

# Adaptable Cardiovascular Disease Risk Prediction from Heterogeneous Data using Large Language Models

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## Abstract

Cardiovascular disease (CVD) risk prediction models are essential for identifying high-risk individuals and guiding preventive actions. However, existing models struggle with the challenges of real-world clinical practice as they oversimplify patient profiles, rely on rigid input schemas, and are sensitive to distribution shifts. We developed ADACVD, an adaptable CVD risk prediction framework built on large language models extensively fine-tuned on over half a million participants from the UK Biobank. In benchmark comparisons, ADACVD surpasses established risk scores and standard machine learning approaches, achieving state-of-the-art performance. Crucially, for the first time, it addresses key clinical challenges across three dimensions: it flexibly incorporates comprehensive yet variable patient information; it seamlessly integrates both structured data and unstructured text; and it rapidly adapts to new patient populations using minimal additional data. In stratified analyses, it demonstrates robust performance across demographic, socioeconomic, and clinical subgroups, including underrepresented cohorts. ADACVD offers a promising path toward more flexible, AI-driven clinical decision support tools suited to the realities of heterogeneous and dynamic healthcare environments.

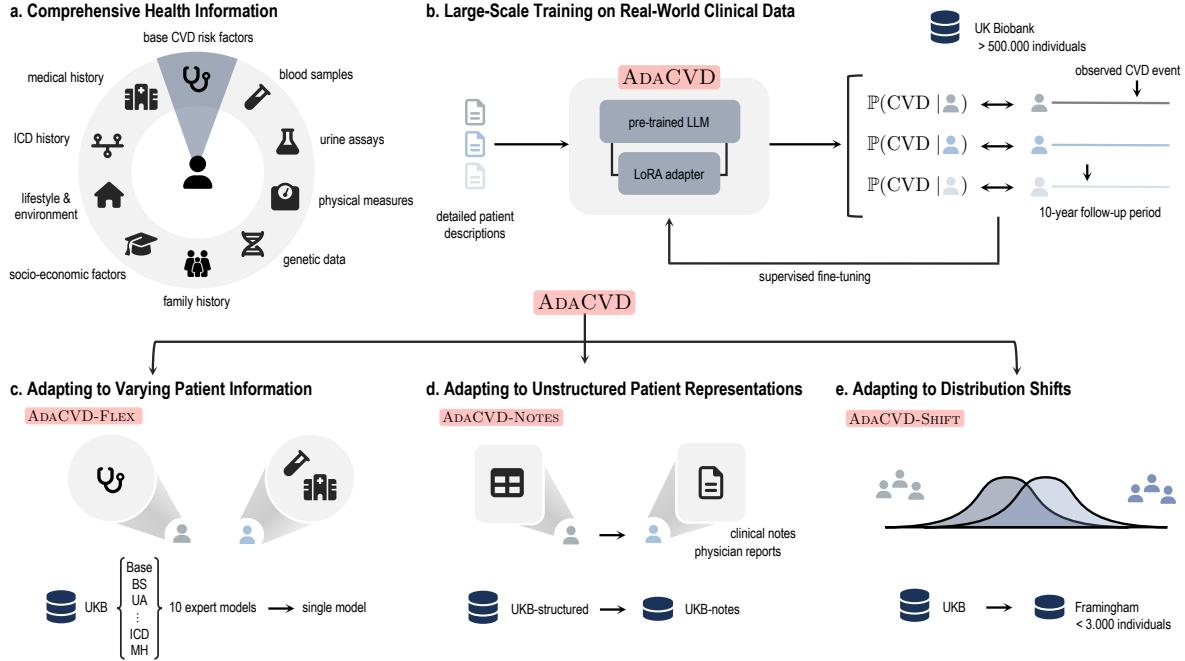
## 1 Introduction

Cardiovascular disease (CVD) remains the leading cause of mortality worldwide [1]. Accurately predicting CVD risk before symptoms manifest is an important prerequisite to initiating targeted interventions that mitigate adverse outcomes. Current clinical guidelines [2–5] recommend risk assessment models that estimate the future risk of CVD based on small sets of well-established risk factors. The most prominent example is the Framingham Risk Score, a pioneering model developed from the Framingham Heart Study [6], which played a key role in identifying several major risk factors. While these base risk factors are easily measurable, less easily quantifiable factors, such as a patient’s lifestyle, also play a significant role [7]. Several studies [8, 9] have demonstrated the potential of integrating more comprehensive health information on patients, combined with the use of stronger machine learning (ML) models that can agnostically discover the complex, non-linear interactions between a broader range of input features and disease outcomes. These methods have demonstrated increased predictive ability, enabling more personalized risk assessment.

