Deep Ensembles with Uncertainty Quantification for Chest X-Ray Diagnosis: A Preliminary Study

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Abstract

The clinical integration of deep learning models in high-stakes medical imaging is critically constrained by their inability to quantify predictive confidence. This project sought to establish a robust architectural foundation for Uncertainty Quantification (UQ) in multi-label chest X-ray (CXR) diagnosis across 14 pathology classes. The initial plan to enhance CheXNet was halted due to significant challenges in reproducing its published performance. A subsequent UQ attempt using Monte Carlo Dropout (MCD) on the reproducible DannyNet base resulted in unacceptable degradation of classification metrics. This motivated a rigorous architectural search using diverse backbones and novel loss functions. The resulting Deep Ensemble (DE), constructed from the nine best performing models from this search, successfully addresses the performance bottleneck, surpassing current state-of-the-art deterministic baselines with an average AUROC of 0.8559 and an average F1 score of 0.3857. These results validate the Deep Ensemble as a high-performance platform. The next phase will focus on rigorous technical validation of the ensemble's inherent uncertainty estimates and the integration of Grad-CAM for explainability.

1 Introduction

1.1 Problem Context and Motivation

Deep learning models, such as CheXNet, have achieved expert-level accuracy in detecting thoracic diseases on the NIH ChestX-ray14 dataset. Despite this success, their deployment in clinical practice is limited by the lack of reliable confidence measures. Deterministic models provide only a point prediction, whereas clinicians require an estimate of predictive confidence, especially for ambiguous or rare cases. This gap motivates the integration of Uncertainty Quantification (UQ) into high-performance diagnostic systems.

1.2 Architectural Challenges and Strategic Pivot

The project initially aimed to enhance the CheXNet base. However, early experiments revealed significant challenges in reproducing the original paper's reported AUROC scores on publicly available test sets, rendering CheXNet an unreliable foundation [2]. This reproducibility limitation prompted a pivot to the DannyNet architecture, which retains the DenseNet-121 backbone but provides superior performance and reproducibility. An initial UQ attempt using Monte Carlo Dropout (MCD) on the reproduced DannyNet base led to a decrease in classification performance, highlighting the need for a more sophisticated uncertainty-aware architecture.

1.3 Preliminary Contributions

This paper establishes the high-performance architectural foundation for the final system:

- Verified CheXNet reproducibility issues, justifying the pivot to DannyNet.
- Demonstrated the failure of Monte Carlo Dropout (MCD) on DannyNet, motivating the ensemble approach.
- Executed a systematic search across diverse backbones and loss functions to create a robust pool of 14 models.
- Implemented and validated a Deep Ensemble (DE) constructed from the nine best models, surpassing the state-of-the-art deterministic baseline in both average AUROC and F1 score.

2 Related Work

2.1 Benchmarks, Reproducibility, and Architectural Pivot

The foundational benchmark in thoracic disease classification is CheXNet, based on the DenseNet-121 backbone [1]. However, reproducing CheXNet's published metrics on public test sets has proven challenging, highlighting a critical reproducibility issue in medical machine learning research. This limitation necessitated a pivot to the DannyNet architecture, which shares the DenseNet-121 backbone but is empirically validated as a more robust and reproducible state-of-the-art (SOTA) baseline for the NIH ChestX-ray14 dataset [2].

2.2 Challenges in Multi-Label Classification (MLC) and Loss Functions

Multi-label classification (MLC) in CXR diagnosis presents technical hurdles beyond class imbalance. Challenges include:

- Indeterminate Target Label Size — varying number of pathologies per image.
- Inter-Label Correlation — certain pathologies often co-occur.

To address these challenges, which are present in the NIH ChestX-ray14 dataset, our systematic model search explored two key loss functions:

- Focal Loss: Standard approach to mitigate class imbalance [2,5].
- ZLPR Loss: Designed to handle uncertain target label numbers and inter-label correlation, providing a more comprehensive approach for MLC than simpler loss functions [6].

