Deep Learning to Estimate Biological Age from Chest Radiographs

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Introduction

- Aging is a fundamental cause of cancer, cardiovascular, and neurological diseases via chronic inflammation, cellular damage and senescence, and genomic instability.
- Chronological age (years since birth) is an imperfect measure of aging, but is routinely used in clinical care to stratify risk
- Biological age is a number in years that quantifies an individual's decline in function
- Biological age is currently estimated via DNA methylation, co-morbidities, or functional tests, but are rarely used clinically due to mixed results for chronic disease prediction and difficulty in obtaining source data.
- Chest radiographs (chest x-rays or CXRs) are the most common diagnostic imaging test

Purpose

- To develop a deep learning model (CXR-Age) that estimates biological age from a single chest x-ray image
- To assess whether CXR-Age predicts all-cause mortality better than chronological age

Methods

- A Resnet34 CNN was pretrained to predict chronological age using publicly available cohorts
- The CNN was then fine-tuned to predict a "biological age" in 25% of the PLCO CXR Arm
- Biological age labels **for training only** were defined as:

  BA = CA + (E-D)

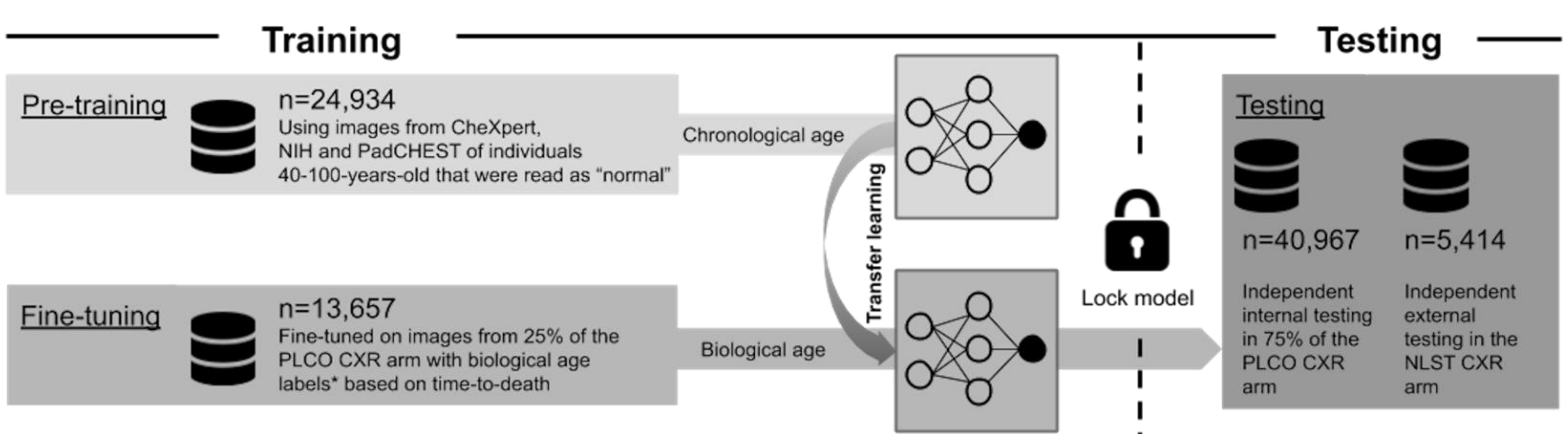
- BA is the biological age label, CA is chronological age at the time of the CXR, E is an expected age at death according to US Social Security Life Tables, and D is actual age at death
- For those who survived during follow-up D was estimated using a risk-factor based survival model developed in the control arm of PLCO

Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) Screening Trial

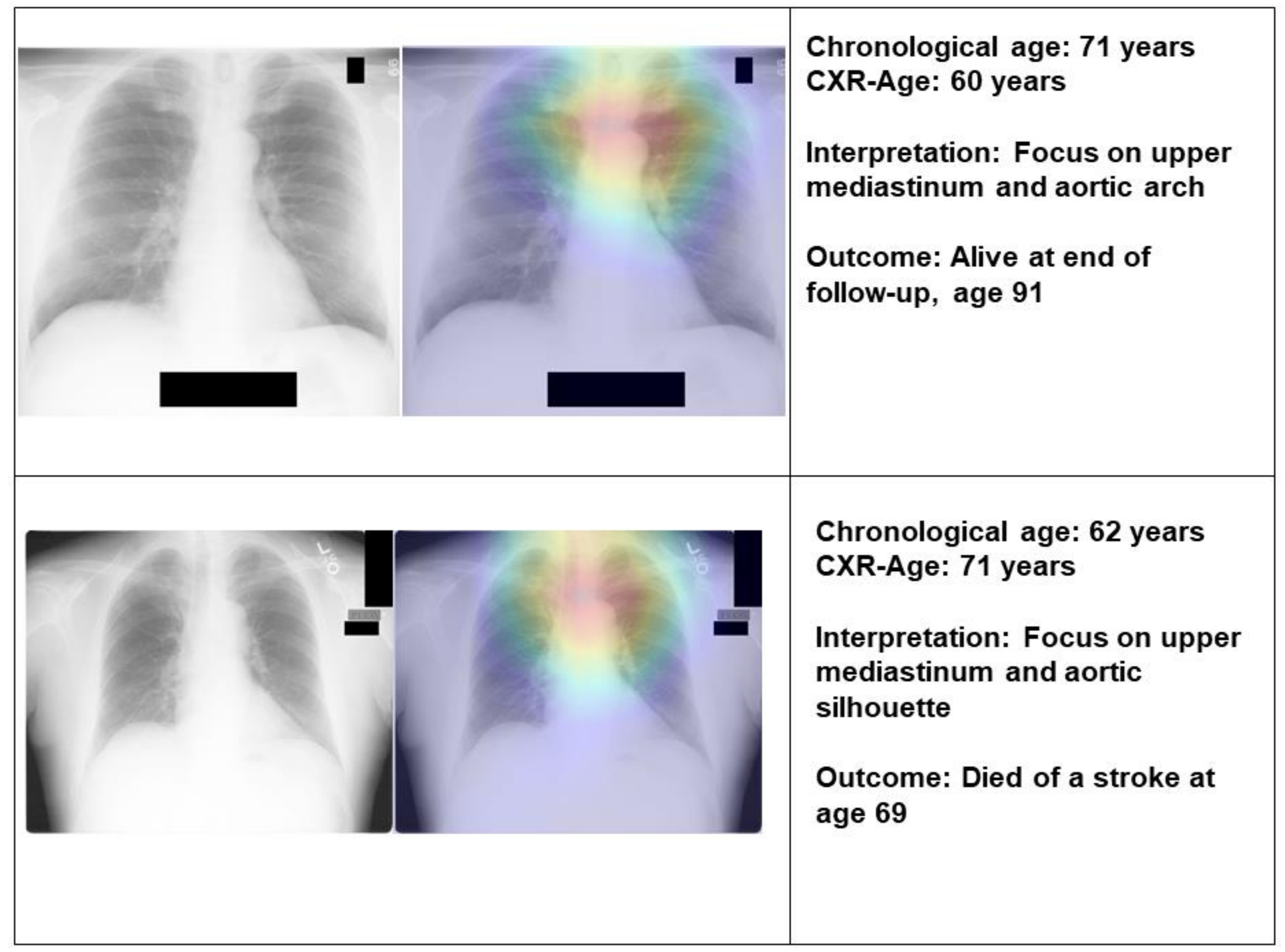
- RCT of no screening vs screening with CXR
- 55-74 years old
- Non-smokers and smokers
- Enrolled @ 10 US sites
- **Outcome:** Median 18-year follow-up for mortality

National Lung Screening Trial (NLST)