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**Figure 1: Overview of our approach to adaptable cardiovascular disease (CVD) risk assessment.** **a.** We integrate a broad spectrum of health-related information on individuals for assessing their CVD risk. Information is categorized into ten different groups. **b.** ADACVD is built by fine-tuning a pre-trained large language model on real-world clinical data from the UK Biobank. **c-e.** We adapt ADACVD along three key axes to address the challenges of real-life clinical practice. These are **c.** handling varying patient information, **d.** dealing with unstructured patient representations, and **e.** adapting to distribution shifts.

However, both traditional medical risk scores and machine learning methods for CVD risk prediction face several critical challenges that hinder their broader clinical applicability. First, these models rely on fixed, pre-defined, and rigid sets of input variables, restricting their ability to flexibly incorporate diverse, varying, or evolving patient information. Second, they require complete and consistently formatted inputs—typically in structured, tabular forms—for accurate estimation and inference. However, in real-life clinical settings, data is often incomplete and unstructured, with documentation typically taking place in the form of clinical notes. Third, due to their rigidity, these models are usually constrained to specific populations or environments, i.e., particular geographical regions or environments with the same data collection standards. This restriction hinders knowledge transfer between diverse healthcare environments and results in models that are poorly generalizable, for example, when facing distribution shifts. Collectively, these limitations are in stark contrast to the demands of clinical reality. Current models lack the flexibility needed for reliable deployment in diverse healthcare settings and often exhibit inconsistent performance. This underscores a pressing need for more flexible, robust, and context-aware approaches to CVD risk prediction—ones that can adapt to the messy, unstructured, and heterogeneous nature of real-world clinical data.

Recently, large language models (LLMs; [10–12]) have received significant attention for their impressive range of capabilities across multiple domains. Early demonstrations of these models on clinical tasks and medical benchmarks indicate their potential to enhance or automate many aspects of clinical practice [13, 14]. Notably, LLMs have been shown to encode broad clinical knowledge, allowing them to pass the US medical licensing exam with similar performance to human experts [15, 16]. Further, they have demonstrated the ability to efficiently extract relevant information from clinical texts [17] and have surpassed medical experts in clinical text summarization [18]. The tasks analyzed thus far have primarily focused on text processing and multiple-choice question answering, yet these capabilities point to a broader and largely untapped

opportunity: supporting real-world clinical decision-making by enabling models to integrate heterogeneous patient data, interpret clinical notes, and operate effectively despite missing or unstructured inputs.

In this work, we present ADACVD, an adaptable CVD risk prediction model that extends beyond traditional risk scores by offering several important dimensions of flexibility. We build upon the well-established pre-training and fine-tuning paradigm by using a pre-trained LLM as a starting point, and then extensively fine-tuning it on real-world data from the UK Biobank (Figs. 1a and 1b). The UK Biobank is one of the largest biomedical databases comprising detailed health information of approximately half a million individuals across the UK, including blood samples, medical history, lifestyle factors, and genetic information. Our model reaches state-of-the-art performance in predicting the 10-year CVD risk of individuals, outperforming established medical risk scores and matching the performance of standard but more rigid ML models that use tabular inputs. Importantly, what sets ADACVD apart is its ability to flexibly adapt to the dynamic and often messy realities of clinical care. We view the three critical challenges mentioned above as three distinct dimensions of clinical complexity—each reflecting a different form of distributional or contextual variation—and demonstrate that our model can address them through quick, flexible, and data-efficient adaptation. To this end, we use our strong foundational model ADACVD as a basis to evaluate its adaptability across three distinct directions:

- i. Handling varying patient information and allowing to flexibly incorporate all available information of an individual's health status, without being constrained by fixed input features (**ADACVD-FLEX**; Fig. 1c).
- ii. Dealing with diverse patient representations, from structured to unstructured patient descriptions, including clinical notes and physician reports (**ADACVD-NOTES**; Fig. 1d).
- iii. Adapting to distribution shifts when switching between heterogeneous environments (**ADACVD-SHIFT**; Fig. 1e).

