A comparison of self-supervised pretraining approaches for risk prediction from chest radiograph images

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Abstract

Deep learning is the state-of-the-art for medical imaging tasks, but requires large, labeled datasets. For risk prediction, large datasets are rare since they require both imaging and follow-up (e.g., diagnosis codes). However, the release of publicly available imaging data with diagnostic labels presents an opportunity for self and semi-supervised approaches to improve label efficiency for risk prediction. Though several studies have compared self-supervised approaches in natural image classification, object detection, and medical image interpretation, there is limited data on which approaches learn robust representations for risk prediction. We present a comparison of semi- and self-supervised learning to predict mortality risk using chest x-ray images. We find that a semi-supervised autoencoder outperforms contrastive and transfer learning in internal and external validation.

Keywords: Deep learning, risk prediction, chest radiographs, self-supervised pretraining

1. Introduction

Deep learning [5,24] is the state of the art for medical image segmentation [18] and interpretation [17] tasks ; however, deep learning requires large, labeled datasets, which are rare. One solution is transfer learning, where models are initially trained to classify objects in large natural image data (e.g., ImageNet [11]), and then fine-tuned for the target task. However, ImageNet-based transfer learning may provide limited benefit beyond training models entirely from scratch [30]. In contrast, self-supervised techniques use unlabeled medical images to learn compressed, expressive representations. Due to the feasibility of releasing unlabeled image data, this strategy is promising for medical image analysis [34].

Beyond image interpretation, deep learning can estimate future disease risk [25,28,33,26,31] using datasets with imaging and follow-up. These tasks differ from common pretraining tasks (e.g., object detection, segmentation, etc.) in that there is not necessarily a localizable pathology (object of interest) on the image. For example, abstract concepts like frailty, posture, and gestalt suggestive of old age may indicate higher disease risk [41]. In addition, labels are scarce as follow-up information (diagnosis dates, dates of death, etc.) is protected health information. Here, self- and semi-supervised techniques can improve risk prediction by using unlabeled data to improve label efficiency.

Chest radiographs (x-ray or CXR) are an ideal test-bed for risk prediction approaches because they are the most common diagnostic imaging test [32]. Studies have shown that

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deep learning models can accurately interpret CXRs [5], and self-supervised techniques [34] improve CXR interpretation beyond transfer learning [37]. These efforts have been supported by the public release of large datasets with radiologists' interpretation of CXRs including: Stanford University's CheXpert [17], Chest x-ray 14 from the National Institutes of Health's Clinical Center [40], PadCHEST from San Juan, Spain [4], and MIMIC-CXR from Boston, MA [19] ($>$ 1 million total images). For risk prediction, these datasets are "unlabeled" in that there is no follow-up information. It is not yet known whether self- and semi-supervised techniques can leverage such data to improve label efficiency.

In this study, we evaluate self- and semi-supervised pretraining techniques for predicting mortality risk from CXRs. Our specific contributions are:

- We introduce a novel semi-supervised autoencoder for representation learning
- We evaluate pretraining strategies using target variables with varying class imbalance.
- We investigate the generalizability of representations in an external validation dataset.
- We assess whether representations can predict disease history and risk factors.

2. Related Work

2.1. Self-supervised learning approaches

Self-supervised learning specifies a pre-training task on unlabeled datasets to improve performance on a target task with limited labeled data [15]. Most self-supervised learning strategies fall into 1) autoencoder/bottleneck and 2) contrastive learning-based approaches.

2.1.1. Autoencoder-based approaches

Autoencoders have two parts: 1) an "encoder" network that compresses the input image into a low-dimensional encoding and 2) a subsequent "decoder" model that reconstructs the original input image from the encoding [35, 43]. In [43], the authors combine a masked autoencoder (input is randomly occluded) with a vision transformer [21] to improve classification of thoracic diseases beyond contrastive learning and ImageNet pretrained models; however, this study only had internal validation. In [35], the authors used a convolutional autoencoder to predict lung nodule malignancy from chest computed tomography images and found a modest improvement over training from scratch. In [14]. the authors show that more generalizable representations are obtained via a variational autoencoder trained on both labeled and unlabeled data with self-ensembling [23]; however, this work lacked external validation.

2.1.2. Contrastive Learning Approaches

In contrastive learning, a model is trained to create image representations such that "positive pairs" (e.g., images from the same patient) have similar representations and "negative pairs" (e.g., images from different patients) have dissimilar representations [2,39,15,16]. Contrastive-learning improves performance on natural image classification tasks [8, 42]; however, a challenge is how to efficiently sample negative pairs since these are quadratic in the dataset size. Some use large batch sizes so that the model sees a diversity of negative pairs at each gradient update; however, this is GPU-memory intensive. The Patient

Contrastive Learning (PCLR) approach is one such strategy [12] Appendix: Contrastive Learning Methodology.

Others have proposed using a "memory bank" approach where representations of previously sampled images are stored. Then, representations from the current mini-batch are "negative pairs" with these stored representations. Thus, the min-batch size is decoupled with the size of the memory bank. One such implementation is momentum contrast or MoCo [15], further described in Appendix: MoCo Methodology

Some approaches avoid using negative pairs entirely (BYOL, DINO, etc.) [6,13]. Instead, a teacher and student network receive augmented views of the same image, and the student must output a "prediction" that matches the teacher's prediction. Typically, the teacher is a moving average of previous student networks.

2.2. Comparisons of self-supervised and transfer-based pretraining

One study compared fully-supervised ImageNet pretraining vs. self-supervised pretraining, including SimCLR, SwAV (Swapping Assignments between multiple Views of the same image) [7], DINO [39], and an ensemble approach (Dynamic Visual Meta-Embedding - DVME) on medical image interpretation tasks. For CXR interpretation, no method consistently outperformed; however, self-supervised learning consistently outperformed transfer learning from ImageNet. It is unknown whether these results hold when using in-domain pretraining or in risk prediction tasks. In [2], the authors combined semi-supervised learning with end-to-end contrastive learning as a pretraining method. They compared two image augmentation methods: MICILe (two crops of the same image) vs. SimCLR (rotation, zoom, etc. of the same image). No difference was observed in CXR intepretation tasks. Another work compared [37] a modified MoCo pretrained on CheXpert vs. pretrained on ImageNet. Models were fine-tuned on CheXpert and Shenzhen hospital CXR datasets using 1) an additional linear layer or 2) end-to-end fine-tuning. MoCo models pretrained on CXRs performed better than ImageNet pretrained for all tested label fractions.

These results are corroborated by findings [10] that demonstrate that the pretraining task domain and the quality of the pre-training data are crucial factors for performance. Findings in medical imaging tasks [30] show that simple architectures trained entirely from scratch outperform large models pretrained using ImageNet. To our knowledge, no studies have tested pretraining strategies on risk prediction from medical imaging.

3. Methods

3.1. Datasets

In our study, we test use two medical imaging datasets for pretraining: CheXpert [17] and NIH CXR-14 [40] (Appendix Figure A.6). CheXpert contains 224,316 frontal posterior-anterior (PA) and lateral CXRs taken at Stanford Hospital between October 2002 and July 2017. NIH CXR-14 contains CXRs taken at the NIH Clinical Center between 1992 and 2015 (108,948 images from 32,717 patients). Only frontal, PA CXRs from patients aged 18 to 100 years were included (29419 CXRs from CheXpert and 64628 from NIH CXR-14). Since no follow-up is available, we use age, sex, and acute findings (Appendix Table F.6) from the radiologist's read for semi-supervised pre-training. For hyperparameter optimization,

CheXpert and NIH CXR-14 were split into training ($N = 74984$) and tuning ($N = 19063$) datasets using a random 80%-20% split by patient. These datasets are used solely for pre-training; no results are reported.

All models were fine-tuned using data (Appendix Figure A.5) from the Prostate, Lung, Colorectal, and Ovarian cancer screening trial (PLCO) [27,29]. PLCO was a randomized trial where adults 55-74 years were randomized to either a CXR or control (no imaging) with a maximum of 18 years of follow-up. The test dataset includes CXRs from PLCO (40,000 T_{min} - earliest CXR for each participant) and the CXR arm of the National Lung Screening Trial (NLST; 5,414 T_{min} CXRs) [1]. The NLST enrolled adults 55-77 years who had a heavy smoking history. NLST participants had max 12 years of follow-up. Models were trained to predict all-cause mortality 1 and 12 years after the CXR.