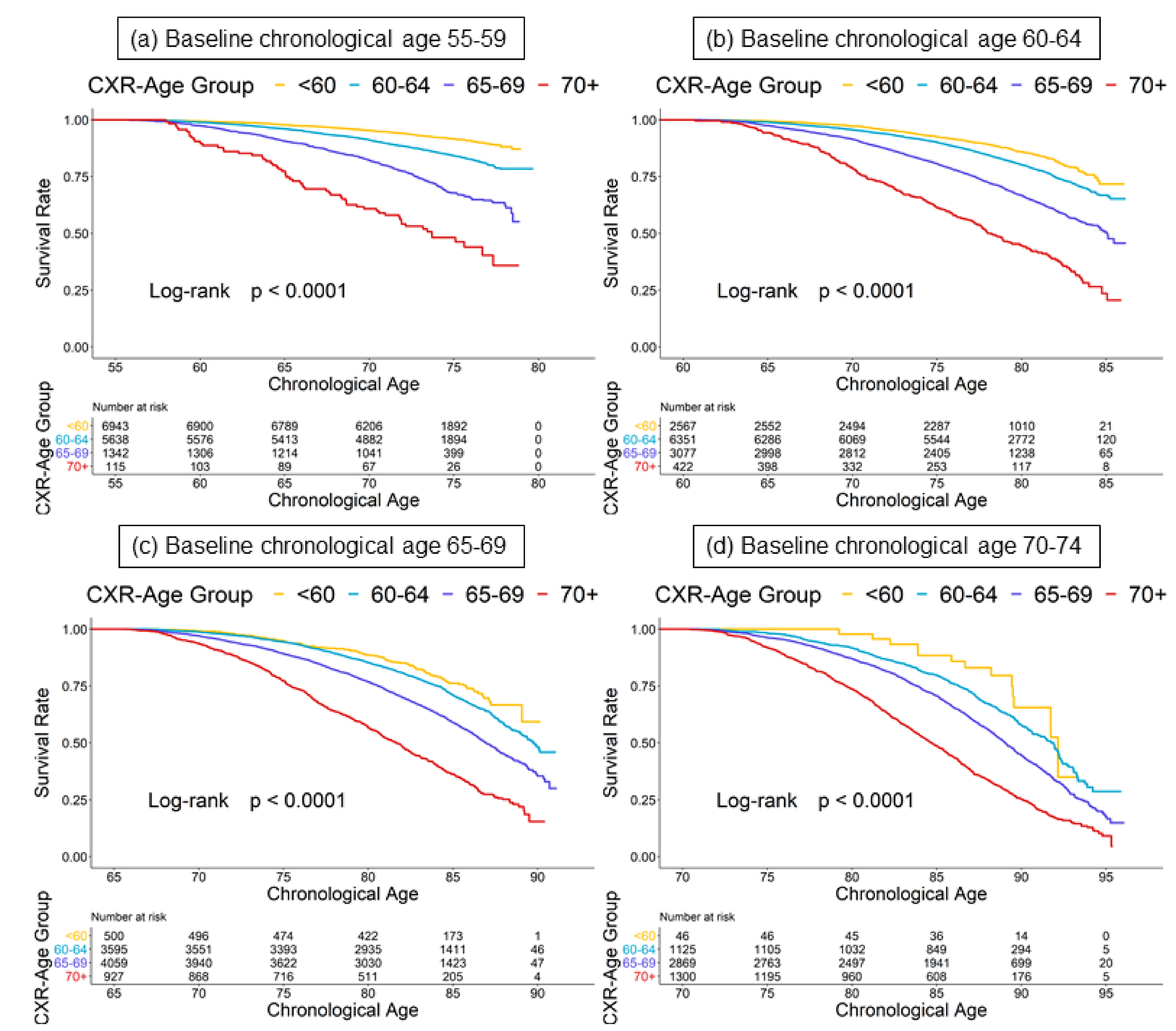
- RCT of no screening CXR vs CT
- 55-74 years old
- Current or former heavy smokers
- Enrolled @ 23 US sites
- **Outcome:** Median 12-year follow-up for mortality



Results



Gradient-Weighted Class Activation Maps (Grad-CAM) localize anatomy contributing to CXR-Age estimates to the upper mediastinum and aortic arch, areas that tend to dilate and become tortuous with age



Kaplan-Meier survival curves by CXR-Age group in PLCO testing data for individuals with a baseline chronological age of (a) 55-59 years, b) 60-64 years, c) 65-69 years, and d) 70-74 years. CXR-Age shows a graded association with longevity in individuals with similar baseline chronological age.

	Observed All-Cause Mortality		Observed Cardiovascular Mortality	
	PLCO Testing C-statistic (95% CI)	NLST Testing C-statistic (95% CI)	PLCO Testing C-statistic (95% CI)	NLST Testing C-statistic (95% CI)
Risk Factors + Findings + Chronological Age	0.741 (0.74,0.74)	0.692 (0.68,0.70)	0.795 (0.79,0.80)	0.735 (0.72,0.75)
Risk Factors + Findings + Chronological Age + CXR-Age	0.751 (0.75,0.75)†	0.705 (0.70,0.71) †	0.808 (0.80,0.81) †	0.755 (0.74,0.77) †

CXR-Age predicts mortality with incremental value to a risk factor and findings regression model

†Significant at $p < 0.001$ against model with Risk Factors + Findings + Chronological age

* Risk factors included: sex, smoking status, diabetes, hypertension, BMI, past myocardial infarction, past stroke, past cancer

Conclusion

- A convolutional neural network can estimate biological age from a chest x-ray image, and this biological age predicts mortality better than chronological age

References

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