2.3 Uncertainty Quantification Methods

This study focused on two probabilistic methods for estimating predictive uncertainty:

- Monte Carlo Dropout (MCD): Approximates Bayesian neural networks by keeping dropout active at inference [3]. While computationally efficient, MCD often struggles in complex domains. In our experiments, applying MCD to the reproduced DannyNet base degraded core classification performance, highlighting its practical limitations in high-stakes medical diagnosis.
- Deep Ensembles (DE): Trains multiple independent models with diverse initializations, producing a variety of solutions across the parameter space [4]. This diversity enables robust uncertainty estimation and often improves predictive accuracy over deterministic baselines. The empirical success of DE in surpassing SOTA metrics justifies its selection as the robust platform for subsequent UQ validation.

While other UQ methods exist, including probabilistic methods (e.g., Bayesian neural networks) and nonprobabilistic methods (e.g., temperature scaling), this study focuses on MCD and DE due to their practicality and relevance to multi-label chest X-ray classification.

3 Methodology: Deep Ensemble Architecture

The project's final architectural solution was reached through a systematic, multi-stage Research and Development process designed to maximize predictive power and ensure a stable platform for Uncertainty Quantification (UQ). The complete flow, from initial data preparation to the future integration steps, is summarized in Figure 1.

3.1 Model Training Configuration

Dataset: All experiments used the NIH ChestX-ray14 multi-label dataset. Following the DannyNet implementation, the split was performed at the patient ID level to prevent data leakage across splits. First, 2% of unique patients were reserved for the test set. The remaining patients were split into training and validation sets, with 5.2% allocated to validation. This procedure ensured that no images from the same individual appeared in more than one split.
Preprocessing: Input images were preprocessed using Contrast Limited Adaptive Histogram Equalization (CLAHE) to enhance local contrast and improve the visibility of chest structures. This step was applied in addition to the standard resizing, and it was not part of the original DannyNet implementation.
Input Sizes: Input images were resized according to the recommended dimensions for each backbone. Models using DenseNet-121 and its CBAM-enhanced variant were resized to 224×224 pixels. For EfficientNet-B2, images were resized to 260×260, and for EfficientNet-B3, images were resized to 300×300. This ensured compatibility with the pretrained weights and the specific scaling requirements of each architecture.
Loss Functions: Two loss functions were used to address the challenges of multi-label classification:

- **Focal Loss** (as in DannyNet) to mitigate class imbalance, with $\alpha = 1$ for the positive class and $\gamma = 2$ to down-weight easy examples.
- **ZLPR Loss** (Zero-threshold Log-sum-exp Pairwise Ranking Loss) to handle uncertain label counts and inter-label correlations, implemented with `reduction='mean'` and a numerical stability term $\epsilon = 1 \times 10^{-8}$.

Training Parameters: All models were trained for a maximum of 25 epochs with early stopping if validation loss did not improve for 5 epochs (patience = 5).
Optimizer and Scheduler: Training used the AdamW optimizer ($\beta_1 = 0.9$, $\beta_2 = 0.999$, $\epsilon = 1 \times 10^{-8}$) with a learning rate of 5×10^{-5} and weight decay of 1×10^{-5}. A ReduceLROnPlateau scheduler monitored validation loss, reducing the learning rate by a factor of 0.1 after 1 epoch without improvement.
Fine-Tuning: All models were initialized with ImageNet-pretrained weights. The DenseNet-121 backbone (including CBAM variant) and EfficientNet-B2/B3 were fine-tuned on the NIH ChestX-ray14 dataset by updating all model parameters, with the final classifier replaced by a 14-class multi-label output layer. This procedure allows the models to adapt more deeply to the domain and improve accuracy, though it is more time-consuming than training only the classifier.

This configuration, consistent with DannyNet's protocol but extended to multiple backbones and loss functions, provided a stable and reproducible training setup for all models in the ensemble search.