3.2. Pre-training approaches

We compare pre-training approaches: semi- and unsupervised autoencoder, semi- and unsupervised end-to-end contrastive learning (Patient-Centered Learning of Representations - PCLR), semi- and unsupervised MoCo, transfer learning, and training from scratch.

3.2.1. Semi-Supervised Autoencoder architecture

The Semi-Supervised Autoencoder architecture has three components (Figure 1):

1. An image encoder $f(\cdot)$, which given input image x_i, outputs a 512-dimensional encoding $f(x_i) = h_i$. The encoder consists of 4 convolutional blocks, each with a convolutional layer (7x7 filters), batch normalization, ReLU activation, and max-pooling (3x3 window and 2x2 stride) (Figure 1). This architecture was previously shown to outperform transfer learning in medical image interpretation [30].

2. A prediction module, which uses image encodings h_i to classify 14 radiologist findings, (see Section 3.1) sex, and a continuous estimate of age. This encourages representations useful to identify important pathology and demographics.

3. An image decoder $g(\cdot)$, which reconstructs the input image x_i given encoding h_i. The decoder has 4 backward basic blocks, all with upsampling, batch norm, ReLU activation, and last layer sigmoid activation (Figure 1).

3.2.2. Semi-Supervised Autoencoder Loss

The model weights are optimized using a three-part loss function:

1. First, reconstruction error using mean-squared error (MSE) of predicted $\hat{x}$ vs. original $n * m * p$ images x:

$$recon_{x,\hat{x}} = \frac{1}{nmp} \sum_{i=1}^{n} \sum_{j=1}^{m} \sum_{k=1}^{p} (x_{i,j,k} - \hat{x}_{i,j,k})^2 \tag{1}$$

2. Second, a composite cross-entropy loss for multi-label classification (findings and sex) and MSE loss for age. Let n be the number of categorical labels. The total classification and regression loss for encoding h_i, with ground truth classification labels Y_i and

predicted labels $\hat{Y}_i$, ground truth age age_i and predicted age $\hat{age}_i$, can be written as:

$$reg_{h_i} = (age_i - \hat{age}_i)^2 \; and \; cls_{h_i} = -\frac{1}{m}\sum_{i=1}^{m}(Y_i \cdot \log \hat{Y}_i + (1 - Y_i) \cdot \log(1 - \hat{Y}_i)). \quad (2)$$

3. Third, an L1 Regularization on the encodings h_i [3].

The overall loss is given by:

$$Loss_{autoencoder} = \lambda_{recon} * recon_{x,\hat{x}} + \lambda_{reg} * (reg_{h_i} + cls_{h_i}) + \lambda_{norm} * norm \quad (3)$$

Here, λ_{recon}, λ_{reg}, and λ_{norm} control the contributions of reconstruction, classification, and normalization to the overall loss. We chose $(1, 20, 0.0001)$ as defaults to scale each equally. We tested the sensitivity of λ and found little impact (Hyperparameter Sensitivity Analysis).

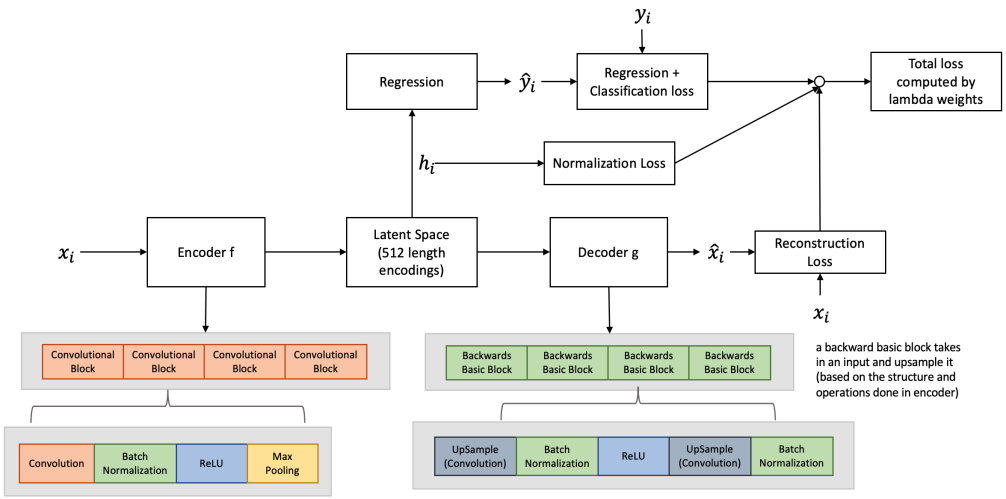

Figure 1: Autoencoder architecture for an input CXR x_i and corresponding label y_i.

3.2.3. Other Approaches

Transfer Learning & Train From Scratch We tested transfer learning [38], where the pretraining task was to predict sex, the radiologist findings, and age. We also tested a model that was trained with randomly initialized weights on the PLCO training dataset ("train from scratch"). All approaches use the encoder architecture described above (Section 3.3.1). The transfer learning loss was just the composite cross-entropy and multi-label classification loss (see 3.3.2). A binary cross-entropy loss was used for training from scratch.

Contrastive Learning We used two implementations of contrastive learning: 1) an end-to-end Patient Contrastive Learning of Representations (PCLR) [12] and Momentum Contrast-CXR (MoCo-CXR) [37] A detailed explanation of both approaches are in Appendix: Contrastive Learning Methodology and .

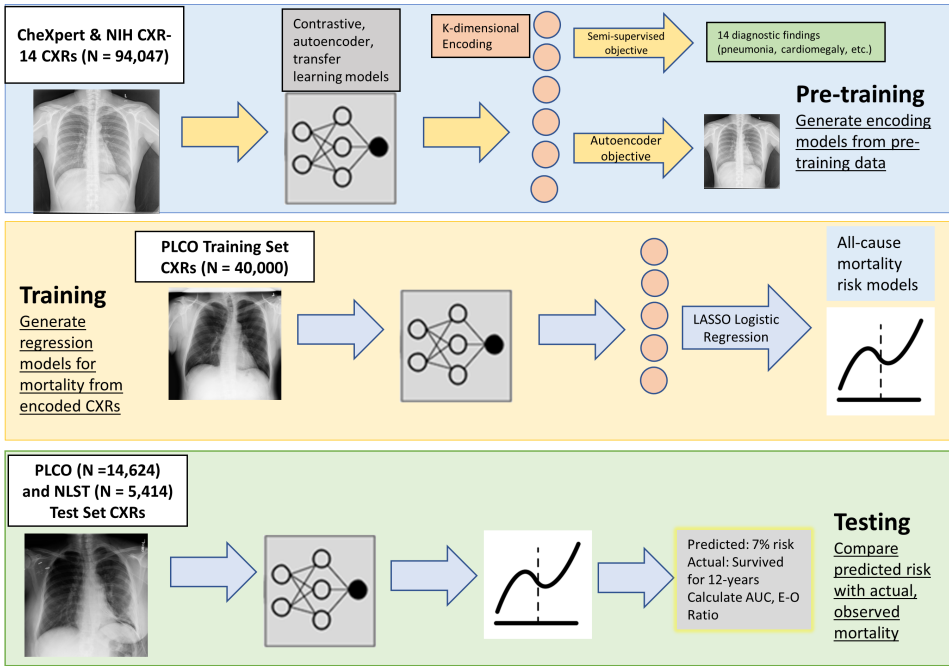

Figure 2: Overview of experimental procedure.

3.2.4. Model Optimizers and Optimizations

All models were trained for 100 epochs, batch size 64, using the Adam optimizer [20] with a maximum learning rate of $1e-5$ and the 1-cycle policy [36]. For each strategy, the model with the lowest validation loss during training was chosen for downstream experiments.