In an extensive evaluation, we compare ADACVD to relevant baselines using different levels of patient information. We show how integrating various aspects of an individual's health status significantly improves risk assessment. In a stratified evaluation, we show that this is consistent across relevant demographic, socioeconomic, and clinical subgroups. Notably, the incorporation of detailed information is especially beneficial for elderly individuals, current smokers, individuals without formal higher education, and individuals with diabetes. Given the importance of incorporating comprehensive patient information for risk prediction, the key challenge lies in doing so flexibly, while accommodating data variability and incompleteness. We demonstrate that ADACVD can handle heterogeneous and incomplete patient inputs at inference time, effectively leveraging all available information without being constrained by a fixed input schema. Beyond flexibility with respect to the input content, we further demonstrate flexibility with respect to input format. Although the model is extensively fine-tuned on structured patient representations, we show that it can transfer to unstructured textual formats, such as clinical notes and physician reports. Notably, this transfer is highly data-efficient, requiring up to 100 times fewer examples compared to training from scratch. Lastly, when evaluated on a patient cohort from the Framingham Heart Study [19], ADACVD demonstrates robustness and strong adaptability to distribution shifts.

## 2 Results

### Constructing Patient Representations and Model Training

In the clinic, natural language text is the dominant form of documentation and information exchange. Clinical notes, physician reports, and discharge summaries typically contain detailed textual descriptions of patients, capturing a wide range of observations, diagnostics, and contextual information. These patient descriptions are rich in information but pose challenges to risk prediction models as they move away from clearly defined and structured sets of input features. Yet this variability reflects the demands of real-world

### a. Structured Patient Representation

Patient Description:  
Age: 41 years;  
Gender: Female;  
Cholesterol: 5.2 mmol/L;  
Cholesterol lowering medication: No;  
Smoking status: Previous;  
Body mass index (BMI): 24.8 Kg/m<sup>2</sup>;  
...

### b. Unstructured Patient Representation

The patient is a 56-year-old non-smoking male. He is severely obese (BMI 44.8). His systolic blood pressure is 166.5 mmHg. He has a history of high blood pressure, diagnosed at the age of 40, and is currently taking medication for both high blood pressure and cholesterol. He has a family history of high blood pressure and heart disease. His physical activity levels are low.

**Figure 2: Overview of the patient representations used for training and evaluating ADACVD.** We generated two types of patient descriptions of over half a million individuals using real-world data from the UK Biobank and the Framingham Heart Study. **a.** Example of a structured patient description, where patient information is serialized into a predefined text format. **b.** Example of a free-text patient summary, simulating clinical notes. These representations are not standardized, capturing the variability found in real-world clinical documentation.

clinical practice: Given *any* information on a patient—regardless of structure or format—we are interested in understanding their risk of developing cardiovascular disease.