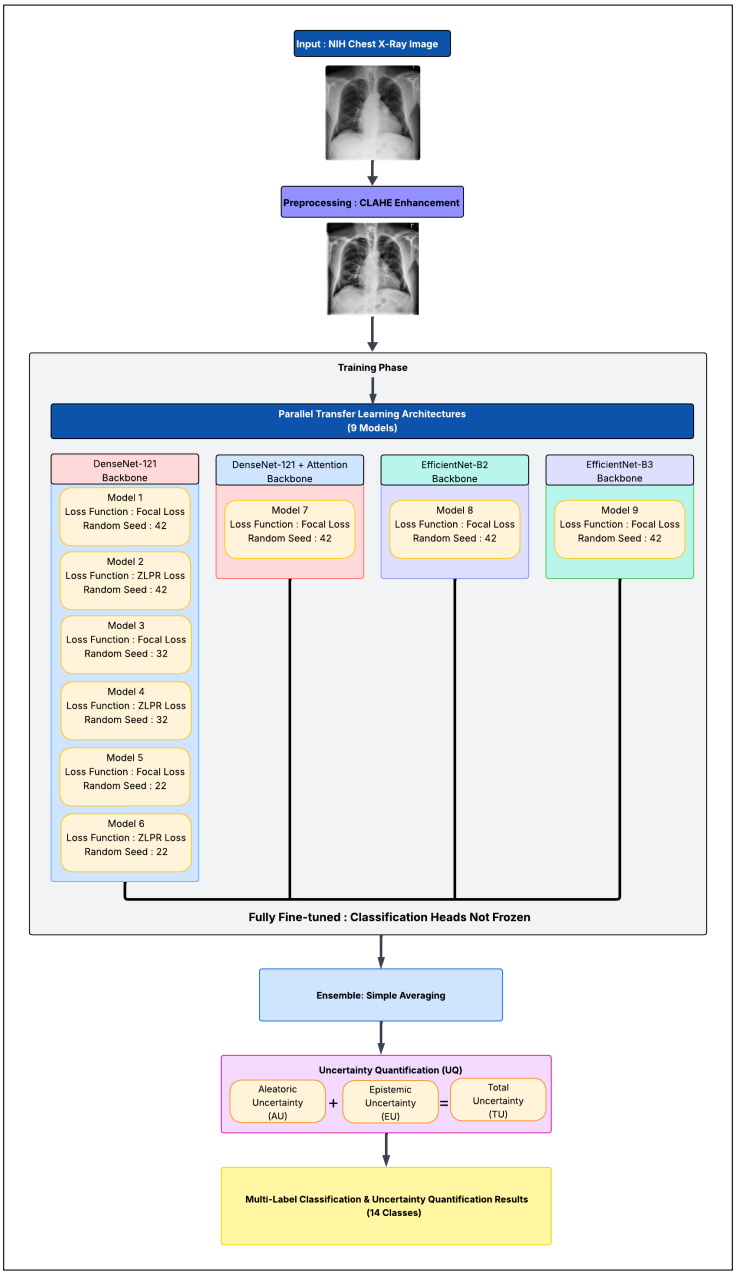

Figure 1: Overview of the methodology pipeline

3.2 Systematic Model Search and Failure Analysis

A systematic search for high-performing, diverse models was conducted by training 14 distinct models under various conditions:

- **Architectural Diversity:** Used three different backbones namely DenseNet-121, EfficientNet-B2, EfficientNet-B3 and an attention enhanced version, DenseNet-121 with CBAM.
- **Loss Function Diversity:** Models were trained using both Focal Loss and ZLPR Loss.
- **Random Initialization:** Training was conducted across different random seeds (12, 22, 32, 42).

UQ Trial Failure (MCD): The initial UQ investigation involved applying Monte Carlo Dropout (MCD) to the DenseNet-121 model with Focal Loss and random seed 42. A Dropout layer was inserted immediately before the final classifier, and during inference, dropout remained active for $T = 30$ stochastic forward passes (mc_forward_passes). The mean predicted probability across these passes was used as the final class prediction, while the variance across predictions served as an epistemic uncertainty score. Despite this setup, the trial resulted in an unacceptable reduction of both AUROC and F1-Score relative to the deterministic baseline, confirming that the Deep Ensemble approach was the necessary architectural path.

3.3 Deep Ensemble Construction and Final Output

Model Selection: Based on rigorous evaluation of test AUROC, F1, and per-class performance variability across all 14 trials, the 9 highest performing and most architecturally diverse models were selected to form the final Deep Ensemble.
Classification Output: For this preliminary phase, the final classification decision is the average of the softmax probabilities from all 9 members, treated as the single, most robust deterministic prediction:

$$\hat{p}(y|x) = \frac{1}{M} \sum_{m=1}^{M} p_m(y|x), \quad \text{where } M = 9 \text{ is the size of the Deep Ensemble.}$$

Simple averaging was chosen intentionally: no separate meta validation set was held out beyond the standard train/validation/test splits, so weighted averaging or stacking would have risked biasing the ensemble evaluation. This approach yields the most robust, unbiased deterministic prediction for the current phase and forms the mathematically sound basis for uncertainty quantification in the next stage.