3.3. Experiments

Experimental steps are outlined in Figure 2. After pretraining, we perform forward propagation on all PLCO and NLST images. The extracted encodings from PLCO are divided into training and testing sets (80% - 20% split). The testing set (N = 40,000) is fixed for all experiments, and we randomly sample from the training set to generate 15 datasets for each sample size (40000, 20000, 10000, 5000, 2000, 1000, 500, and 200). Identical training and testing sets were used for all models to ensure fairness. We test the effect of imbalanced outcomes by training on 1-year (event rate 0.456%) and 12-year mortality (14.205%).

PLCO encodings were scaled and centered and 0 variance encodings were removed. Testing encodings were transformed using training data statistics. A LASSO logistic regression was trained to predict mortality risk using extracted image encodings. λ for LASSO was selected using cross-validation AUC [22]. Pretraining strategies were assessed using discrimination and calibraiton of downstream predictions. We used mean AUC for discrimination and mean E/O Ratio (expected/observed ratio) for calibration across the 15 trials for each training set size and mortality time horizon.

4. Results

4.1. Effect of pre-training strategy on discriminative accuracy

In Figure 3 and Figure 4, we compared discrimination for 12- and 1-year all-cause mortality. We found that semi-supervision outperformed other models in external validation for most training set sizes. In particular, the semi-supervised autoencoder and transfer learning from diagnostic labels (with no self-supervision) had highest AUC when the training set was small, while semi-supervised contrastive learning excelled with >5000 samples and for 1-year mortality. Among the fully self-supervised models, contrastive learning (PCLR) performed the closest to semi-supervised methods and even outperformed semi-supervised MoCo in external validation for 12-year mortality. Often, training a model from scratch outperformed self-supervised approaches. For all approaches, the gap between internal and external validation AUC was higher for 12-year mortality than 1-year, potentially due to overfitting. This gap was still pronounced for 1-year mortality for transfer learning, unsupervised PCLR, and training from scratch ($> 5\%$ drop in AUC) (Figure 3 and Figure 4).

4.2. Effect of pretraining strategy on calibration

We assessed calibration using the E-O Ratio (Appendix Table D.2, Appendix Table D.3, Appendix Table D.4, Appendix Table D.5). In internal validation, we find that all models are well-calibrated for 12-year mortality (except train from scratch which over-predicted risk), and all models over-predicted risk for 1-year mortality. In external validation, the semi-supervised autoencoder and transfer learning were well-calibrated, especially for 1-year mortality. Contrastive learning approaches consistently under-predicted risk for both 12- and 1-year mortality. Unsupervised models followed a similar trend, except contrastive learning alone was well-calibrated in 12-year external validation, whereas the unsupervised autoencoder was well-calibrated for 1-year external validation. In general, semi-supervised models had better calibration in external validation than their self-supervised counterparts.

4.3. Comparison of pretraining strategies to predict risk factors

To assess whether some representations were more suited to certain disease processes (e.g., cardiovascular vs. lung disease), we used generated encodings to develop prediction models for prevalent risk factors, disease history, and radiologist findings (Appendix: Intermediate Risk Factors Results). We found that the semi-supervised autoencoder predicted all risk factors better than other pretraining approaches in internal and external validation.

5. Discussion

In this study, we tested several pretraining approaches to predict mortality risk from CXR images. Our major findings were that 1) using diagnostic labels in pre-training is better than self-supervised and no pretraining, 2) self-supervised pretraining is no better than training from scratch in most cases, and 3) a semi-supervised autoencoder and transfer learning representations were strongly associated with risk factors. We found that autoencoder representations were robust to hyperparameter choices and were generally well-calibrated. Unlike previous studies of medical imaging pretraining, our study focuses on risk prediction and

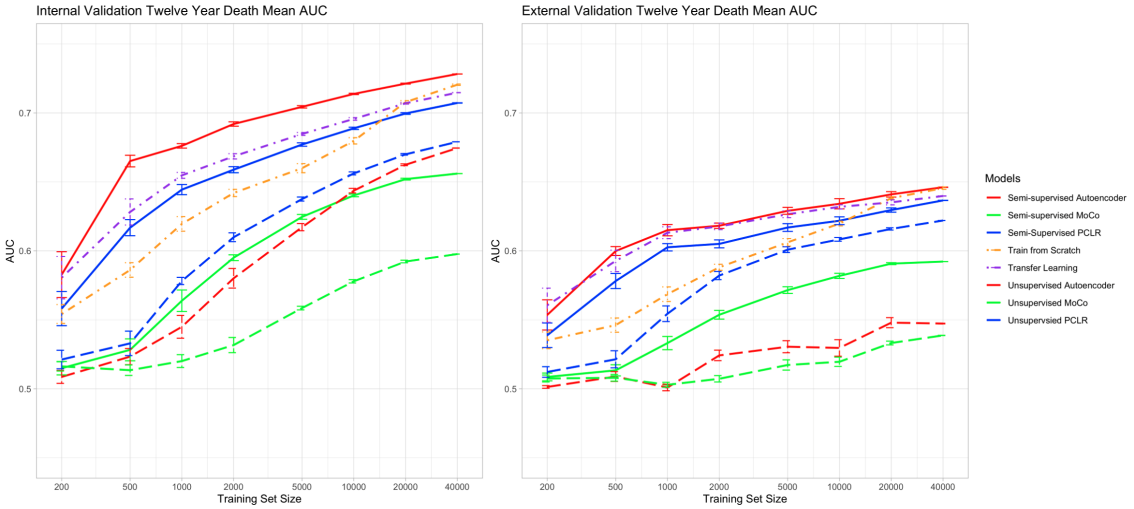

Figure 3: Comparison of approaches to predict 12-year mortality. Training set size (x-axis) vs. mean AUC (y-axis) in PLCO internal (left) and NLST external validation (right) data.

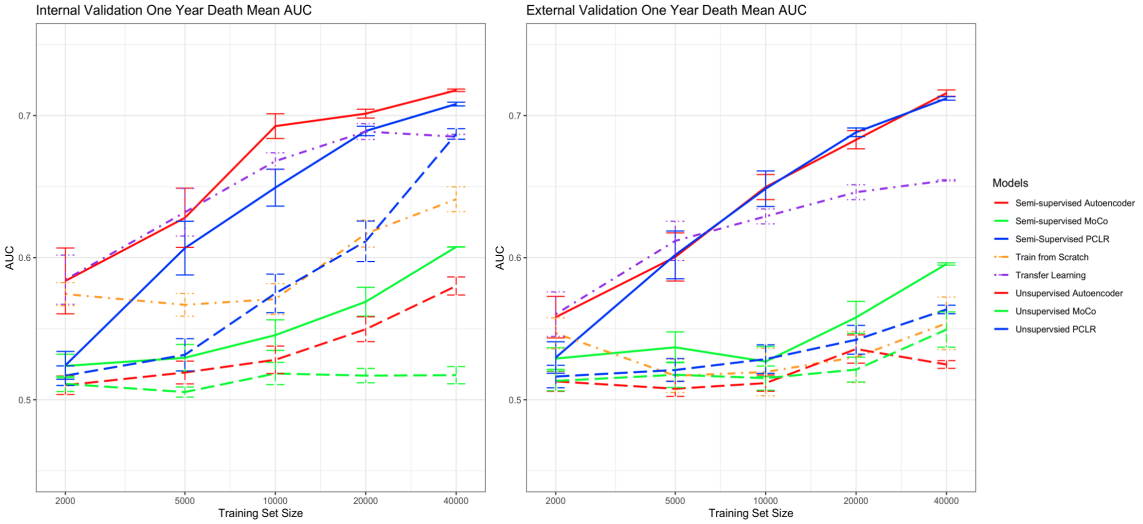

Figure 4: Comparison of approaches to predict 1-year mortality. Training set size (x-axis) vs. mean AUC (y-axis) in PLCO internal (left) and NLST external validation (right) data.

tests representations in internal and external validation. The semi-supervised autoencoder is publicly available at https://github.com/circ-ml/cxr-encoder. For future work, we plan to test other common imaging modalities (e.g., retinal fundoscopy, CT) and other incident disease states. Here, we focused on a single architecture that was successful in CXR tasks, but we plan to test other architectures.