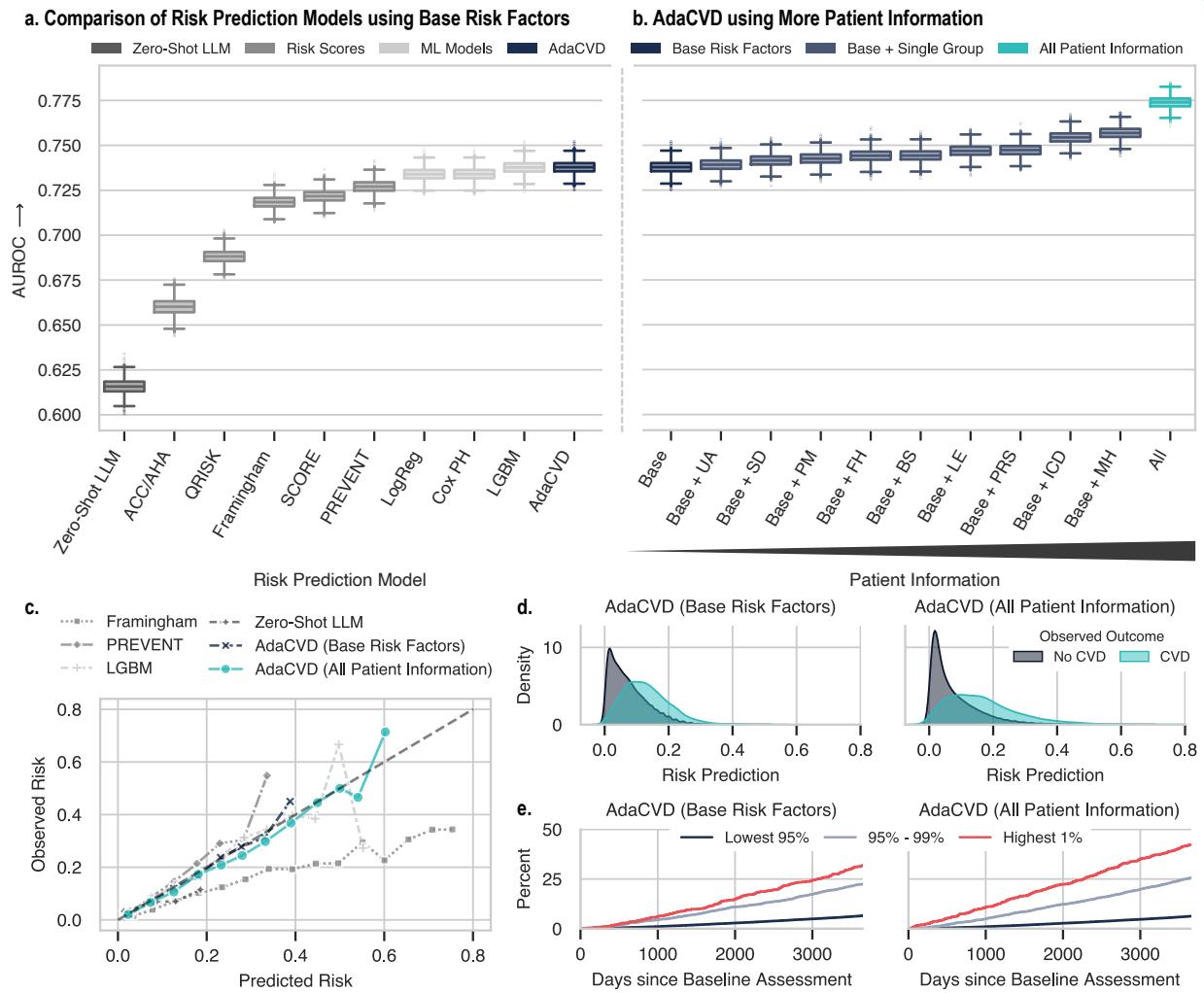
To train ADACVD on realistic clinical inputs, we generated patient descriptions of over half a million individuals using data from the UK Biobank [20] and the Framingham Heart Study [19]. We used two different approaches, resulting in two types of patient representations of increasing complexity. In the first version, we serialized patient data into a highly structured text format (see Fig. 2a). In the second version, we generated free-text patient summaries (see Fig. 2b) that simulate clinical notes (see Methods for details). The patient information used to create these descriptions varies across experiments throughout this work. Established CVD risk prediction models typically rely on a small set of well-known risk factors, such as age, cholesterol levels, blood pressure, smoking status, and diabetes; referred to here as the base risk factors. Beyond these, we defined nine additional information categories that capture broader aspects of patient health: Lifestyle & Environment, Sociodemographic factors, Physical Measures, Urine Assays, Blood Samples, Family History, Polygenic Risk Scores, ICD Codes, and Medical History.

We developed our model ADACVD to flexibly reason over these diverse patient representations. Our approach follows the well-established pre-training and fine-tuning paradigm, utilizing a pre-trained transformer-based LLM with general language understanding capabilities as a foundation and tailoring it to the specific task of CVD risk prediction. Specifically, we fine-tuned Mistral-7B-Instruct [21] on over 467 063 structured patient representations from the UK Biobank (UKB-structured) to predict the 10-year risk of developing CVD. To reduce computational demands, we used low-rank adaptation (LoRA; [22]), a parameter-efficient fine-tuning method that updates only a small fraction of model weights.

## 2.2 Benchmarking Performance Using Base Risk Factors

We first evaluated model performance in a controlled setting using only the base risk factors that are commonly used by established CVD risk scores. These base risk factors include age, gender, smoking status, diabetes, total and HDL cholesterol, cholesterol medication use, blood pressure, blood pressure medication use, body mass index (BMI), ethnic background, and estimated glomerular filtration rate (eGFR).