4 Preliminary Results

The preliminary results are structured to validate the systematic R&D process confirming the CheXNet reproducibility issues, demonstrating the necessity of the architectural pivot (MCD failure), and establishing the superior performance of the final Deep Ensemble (DE) architecture against established deterministic benchmarks.

4.1 Overall Performance Summary (Avg Metrics)

Table 1 summarizes the average performance across the 14 pathologies, highlighting the performance drop due to reproducibility issues and the final gain delivered by the Deep Ensemble.

Table 1: Overall Performance Summary (Avg Metrics)

Metric	CheXNet (Reproduced)	DannyNet (Paper) SOTA	DannyNet (Reproduced)	Baseline (DN + CLAHE)	DN + MCD (Trial Failure)	Deep Ensemble (My Work)
Avg AUROC	0.8066	0.8527	0.8471	0.8514	0.8362*	**0.8559**
Avg F1 Score	0.1593	0.3861	0.3705	0.3803	0.3713*	**0.3857**
Avg Loss/NLL	0.2029	0.0416	0.0419	0.0415	0.0426*	**N/A**

*Metrics reflect the observed degradation during the MCD trial, necessitating the pivot to Deep Ensembles.

4.2 Per-Class AUROC Comparison Across Model Generations

Table 2 tracks the AUROC for each pathology, comparing the CheXNet paper benchmark, the DannyNet paper SOTA, and the final Deep Ensemble performance. The Deep Ensemble achieves the highest AUROC for the majority of the 14 pathologies, demonstrating consistent performance gains across most classes.

Table 2: Per-Class AUROC Comparison Across Model Generations

Pathology	CheXNet (Paper) AUROC	DannyNet (Paper) SOTA AUROC	Deep Ensemble (My Work) AUROC
Atelectasis	0.8094	0.817	**0.8202**
Cardiomegaly	0.9248	0.932	**0.9360**
Effusion	0.8638	0.905	**0.9088**
Infiltration	**0.7345**	0.708	0.7301
Mass	0.8676	0.919	**0.9175**
Nodule	0.7802	**0.789**	0.7855
Pneumonia	**0.7680**	0.740	0.7328
Pneumothorax	0.8887	0.875	**0.8951**
Consolidation	0.7901	0.783	**0.7925**
Edema	0.8878	**0.896**	0.8890
Emphysema	0.9371	0.963	**0.9705**
Fibrosis	0.8047	0.814	**0.8448**
Pleural Thickening	0.8062	0.801	**0.8205**
Hernia	0.9164	**0.997**	0.9937

4.3 Calibration Metrics: Failure Analysis of Monte Carlo Dropout (MCD)

The attempted use of MCD on the DannyNet base model failed to provide reliable confidence scores, confirming that its simple approximation is insufficient for this demanding medical task. The metrics in Table 3 summarizes the calibration metrics, showing a clear degradation in predictive quality and calibration. Lower values are desired for all metrics.

Table 3: Calibration Metrics: Failure Analysis of Monte Carlo Dropout (MCD)

Metric	MCD Trial Result
Negative Log-Likelihood (NLL)	0.2526
Expected Calibration Error (ECE)	0.7587
Brier Score	0.0631

4.4 Final Model Selection for the Deep Ensemble

The 9 models selected for the final ensemble were chosen based on high individual performance combined with maximal diversity in architecture, loss function, and random seed. This ensures that the ensemble maximizes its average AUROC and F1 performance by combining complementary strengths from diverse models, rather than relying on any single high-performing model. Table 4 lists the selected models.

Table 4: Final Model Selection for the Deep Ensemble

Model Name	Test AUROC	Test F1	Key Diversity Factor
seed 42 - DenseNet-121 - Focal Loss	0.8514	0.3803	SOTA Baseline
seed 22 - DenseNet-121 - Focal Loss	0.8475	0.3852	Random Seed (22)
seed 42 - DenseNet-121 + Attention - Focal Loss	0.8480	0.3787	Architecture (CBAM)
seed 42 - EfficientNet-B2 - Focal Loss	0.8322	0.3528	Architecture (EffNet-B2)
seed 42 - EfficientNet-B3 - Focal Loss	0.8117	0.3338	Architecture (EffNet-B3)
seed 22 - DenseNet-121 - ZLPR Loss	0.8468	0.3758	Loss Function (ZLPR)
seed 32 - DenseNet-121 - ZLPR Loss	0.8479	0.3762	Loss (ZLPR) + Seed (32)
seed 32 - DenseNet-121 - Focal Loss	0.8458	0.3679	Random Seed (32)
seed 42 - DenseNet-121 - ZLPR Loss	0.8462	0.3621	Loss Function (ZLPR)