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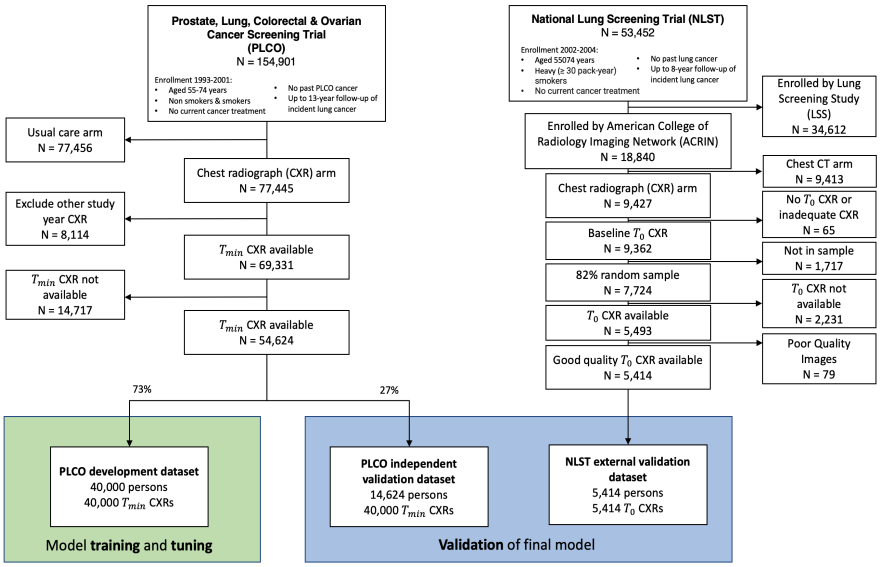
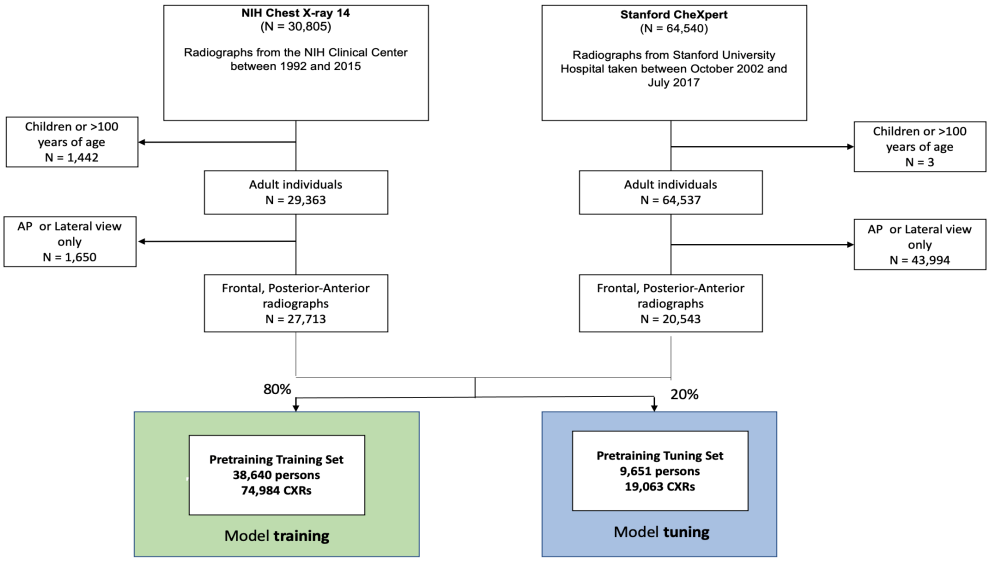
Appendix A. Image Preprocessing

Image preprocessing steps followed our previous work [31]. For PLCO CXRs, we converted original TIF files to PNG with a short-axis dimension of 512 using ImageMagick. A previously developed CNN was used to identify rotated PLCO radiographs and ImageMagick was used to correct these. Similar preprocessing steps were used for NLST, though first CXRs were converted from native DICOM to TIF using the DCMTK toolbox. All input PNG images to the model were resized to 224 x 224 pixels using random cropping along the longer axis. Random data augmentation was used during training, including up to 5 degrees of rotation, up to 20% zoom in/out, and up to 50% brightness and contrast adjustment. No augmentation was used during validation and testing.



Appendix Figure A.5: CONSORT diagram for PLCO and NLST training and testing datasets. Only the earliest (T_{min}) CXR from each patient was used.



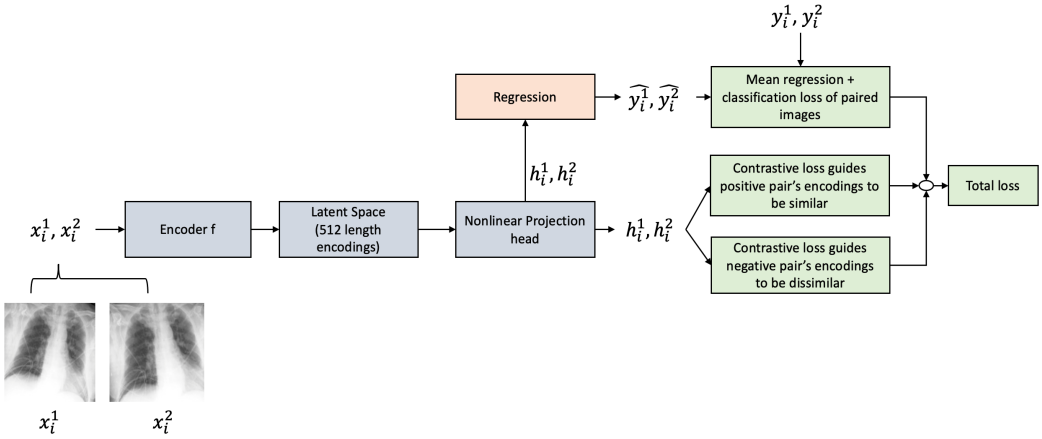
Appendix Figure A.6: CONSORT diagram for pretraining datasets NIH Chest X-ray 14 and CheXpert. Only adult, frontal, and posterior-anterior radiographs are kept.

Appendix B. End-to-end Contrastive Learning Methodology (PCLR)

We implemented the same data selection method used in PCLR [12] but with a different model architecture. For training, first, a mini-batch of images from unique patients was randomly sampled. To create "positive pairs," a second image from each of these patients was randomly sampled, otherwise, an augmented version of the first image was used. All individual images were randomly transformed as described in Appendix A
The Contrastive Learning approach used an identical image encoder architecture as the Autoencoder-Classifier but trained with different loss functions and input data structure. The major differences in this approach are as follows:

1. A Nonlinear projection head using the ReLU activation function that maintains 512-dimensional encodings and projects image encodings onto a nonlinear space. The results of [8] demonstrate that the incorporation of a nonlinear projection head leads to an improvement in the quality of the representation learned by contrastive learning models. The aim of the projection head is to learn a compact, meaningful and discriminative representation of the input data that can be effectively used in later downstream tasks.

2. A Contrastive loss function is used to train the encoder and projection head. Contrastive loss $cl_{i,j}$ will be low for positive pairs and high for negative pairs, which encourages the model to generate similar encodings (based on cosine similarity) for CXRs from the same patient and dissimilar encodings for CXRs from different patients.



Appendix Figure B.7: Contrastive Learning model architecture for an input x-ray image pair (x_i^1, x_i^2)
and corresponding label (y_i^1, y_i^2).