ADACVD achieved state-of-the-art performance for CVD risk prediction when using only the base risk factors, with an area under the receiver operating characteristic curve (AUROC) of 0.738 (Fig. 3a). The predictions are well-calibrated (Fig. 3c), meaning that the predicted risk matched the observed risk. Its performance matched the performance of gradient-boosted trees (AUROC: 0.738), which are specifically designed for and known to excel with this setting of structured tabular inputs. Performance was superior to simpler ML models, including logistic regression and the Cox proportional hazards model. Notably, all ML models surpassed established medical risk scores, which showed great variability in performance (Fig. 3a). Among these scores, PREVENT [23] achieved the highest AUROC (0.727); QRISK [24] and ACC/AHA [25] were significantly worse (AUROC 0.688 and 0.660).



**Figure 3: Evaluation of AdaCVD.** **a.** Comparison of CVD risk prediction models using only a limited set of base risk factors. Predictive performance is measured by the area under the receiver operating characteristic curve (AUROC; y-axis), reflecting the models' ability to distinguish between individuals who develop CVD and those who do not. AdaCVD outperforms established medical risk scores and machine learning baselines. Zero-shot LLMs perform poorly. **b.** Predictive performance of AdaCVD improves as additional patient information is incorporated. Acronyms: Urine Assays (UA), Sociodemographic factors (SD), Physical Measures (PM), Family History (FH), Blood Samples (BS), Lifestyle & Environment (LE), Polygenic Risk Scores (PRS), ICD Codes (ICD), and Medical History (MH). Each feature group includes the base risk factors. The All Patient Information setting integrates all feature categories. **c.** Calibration plot comparing predicted and observed risk across binned risk strata. The diagonal line indicates perfect calibration. AdaCVD model's using different inputs are all well-calibrated. **d.** Risk prediction distributions for individuals that developed CVD vs. those who did not, using either base risk factors (left) or all patient information (right). Distributions become more separable with comprehensive inputs. **e.** Event curves stratified by predicted risk percentiles (lowest 95%, 95 – 99%, and highest 1%) when using only the base risk factors (left) and when incorporating all patient information (right). The x-axis denotes the 10-year follow-up period (in days); the y-axis shows the observed incidence for each risk group up until that day; the rightmost points indicate the observed 10-year incidence rates for each risk group. The event curves show clearer separation and improved risk stratification when using all patient information.

Across five open-access LLMs of small (2-3B parameters) and medium size (7-8B parameters), post-fine-tuning performance was similar for models of comparable sizes, and predictions were highly correlated (Supplementary Fig. 9a–b). In contrast, zero-shot LLMs performed poorly (AUROC: 0.616) and inconsistently followed instruction formats (Fig. 3a and Supplementary Fig. 9a), emphasizing the relevance of domain-specific fine-tuning.

## 2.3 Incorporating Broader Patient Information Improves Risk Prediction

A major limitation of established CVD risk scores is that they incorporate only a limited set of input features for risk prediction. While these base risk factors are essential, they do not capture the full complexity of an individual's health profile. In particular, it is well known that other factors, such as a patient's lifestyle, also play a significant role [7].

To assess the relevance of broader patient information, we evaluated models trained with additional feature groups beyond the base risk factors. Figure 3b shows the performance improvements with the inclusion of additional patient information. Compared to using only the base risk factors (AUROC 0.738), incorporating all patient information improves risk prediction by 4.9% (AUROC 0.774). Feature groups with the largest individual performance gains included lifestyle & environment (+1.23%), polygenic risk scores (+1.29%), ICD codes (+2.25%), and medical history (+2.58%).

Using all patient information led to a broader and more distinct separation in the distribution of predicted risks between individuals who did and did not develop CVD (Fig. 3d). Furthermore, risk stratification based on predicted percentiles showed enhanced separation of event curves (Fig. 3e), which implies improved identification of high-risk individuals.

The patient description lengths varied across feature groups and individuals. An interesting comparison arises between two groups: ICD codes and medical history. Although both represent similar clinical content, they differ significantly in structure and length: ICD codes are concise lists of standardized codes (median length: 201 tokens<sup>1</sup>), while medical history consists of longer, self-reported, questionnaire-style narratives (median length: 469 tokens). Despite these differences, both formats demonstrated comparably strong predictive performance, indicating that ADACVD can effectively extract clinical signals from both highly standardized, sparsely occurring codes and more naturalistic, narrative inputs.

