-RADS recommendations by multimorbidity burden	Real-world LCSC
LDCT screening outcomes; biopsies, complications	Real-world LCSC
Competing other-cause mortality	CISNET, NLST, PLCO, real-world LCSC

CISNET, Cancer Intervention and Surveillance Modeling Network; HPFS, Health Professionals Fellow-Up Study; LCSC, lung cancer screening cohort data (Aims 1 and 2 in the PLuS study); LDCT, lung cancer screening with low-dose CT; NHS, Nurses' Health Study; NLST, National Lung Screening Trial; PLCO, Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial; SEER, Surveillance, Epidemiology, and End Results.

average annual public transportation expenditures, and proportion with access to the internet.[53]

Data collection and management

Data elements will be collected and managed locally by investigators at each of the four sites and subsequently transferred securely to the Data Coordinating Center (DCC) at the University of Florida for quality control and analysis. The data elements will include both structured and unstructured health information collected at our participating healthcare systems. All four healthcare systems will work towards data harmonisation and use identical methods to abstract the data via the EHR and NLP methods. The study site will be linked to respective cancer registries to determine the timing of lung cancer diagnosis after LDCT, as well as other essential variables.

Patient and public involvement

There is no patient and public involvement in the design and conduct of the study.

Sample size and power analysis

The preliminary data collected from the four study sites will include ~40 000 unique individuals in the LCS cohort and ~800 incident lung cancer cases (based on an estimated 2% lung cancer rate) for the period 2016–2022. To estimate the sample size, we focused our calculation on the outcome for Aim 2, since the procedure-related complications were selected by the members of the research team to be the least likely of the LCS outcomes and would allow for a feasible sample.

We estimate that at least 70% of those undergoing LSC with LDCT will have at least one consequential comorbidity, and about 20% will have COPD.[54–56] Based on the prior literature, <5% of individuals who have LCS with LDCT receive subsequent invasive diagnostic procedures, and ~15%–20% of individuals undergoing an invasive diagnostic procedure will have procedure-related complications, even if those individuals have no major chronic co-existing conditions at the time of the diagnostic procedure.[57 58] Given these assumptions, the study is powered to identify a minimally detectable risk difference as small as 5% for procedure-related complications. This estimate considers 80% power and the probability of type I error of 0.05, which should be able to detect small effect sizes for minimally detectable risk differences of false-positive LCS results ranging between 1.3% and 1.9% across levels of comorbidity.

Analytical plan

The first aim will characterise the receipt of LCS by examining the burden of chronic comorbidities, functional limitations and impaired pulmonary function using descriptive statistics to fully characterise our patient population (including means and SD for continuous variables and χ^2 tests or contingency table analysis for categorical variables). As an exploratory sub-aim, we will examine this burden by race/ethnicity, SES and age. Additionally, to increase the generalisability of the estimates, we will generate a weighted variable for each observation based on the inverse of its selection probability and report weighted prevalence estimates of comorbidity, functional limitations and impaired pulmonary function. Two-sample proportion tests will be used to examine if the prevalence of comorbidity, functional limitations and impaired pulmonary function differ by race/ethnicity, SES or age. We will use multivariable logistic regression models to calculate adjusted ORs and 95% CIs of comorbidity, FRIs, and impaired pulmonary function, adjusting for race/ethnicity, SES, age, and other relevant covariates (eg, smoking status, calendar year screened and geographical location).

The second aim will examine the LCS outcomes following LDCT. We will first quantify potential harms (eg, false-positive results, procedure-related complications) and benefits (early-stage lung cancer at diagnosis) of LCS. Descriptive statistics will be conducted for the outcomes and will be stratified by measures of comorbidity, functional limitation and baseline pulmonary function. We will estimate the cumulative risk of these LCS outcomes over 7 years of screening performed during 2016–2022 using discrete-time survival models, which inherently account for the fact that the risk of an event only accrues at the time of screening exam.[59] Thus, time in the models will be indexed by the number of prior screening examinations rather than calendar time.

Additionally, using separate discrete-time survival models, we will estimate the hazard for each outcome of interest by comorbidity, functional limitations and impaired pulmonary function, adjusted for relevant covariates (eg, geographic location, SES, race/ethnicity, age, smoking status). We will model each LDCT scan as a separate observation and calculate the probability of an event within the following year, using comorbidity score, functional limitations, and pulmonary function at the beginning of each interval for each separate observation as time-varying, because they can change with each observation. Models will be pruned by backward selection using the Akaike information criterion to balance the predictive power of the model against model parsimony.[60] To estimate the cumulative probability of each outcome associated with LCS for persons of a given comorbidity level, functional limitation level or pulmonary function level, we will aggregate discrete hazards to estimate the average number of LCS examinations until a person first experiences an event as well as the cumulative probability of experiencing at least one event over 6 years of screening. To address missing data, logistic regression models will be used to identify the factors related to the probability of missing data and determine whether there is any distinct pattern of missingness. The issue of potential loss of power and bias due to missing data will be further addressed by using multiple imputation methods if the variables are missing at random. Before performing the statistical analysis for Aim 3, we will generate 10 imputed datasets, analyse them separately and then combine the results using established methods.[61] Sensitivity analyses