PCLR Loss To make image encodings $p(h_i)$ produced by the projection head p similar for positive pairs and dissimilar for negative pairs, we used the contrastive loss function

introduced in SimCLR [9]. Let (z_i, z_j) be positive pairs, remaining (z_i, z_k) be negative pairs, τ be the temperature of the similarity function, loss of a positive pair (z_i, z_j) (in total of N pairs of input) using cosine similarity sim as the distance between two encodings can be written as:

$$l_{i,j} = -\log \frac{exp(sim(z_i, z_j)/\tau)}{\sum_{k=1}^{2N} \mathbb{1}_{k \neq i} exp(sim(z_i, z_k)/\tau)} \tag{4}$$

Given a batch of M patients, we will have a total of 2M encoded images and M-positive pairs. Two adjacent encoded images h_i, h_{i+1} will be positive pairs. Thus total loss will be the sum of all losses between positive pairs is:

$$C_{batch} = \frac{1}{2M} \sum_{i=1}^{M} [l_{i,i+1}]_{i \in 2\mathbb{Z}} \tag{5}$$

Appendix C. MoCo Methodology

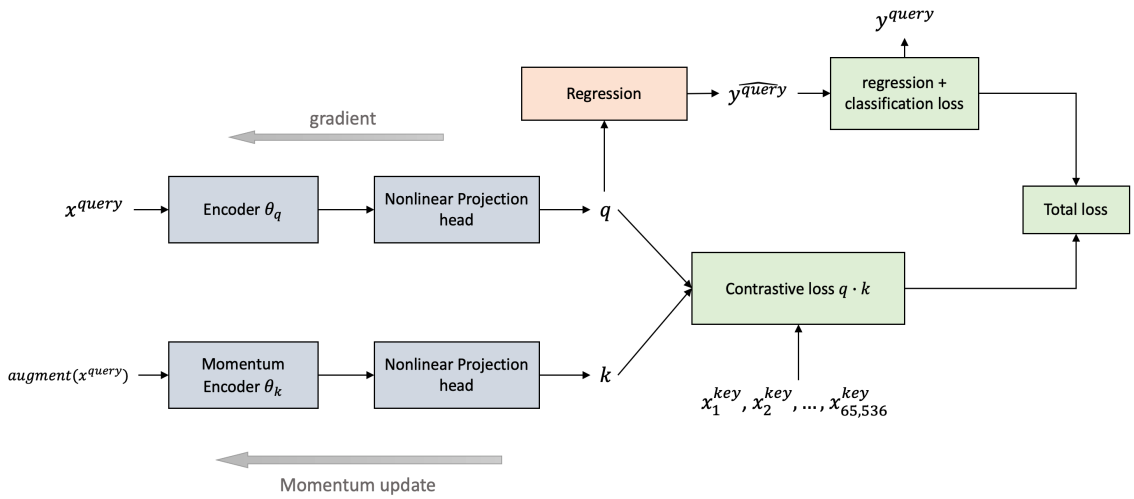
We used the MoCo pretraining technique as described in[15] with a batch size of 32 anchor images. A heavy image augmentation technique, similar to the procedure used in SimCLR, is employed as a pretraining task.
The MoCo pre-training procedure is as follows Figure C.8:

1. An image encoder θ_q used to generate a 512-dimensional image encoding for anchor image (or query, which is the name used in [15]). The structure of this image encoder is the same as that of a complete autoencoder. The image encoding is then projected onto a 128-dimensional vector space using a nonlinear projection head, denoted by $g(\cdot)$.

2. A momentum encoder θ_k is used to encode the positive and negative pair for the query. The structure of θ_k is exactly the same as θ_q, but no back-propagation is performed. The weights were updated using $\theta_k \leftarrow m\theta_k + (1-m)\theta_q$ [15] where m is the momentum hyperparameter which controls the speed of momentum encoder's update. We set $m = 0.999$ as suggested.

3. A first-in-first-out (FIFO) queue, comprised of previous image encodings (keys), enqueues the latest mini-batch's encodings, and dequeues the earliest mini-batch's encodings. Since MoCo is more effective when the dictionary size is large, we used 65,536 for the queue size as suggested by the authors.

4. A contrastive loss function Equation 4 was used to train the overall model with back-propagation performed only on the parameters of θ_q. It uses the query image and its augmented version as a positive pair, which is encoded by θ_k, and the rest of the keys in the queue as negative pairs. The softmax temperature was 0.07.



Appendix Figure C.8: Momentum Contrastive Learning model architecture for an input x-ray x^{query}, its augmented version as positive pair $augment(x^{query})$, and corresponding label y^{query}.

Appendix D. Calibration of all-cause mortality risk estimates

Lambda	One-Year Death (PLCO)				Twelve-Year Death (NLST)			
	Amplified Classification Parameter	Amplified Image Reconstruction Parameter	Amplified Normalization Parameter	Original Parameter	Amplified Classification Parameter	Amplified Image Reconstruction Parameter	Amplified Normalization Parameter	Original Parameter
200	1.026(0.215)	1.027(0.212)	1.021(0.221)	1.031(0.211)	0.998(0.535)	1.104(0.921)	1.071(0.827)	1.04(0.513)
500	1.054(0.078)	1.056(0.08)	1.05(0.08)	1.047(0.079)	1.218(0.66)	0.925(0.584)	1.098(0.719)	1.137(0.672)
1000	1.014(0.067)	1.01(0.066)	1.009(0.07)	1.008(0.067)	1.601(0.83)	1.127(0.844)	1.285(0.646)	1.166(0.65)
2000	1.021(0.057)	1.024(0.055)	1.026(0.055)	1.023(0.057)	1.857(0.754)	1.229(0.685)	1.127(0.622)	1.483(0.696)
5000	1.025(0.032)	1.024(0.032)	1.024(0.03)	1.023(0.031)	1.433(0.42)	0.99(0.585)	0.631(0.239)	0.835(0.558)
10000	1.143(0.124)	1.136(0.116)	1.168(0.124)	1.262(0.311)	1.133(0.117)	1.03(0.013)	1.031(0.018)	1.034(0.021)
20000	1.227(0.085)	1.221(0.086)	1.224(0.103)	1.162(0.106)	1.223(0.086)	1.031(0.015)	1.033(0.017)	1.036(0.011)
40000	1.212(0.0)	1.206(0.0)	1.209(0.003)	1.187(0.102)	1.21(0.001)	1.029(0.0)	1.031(0.0)	1.031(0.0)

Appendix Table D.1: Calibration Results for Hyperparameter Sensitivity Analysis

PLCO	One-year death					Twelve-Year Death				
	Semi-Supervised Autoencoder	Semi-supervised PCLR	Transfer Learning	From Scratch	Semi-supervised MoCo	Semi-Supervised Autoencoder	Semi-supervised PCLR	Transfer Learning	From Scratch	Semi-supervised MoCo
200	N/A	N/A	N/A	N/A	N/A	1.024(0.21)	1.024(0.206)	1.018(0.116)	1.17(0.831)	1.027(0.211)
500	N/A	N/A	N/A	N/A	N/A	1.052(0.081)	1.052(0.079)	1.106(0.108)	1.142(0.179)	1.057(0.08)
1000	N/A	N/A	N/A	N/A	N/A	1.008(0.061)	1.003(0.066)	1.015(0.06)	1.141(0.115)	1.006(0.067)
2000	1.116(0.417)	1.114(0.412)	1.223(0.316)	1.881(1.59)	1.102(0.435)	1.022(0.057)	1.017(0.055)	1.039(0.036)	1.108(0.096)	1.016(0.058)
5000	1.222(0.249)	1.201(0.249)	1.23(0.259)	1.226(0.445)	1.207(0.252)	1.019(0.029)	1.021(0.033)	1.034(0.025)	1.078(0.054)	1.022(0.032)
10000	1.143(0.124)	1.136(0.116)	1.168(0.124)	1.262(0.311)	1.133(0.117)	1.03(0.013)	1.031(0.018)	1.034(0.021)	1.115(0.031)	1.031(0.016)
20000	1.227(0.085)	1.221(0.086)	1.224(0.103)	1.162(0.106)	1.223(0.086)	1.031(0.015)	1.033(0.017)	1.036(0.011)	1.112(0.026)	1.032(0.017)
40000	1.212(0.0)	1.206(0.0)	1.209(0.003)	1.187(0.102)	1.21(0.001)	1.029(0.0)	1.031(0.0)	1.031(0.0)	1.081(0.032)	1.031(0.0)

Appendix Table D.2: Calibration of semi-supervised and supervised models in the PLCO dataset. Results are not available for some smaller training sets due to insufficient events.