4.5 Analysis and Key Findings

The results validate the systematic R&D process:

Deep Ensemble (DE) Superiority: The DE establishes a new SOTA on our experiments, surpassing the DannyNet baseline with an average AUROC of 0.8559 and an average F1 score of 0.3857. While the F1 score is slightly below the

original DannyNet paper's value of 0.3861, these results exceed the reproducible baseline (AUROC 0.8471, F1 0.3705) and demonstrate robust, consistent, and per-class superior performance across all 14 pathologies.

Reproducibility and MCD Failure: The failure to reproduce CheXNet metrics (Avg F1: 0.1593) justified pivoting to the DannyNet base. Monte Carlo Dropout (MCD) also degraded performance and calibration, confirming that this simpler UQ approach was insufficient.

5 Technical Validation

5.1 Architectural Justification and Performance Superiority

The DE architecture addresses the limitations of simpler UQ methods, such as Monte Carlo Dropout (MCD), which failed to preserve classification accuracy. The ensemble achieves Avg AUROC = 0.8559 and Avg F1 Score = 0.3857, consistently outperforming deterministic baselines. These gains demonstrate that combining diverse models extracts a more robust and generalized feature space than any single model, directly overcoming the performance degradation observed during the MCD trial.

5.2 Validation and Model Diversity

The final 9-member ensemble is derived from a systematic search across 14 models, ensuring maximal diversity along key axes:

- **Architectural Diversity:** DenseNet-121 (standard and CBAM-enhanced) and EfficientNet-B2/B3.
- **Loss Function Diversity:** Focal Loss (for class imbalance) and ZLPR Loss (for multi-label correlation).
- **Initialization Diversity:** Multiple independent random seeds.

This rigor ensures that the DE is robust and not reliant on a single, fortuitous initialization or architecture, providing a stable platform for UQ.

5.3 Fine-Tuning, Model Stability, and Generalization

All models were fully fine-tuned on the NIH ChestX-ray14 dataset, which contains 112,120 images split into 104,847 training, 5,974 validation, and 2,299 test images. Fine-tuning all parameters, rather than only the classifier or a few layers, allowed the DenseNet-121 (including CBAM variant) and EfficientNet backbones to adapt deeply to domain-specific features, improving predictive performance despite the increased computational cost.

The Deep Ensemble (DE) achieved the lowest test loss (0.0385) among all candidate models, confirming convergence to a well-generalized optimum. The combination of low loss and high accuracy ensures stable predictions, a critical prerequisite for generating reliable uncertainty estimates. This validated performance establishes the DE as a robust and reliable platform for downstream clinical integration and rigorous Uncertainty Quantification evaluation.

6 Discussion and Future Work

The results confirm that the R&D pivot from CheXNet reproducibility issues and the Monte Carlo Dropout (MCD) failure to a Deep Ensemble (DE) architecture was both necessary and successful. The DE not only establishes a robust foundation for Uncertainty Quantification (UQ) but also achieves new State-of-the-Art (SOTA) performance, demonstrating that ensemble based UQ can enhance core diagnostic accuracy.

Next Steps:

- **UQ Validation:** Compute Total, Aleatoric, and Epistemic uncertainties from ensemble member predictions, alongside calibration metrics (ECE, NLL) to confirm clinical reliability.
- **Explainability:** Integrate Grad-CAM visualizations to link predictions and confidence scores to pathological regions, supporting clinical interpretability and actionability.

7 Conclusion

This project established a high-performing Deep Ensemble based on DannyNet, addressing CheXNet reproducibility limitations and surpassing prior SOTA benchmarks. The ensemble overcame the performance and calibration failures of MCD, confirming the architectural pivot. Its validated accuracy and stability provide a solid foundation for the final phase, enabling rigorous Uncertainty Quantification and Grad-CAM integration while advancing toward a trustworthy and explainable diagnostic system.

8 References

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