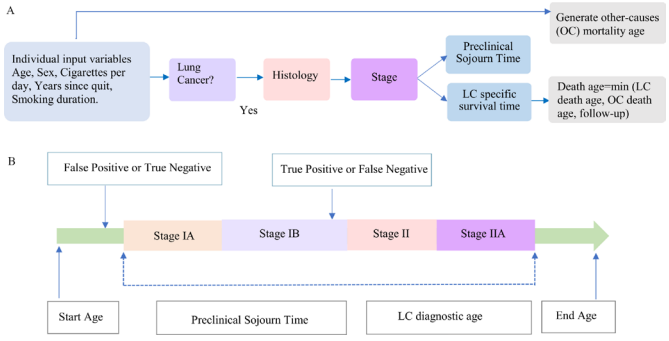

Figure 2 (A) Natural history component of the UM-LCS model. (B) Screening component of the UM-LCS model, example for an individual diagnosed with stage IIIA lung cancer in natural history component. LC, lung cancer; OC, other causes; UM-LCS, University of Michigan Lung Cancer Screening model.

will be based on using inverse probability (of having missing data) weights.[62]

Simulation modelling for Aim 3

The UM-LCS model consists of two main components: a natural history component and a screening component, which together generate an individual history. The natural history component simulates individual lung cancer-related events as well as death from causes other than lung cancer, given an individual's smoking history (figure 2A). The screening component simulates a stage-appropriate preclinical sojourn time (PST) (ie, the period in which an asymptomatic lung cancer develops before being detected once screening occurs), as well as a screening schedule and screening outcomes (figure 2B). For screening-detected cancers, the model simulates a new lung cancer survival time based on the stage at diagnosis. The UM-LCS model inputs are described in table 1. In the proposed study, we will recalibrate some model elements using data generated in Aims 1 and 2. The refined model will then evaluate various measures for the benefits and harms of LCS for vulnerable populations with various multimorbidity conditions under diverse screening scenarios. The reference scenario will be the annual LCS of individuals ages 55 through 80 years who have smoked for 30 pack-years and either currently smoke or quit smoking within 15 years.[11]

We will compare the benefits and harms in diverse screening scenarios by varying starting and stopping ages, frequencies and eligibility criteria based on smoking pack-years, years since quitting and level of multimorbidity. Comparative effectiveness of various LDCT screening strategies according to the level of smoking exposure, overall comorbidity, functional limitations and pulmonary/COPD status will be assessed. Furthermore, the UM-LCS model will be extended to incorporate complications observed in screened individuals given their multimorbidity conditions. We will also determine the threshold of multimorbidity (coexisting conditions, limited functioning and/or impaired pulmonary function) where the benefits and harms of LCS are comparable to those for a predefined subgroup having average health status for the population.

The simulation model outcomes will include (1) screening of eligible populations, (2) LDCT screens and follow-up scans, (3) false-positive screens, (4) lung cancer biopsies, (5) lung cancer incidence, (6) lung cancer mortality, (7) life-years/quality-adjusted life-years gained compared with no screening, (8) number needed to screen to prevent one lung cancer death, (9) overdiagnosis and (10) radiation-related lung cancer death.

DISCUSSION

The PLuS study will generate valuable data on a real-world population undergoing recommended LCS at four diverse healthcare systems. The study is designed to address LCS utilisation among patients with comorbidities, functional limitations and impaired pulmonary function that are largely unknown.

Although the NLST and other trials have shown that LCS with LDCT reduces the risk of lung cancer mortality, the benefits and harms found in prior studies are unknown in older and potentially sicker real-world populations. Compared with LCS trial participants, US adults eligible for LCS are nearly twice as likely to be >70 years old and are substantially more likely to have a history of current smoking.[14] Additionally, of the nearly 8.6 million LCS-eligible adults in the USA, ~3 million have chronic coexisting conditions that may decrease the net benefit of screening for early-stage disease.[56]

The first scientific manuscript for the PLuS study will describe the results of LCS utilisation patterns and present empirical data by multimorbidity. Our study has the potential to inform future updates and refinement of screening guidelines concerning the health status of individuals with multimorbidity. The subsequent papers will describe the rates of benefits and harms of LCS outcomes in the presence of multimorbidity. Finally, using inputs from observational studies, the refined simulation model results will be presented, which will help us to quantify the impact of comorbidity, functional limitations, pulmonary function on screening outcomes and the net benefit of LCS with LDCT on long-term health outcomes in real-world clinical settings. Thus, the current proposed study results will characterise the population with a high comorbidity burden, quantifying for them the benefits and harms of LCS and help guide clinical decision-making for patients with comorbidities who are at risk of lung cancer.

ETHICS AND DISSEMINATION

The study protocol was approved by the Kaiser Permanente Southern California (KPSC)

Institutional Review Board (IRB) under the smart IRB Master Common Reciprocal Institutional Review Board Authorisation Agreement (Reference number: 12430) for all sites except the VA Portland Healthcare System, whose

IRB determined this study to be exempt from review (Exemption number: 4507). The DCC at UF will ensure that the required data elements are reliably collected and mapped into a commonly defined, Health Insurance Portability and Accountability Act (HIPAA)-compliant format, and are managed in a flexible, secure data system. The DCC will establish and maintain systems to collect common data elements across all four participating institutions and provide a secure transfer and distribution infrastructure to meet HIPAA, collaborating institutions and the US federal regulations for data sharing.

The data and the results have the potential to directly benefit public health and will be disseminated by the research team through the presentation of high-quality reports at national and international conferences, and through publications in peer-reviewed journals.

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Competing interests None declared.

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