NLST	One-year death					Twelve-Year Death				
	Semi-Supervised Autoencoder	Semi-supervised PCLR	Transfer Learning	From Scratch	Semi-supervised MoCo	Semi-Supervised Autoencoder	Semi-supervised PCLR	Transfer Learning	From Scratch	Semi-supervised MoCo
200	N/A	N/A	N/A	N/A	N/A	0.997(0.452)	0.864(0.224)	0.881(0.287)	1.435(0.654)	0.796(0.157)
500	N/A	N/A	N/A	N/A	N/A	1.005(0.393)	0.907(0.096)	1.031(0.356)	1.163(0.293)	0.824(0.057)
1000	N/A	N/A	N/A	N/A	N/A	1.01(0.223)	0.86(0.106)	1.017(0.34)	1.18(0.337)	0.793(0.059)
2000	1.215(1.235)	0.673(0.281)	1.251(1.168)	2.272(2.169)	0.648(0.263)	1.204(0.267)	0.877(0.095)	1.073(0.18)	1.217(0.216)	0.802(0.049)
5000	1.802(1.776)	0.701(0.15)	1.093(0.666)	1.874(0.635)	0.76(0.177)	1.161(0.211)	0.905(0.095)	1.143(0.175)	1.212(0.157)	0.841(0.068)
10000	1.506(0.848)	0.713(0.122)	1.127(0.455)	1.722(0.475)	0.7(0.096)	1.268(0.314)	0.935(0.048)	1.22(0.176)	1.278(0.122)	0.874(0.05)
20000	1.332(0.571)	0.717(0.126)	0.977(0.266)	1.555(0.297)	0.785(0.087)	1.372(0.169)	0.963(0.032)	1.19(0.11)	1.186(0.082)	0.872(0.035)
40000	1.113(0.076)	0.716(0.014)	1.055(0.038)	1.684(0.215)	0.806(0.005)	1.275(0.003)	0.973(0.002)	1.238(0.007)	1.099(0.051)	0.868(0.001)

Appendix Table D.3: Calibration of semi-supervised and supervised models in the NLST dataset. Results are not available for some smaller training sets due to insufficient events.

PLCO	One-year death			Twelve-Year Death		
	Unsupervised Autoencoder	Unsupervised PCLR	Unsupervised MoCo	Unsupervised Autoencoder	Unsupervised PCLR	Unsupervised MoCo
200	N/A	N/A	N/A	1.032(0.206)	1.024(0.206)	1.027(0.202)
500	N/A	N/A	N/A	1.048(0.084)	1.052(0.079)	1.052(0.08)
1000	N/A	N/A	N/A	1.006(0.069)	1.003(0.066)	1.003(0.067)
2000	1.209(0.249)	1.114(0.412)	1.112(0.413)	1.02(0.057)	1.017(0.055)	1.014(0.058)
5000	1.135(0.119)	1.201(0.249)	1.202(0.247)	1.024(0.033)	1.021(0.033)	1.019(0.032)
10000	1.227(0.087)	1.136(0.116)	1.133(0.119)	1.033(0.017)	1.031(0.018)	1.028(0.017)
20000	1.218(0.231)	1.221(0.086)	1.219(0.085)	1.035(0.016)	1.033(0.017)	1.031(0.015)
40000	1.204(0.002)	1.206(0.0)	1.201(0.001)	1.034(0.0)	1.031(0.0)	1.031(0.0)

Appendix Table D.4: Calibration of unsupervised models in the PLCO dataset

NLST	One-year death			Twelve-Year Death		
	Unsupervised Autoencoder	Unsupervised PCLR	Unsupervised MoCo	Unsupervised Autoencoder	Unsupervised PCLR	Unsupervised MoCo
200	N/A	N/A	N/A	1.361(1.167)	0.864(0.224)	0.778(0.17)
500	N/A	N/A	N/A	0.831(0.196)	0.907(0.096)	0.806(0.062)
1000	N/A	N/A	N/A	1.2(0.894)	0.86(0.106)	0.781(0.06)
2000	0.935(0.611)	0.673(0.281)	0.638(0.205)	1.104(0.68)	0.877(0.095)	0.794(0.062)
5000	0.965(0.783)	0.701(0.15)	0.712(0.147)	0.566(0.314)	0.905(0.095)	0.784(0.033)
10000	0.958(0.592)	0.713(0.122)	0.675(0.07)	0.389(0.142)	0.935(0.048)	0.805(0.025)
20000	1.196(0.649)	0.717(0.126)	0.723(0.052)	0.379(0.068)	0.963(0.032)	0.826(0.021)
40000	1.004(0.002)	0.716(0.014)	0.711(0.005)	0.388(0.006)	0.973(0.002)	0.831(0.001)

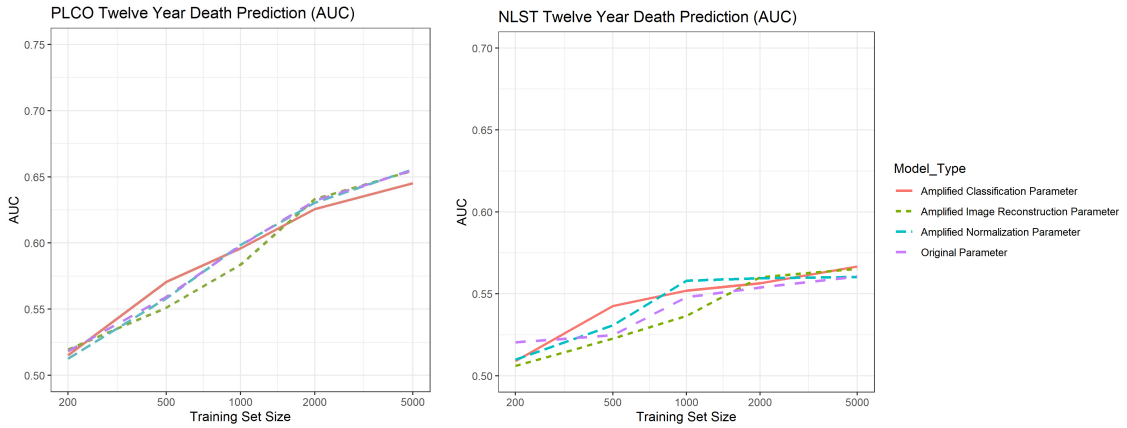
Appendix Table D.5: Calibration of self-supervised models in the NLST dataset.

Appendix E. Hyperparameter Sensitivity Analysis

We performed a sensitivity analysis on the hyperparameters for the Autoencoder-Classifier's loss function $\lambda_{reg}, \lambda_{recon}, \lambda_{norm}$. The default parameters were $(1, 20, 0.0001)$. We tested the following configurations:

- Amplified Classification & Regression parameter λ_{reg}: $(10, 20, 0.0001)$
- Amplified Image reconstruction parameter λ_{recon}: $(1, 200, 0.0001)$
- Amplified Normalization parameter λ_{norm}: $(1, 20, 0.001)$

Using each parameter setting, we trained separate models on a randomly selected set of 7000 radiographs from the pretraining datasets and tested them on PLCO and NLST to predict 12-year mortality: Figure E.9 and Table D.1.
The results for different hyperparameters are generally consistent with each other. However, amplification of the classification loss shows a slight disadvantage for internal validation when the training set size is large, and a slight advantage for both internal and external validation when the training set size is small. It is possible that a larger discrepancy may emerge if a larger subset of images is used for training. Currently, scaling up any of the hyperparameters does not significantly impact the AUC showing the robustness of the approach.



(a) PLCO-1 (b) NLST-1

Appendix Figure E.9: AUC comparisons for 12-year mortality rate between different hyperparameter settings.

Appendix F. Radiologist Findings Supplementary Table

Radiologist Findings	Percent Positive
No Finding	47041/94047 (50.0%)
Pleural Effusion	14528/94047 (15.4%)
Lung Opacity	9736/94047 (10.4%)
Lung Lesion	9094/94047 (9.7%)
Infiltration	8976/94047 (9.5%)
Atelectasis	8809/94047 (9.4%)
Pneumothorax	5070/94047 (5.4%)
Cardiomegaly	4429/94047 (4.7%)
Consolidation	2961/94047 (3.1%)
Pleural Thickening	2366/94047 (2.5%)
Edema	1977/94047 (2.1%)
Pneumonia	1784/94047 (1.9%)
Emphysema	1473/94047 (1.6%)
Enlarged Cardiomediastinum	1436/94047 (1.5%)
Fracture	1411/94047 (1.5%)
Fibrosis	1394/94047 (1.5%)
Pleural Other	1012/94047 (1.1%)
Hernia	191/94047 (0.2%)

Appendix Table F.6: Percent positive labels for all radiologist findings in the pretraining datasets.

Appendix G. Prediction of intermediate risk factors

		PLCO Internal Validation			
	Target Variable	Semi-Supervised Autoencoder	Semi-Supervised MoCo	Semi-Supervised PCLR	Transfer Learning
Continuous Demographics and Risk Factors	Age	0.654 (0.64,0.66)	0.465 (0.45,0.48)	0.392 (0.38,0.41)	0.373 (0.36,0.39)
	BMI	0.823 (0.82,0.83)	0.629 (0.62,0.64)	0.732 (0.72,0.74)	0.656 (0.65,0.67)
	Pack-Years	0.332 (0.31,0.35)	0.205 (0.18,0.23)	0.217 (0.2,0.24)	0.202 (0.18,0.22)
Discrete Demographics and Risk Factors	Black Race	0.947 (0.94,0.95)	0.776 (0.76,0.79)	0.845 (0.83,0.86)	0.794 (0.78,0.81)
	History of Type 2 Diabetes	0.752 (0.74,0.77)	0.669 (0.65,0.69)	0.709 (0.69,0.72)	0.667 (0.65,0.68)
	History of Emphysema	0.799 (0.77,0.82)	0.677 (0.65,0.7)	0.676 (0.65,0.7)	0.684 (0.66,0.71)
	History of Smoking	0.675 (0.67,0.68)	0.622 (0.61,0.63)	0.63 (0.62,0.64)	0.622 (0.61,0.63)
	History of Myocardial Infarction	0.763 (0.75,0.78)	0.673 (0.66,0.69)	0.7 (0.68,0.72)	0.662 (0.65,0.68)
	Hispanic Ethnicity	0.789 (0.76,0.82)	0.728 (0.7,0.76)	0.746 (0.72,0.78)	0.684 (0.65,0.72)
	History of Hypertension	0.696 (0.69,0.7)	0.644 (0.63,0.65)	0.661 (0.65,0.67)	0.649 (0.64,0.66)
	History of Osteoporosis	0.804 (0.79,0.82)	0.76 (0.74,0.78)	0.745 (0.73,0.76)	0.708 (0.69,0.73)
	History of Cancer	0.649 (0.63,0.67)	0.619 (0.6,0.64)	0.629 (0.61,0.65)	0.602 (0.58,0.62)
	Sex	0.999 (1,1)	0.991 (0.99,0.99)	0.987 (0.99,0.99)	0.958 (0.96,0.96)
	History of Stroke	0.672 (0.64,0.7)	0.602 (0.57,0.63)	0.62 (0.59,0.65)	0.593 (0.56,0.62)
Radiologist Findings	Atelectasis	0.753 (0.56,0.95)	0.523 (0.26,0.78)	0.628 (0.43,0.83)	0.576 (0.29,0.86)
	Bone/Chest Wall Lesion	0.761 (0.74,0.78)	0.694 (0.67,0.72)	0.731 (0.71,0.75)	0.665 (0.64,0.69)
	Cardiovascular Abnormality	0.89 (0.88,0.9)	0.786 (0.77,0.81)	0.811 (0.79,0.83)	0.81 (0.79,0.83)
	COPD/Emphysema	0.842 (0.82,0.86)	0.752 (0.73,0.78)	0.785 (0.76,0.81)	0.745 (0.72,0.77)
	Lung Fibrosis	0.704 (0.69,0.72)	0.608 (0.59,0.62)	0.612 (0.6,0.63)	0.629 (0.61,0.65)
	Lung Opacity	0.68 (0.63,0.73)	0.569 (0.52,0.62)	0.562 (0.51,0.61)	0.586 (0.53,0.64)
	Lymphadenopathy	0.725 (0.67,0.78)	0.67 (0.62,0.72)	0.59 (0.52,0.66)	0.563 (0.5,0.63)
	Lung Nodule	0.617 (0.6,0.63)	0.59 (0.57,0.61)	0.593 (0.57,0.61)	0.559 (0.54,0.58)
	Pleural Fibrosis	0.723 (0.7,0.75)	0.646 (0.62,0.67)	0.633 (0.61,0.66)	0.613 (0.59,0.64)

Appendix Table G.7: Comparison of prediction of intermediate risk factors for supervised and semi-supervised models on the PLCO dataset using Pearson Correlation for continuous variables and AUC for discrete variables. Results indicate superior performance of the semi-supervised autoencoder in most target tasks.

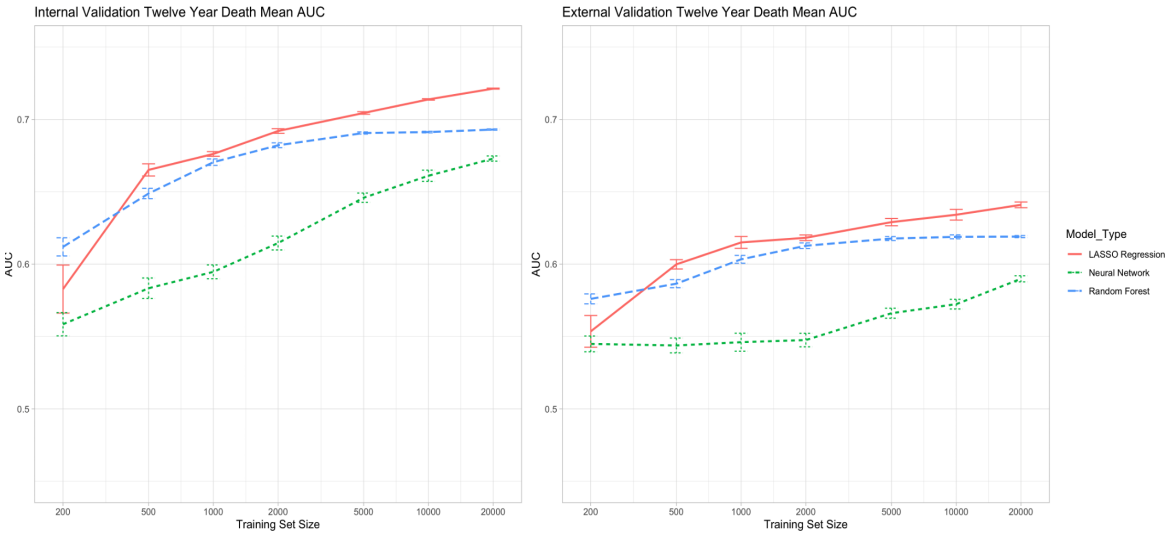
		NLST External Validation			
	Target Variable	Semi-Supervised Autoencoder	Semi-Supervised MoCo	Semi-Supervised PCLR	Transfer Learning
Continuous Demographics and Risk Factors	Age	0.547 (0.53,0.57)	0.465 (0.44,0.49)	0.226 (0.2,0.25)	0.407 (0.38,0.43)
	BMI	0.761 (0.75,0.77)	0.493 (0.47,0.51)	0.63 (0.61,0.65)	0.68 (0.67,0.69)
	Pack-Years	0.181 (0.16,0.21)	0.166 (0.14,0.19)	0.101 (0.07,0.13)	0.156 (0.13,0.18)
Discrete Demographics and Risk Factors	History of Type 2 Diabetes	0.737 (0.72,0.76)	0.651 (0.63,0.68)	0.679 (0.66,0.7)	0.704 (0.68,0.73)
	History of Emphysema	0.609 (0.58,0.64)	0.574 (0.54,0.6)	0.573 (0.54,0.6)	0.637 (0.61,0.67)
	History of Myocardial Infarction	0.669 (0.65,0.69)	0.625 (0.6,0.65)	0.622 (0.6,0.64)	0.657 (0.63,0.68)
	History of Hypertension	0.634 (0.62,0.65)	0.595 (0.58,0.61)	0.608 (0.59,0.62)	0.644 (0.63,0.66)
	History of Cancer	0.637 (0.6,0.68)	0.602 (0.56,0.64)	0.543 (0.51,0.58)	0.576 (0.54,0.61)
	Sex	0.993 (0.99,1)	0.974 (0.97,0.98)	0.905 (0.9,0.91)	0.917 (0.91,0.92)
	History of Stroke	0.596 (0.55,0.64)	0.528 (0.48,0.57)	0.578 (0.53,0.62)	0.601 (0.56,0.64)
Radiologist Findings	Atelectasis	0.611 (0.53,0.69)	0.501 (0.41,0.59)	0.566 (0.47,0.66)	0.588 (0.5,0.67)
	Bone/Chest Wall Lesion	0.608 (0.54,0.68)	0.511 (0.43,0.59)	0.569 (0.49,0.64)	0.507 (0.43,0.58)
	Cardiovascular Abnormality	0.721 (0.67,0.77)	0.77 (0.73,0.81)	0.715 (0.67,0.76)	0.808 (0.76,0.85)
	COPD/Emphysema	0.638 (0.62,0.66)	0.6 (0.58,0.62)	0.643 (0.63,0.66)	0.679 (0.66,0.69)
	Lung Fibrosis	0.606 (0.58,0.63)	0.572 (0.55,0.59)	0.51 (0.49,0.53)	0.542 (0.52,0.56)
	Lung Opacity	0.65 (0.55,0.75)	0.539 (0.43,0.65)	0.496 (0.4,0.59)	0.534 (0.41,0.65)
	Lymphadenopathy	0.615 (0.53,0.7)	0.521 (0.44,0.6)	0.615 (0.54,0.69)	0.526 (0.44,0.61)
	Lung Nodule	0.544 (0.53,0.56)	0.521 (0.5,0.54)	0.527 (0.51,0.54)	0.541 (0.52,0.56)
	Pleural Fibrosis	0.514 (0.49,0.54)	0.558 (0.53,0.58)	0.499 (0.47,0.52)	0.598 (0.57,0.62)

Appendix Table G.8: Prediction accuracy of intermediate risk factors using supervised and semi-supervised models on the NLST external validation dataset. We observed similar findings as in the internal validation (PLCO) results.

		PLCO Internal Validation			NLST External Validation		
	Target Variable	Unsupervised PCLR	Unsupervised Autoencoder	Unsupervised MoCo	Unsupervised PCLR	Unsupervised Autoencoder	Unsupervised MoCo
Continuous Demographics and Risk Factors	Age	0.469 (0.46,0.48)	0.433 (0.42,0.45)	0.196 (0.18,0.21)	0.368 (0.34,0.39)	0.126 (0.1,0.15)	0.121 (0.09,0.15)
	BMI	0.744 (0.74,0.75)	0.73 (0.72,0.74)	0.509 (0.5,0.52)	0.692 (0.68,0.71)	0.464 (0.44,0.48)	0.349 (0.33,0.37)
	Pack-Years	0.246 (0.22,0.27)	0.226 (0.21,0.25)	0.171 (0.15,0.19)	0.153 (0.13,0.18)	0.044 (0.02,0.07)	0.083 (0.06,0.11)
Discrete Demographics and Risk Factors	History of Type 2 Diabetes	0.715 (0.7,0.73)	0.689 (0.67,0.7)	0.635 (0.62,0.65)	0.705 (0.68,0.73)	0.558 (0.53,0.59)	0.58 (0.55,0.61)
	History of Emphysema	0.709 (0.68,0.74)	0.672 (0.64,0.7)	0.64 (0.61,0.67)	0.617 (0.59,0.65)	0.542 (0.51,0.57)	0.567 (0.54,0.6)
	History of Smoking	0.641 (0.63,0.65)	0.629 (0.62,0.64)	0.615 (0.61,0.62)	NA	NA	NA
	History of Myocardial Infarction	0.712 (0.7,0.73)	0.689 (0.67,0.7)	0.631 (0.62,0.65)	0.652 (0.63,0.67)	0.546 (0.52,0.57)	0.571 (0.55,0.59)
	History of Hypertension	0.675 (0.67,0.68)	0.667 (0.66,0.68)	0.606 (0.6,0.62)	0.629 (0.61,0.64)	0.559 (0.54,0.57)	0.564 (0.55,0.58)
	History of Osteoporosis	0.762 (0.75,0.78)	0.747 (0.73,0.76)	0.721 (0.7,0.74)	NA	NA	NA
	History of Cancer	0.633 (0.61,0.66)	0.616 (0.59,0.64)	0.631 (0.61,0.65)	0.563 (0.52,0.6)	0.537 (0.5,0.58)	0.503 (0.47,0.54)
	Sex	0.992 (0.99,0.99)	0.982 (0.98,0.98)	0.943 (0.94,0.95)	0.949 (0.94,0.95)	0.754 (0.74,0.77)	0.728 (0.71,0.74)
	History of Stroke	0.626 (0.59,0.66)	0.585 (0.55,0.62)	0.532 (0.5,0.57)	0.551 (0.51,0.59)	0.504 (0.46,0.55)	0.511 (0.47,0.56)
Radiologist Findings	Atelectasis	0.556 (0.29,0.82)	0.613 (0.47,0.76)	0.54 (0.4,0.68)	0.548 (0.46,0.63)	0.548 (0.47,0.63)	0.551 (0.46,0.64)
	Bone/Chest Wall Lesion	0.727 (0.7,0.75)	0.704 (0.68,0.73)	0.689 (0.67,0.71)	0.569 (0.5,0.64)	0.615 (0.54,0.69)	0.499 (0.42,0.57)
	Cardiovascular Abnormality	0.841 (0.82,0.86)	0.79 (0.77,0.81)	0.736 (0.71,0.76)	0.809 (0.77,0.85)	0.628 (0.57,0.68)	0.639 (0.59,0.69)
	COPD/Emphysema	0.783 (0.76,0.81)	0.775 (0.75,0.8)	0.697 (0.67,0.72)	0.65 (0.63,0.67)	0.597 (0.58,0.61)	0.567 (0.55,0.59)
	Lung Fibrosis	0.647 (0.63,0.66)	0.603 (0.59,0.62)	0.564 (0.55,0.58)	0.6 (0.58,0.62)	0.503 (0.48,0.53)	0.512 (0.49,0.54)
	Lung Opacity	0.607 (0.55,0.66)	0.541 (0.49,0.59)	0.556 (0.5,0.61)	0.533 (0.45,0.62)	0.538 (0.45,0.63)	0.497 (0.42,0.58)
	Lymphadenopathy	0.671 (0.61,0.73)	0.634 (0.58,0.69)	0.58 (0.52,0.64)	0.566 (0.48,0.65)	0.505 (0.41,0.6)	0.565 (0.49,0.64)
	Lung Nodule	0.59 (0.57,0.61)	0.576 (0.56,0.59)	0.572 (0.55,0.59)	0.542 (0.52,0.56)	0.524 (0.51,0.54)	0.513 (0.5,0.53)
	Pleural Fibrosis	0.66 (0.63,0.69)	0.624 (0.6,0.65)	0.607 (0.58,0.63)	0.58 (0.55,0.61)	0.509 (0.48,0.53)	0.519 (0.49,0.55)

Appendix Table G.9: Prediction accuracy of intermediate risk factors using self-supervised models on PLCO (internal validation) and NLST (external validation). Results indicate superior performance of Unsupervised Contrastive Learning and Autoencoder in most tasks.

Appendix H. A Comparison of Results of Different Downstream Task Models



Appendix Figure H.10: The performance of LASSO regression, a neural network with one hidden layer and nonlinear activation, and a random forest with 10 max nodes and 10 trees were evaluated using AUC on 12-year mortality rate prediction with the PLCO dataset. Results showed that LASSO had the best AUC performance across all training sizes. However, the neural network failed to converge in most trials of size 40,000, therefore trial size 40,000 was not included in the final analysis.