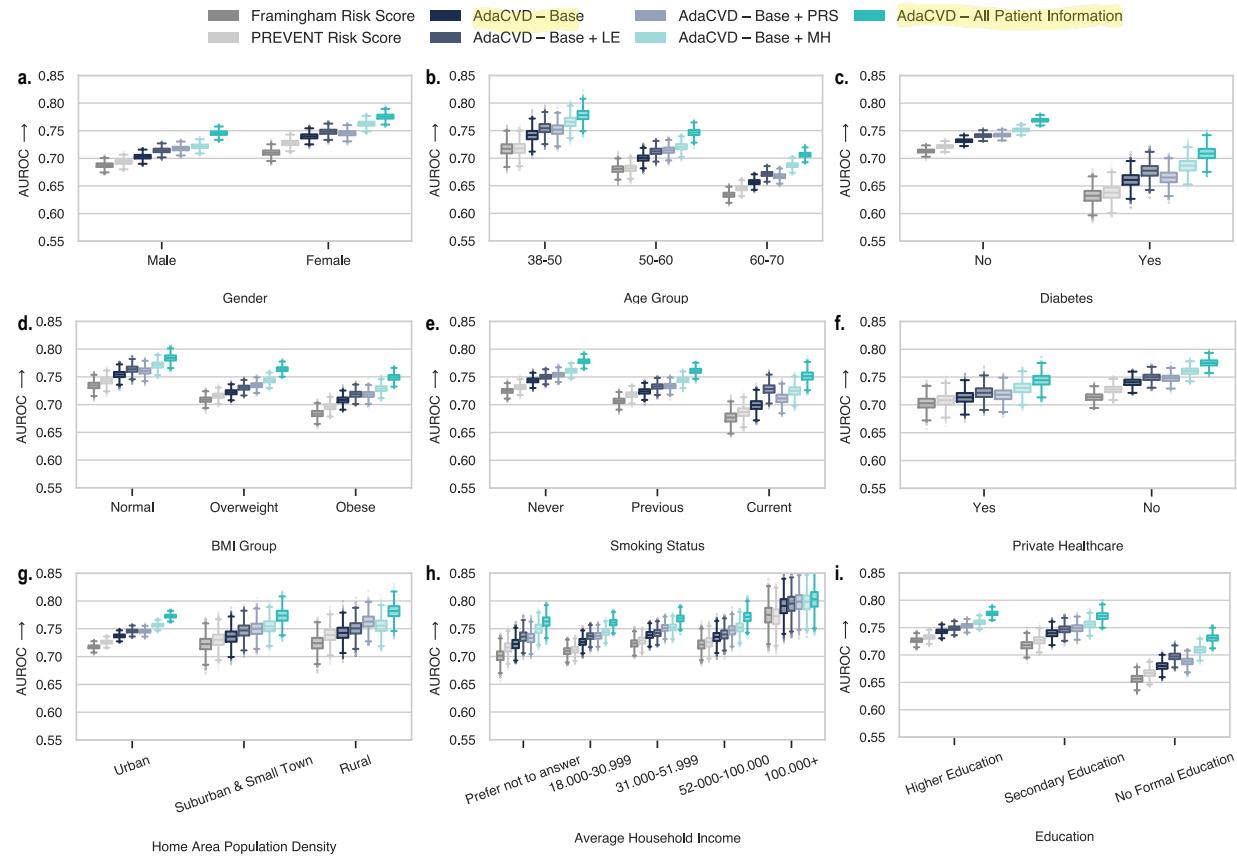
## 2.4 Enhanced Risk Assessment Across Demographic, Clinical, and Socioeconomic Subgroups

To assess potential biases of LLM-based models, we evaluated model performance across demographic, socioeconomic, and clinical subgroups (Fig. 4). All subgroups benefited from the inclusion of broader patient information. Notably, certain groups experienced even more pronounced performance gains. We measure the relative performance gain in percent between the model using only the base risk factors and the model using all patient information. The largest performance improvements were observed in elderly individuals (+7.55%), individuals without higher education (+7.50%), current smokers (+7.46%), and individuals with diabetes (+7.21%). Across all subgroups, the ranking of feature groups remained consistent, with only minor exceptions, indicating that including comprehensive health information does not come at the expense of certain subpopulations.

## 2.5 Adapting to Incomplete and Variable Patient Information

In the above experiments, we operated under ideal conditions where all patient records contained the same set of complete data features. While this is a common assumption in machine learning research, real-world clinical data rarely meets this standard. Patient records are often incomplete or inconsistent, with varying levels of information available for different patients. Therefore, an important requirement for deploying CVD

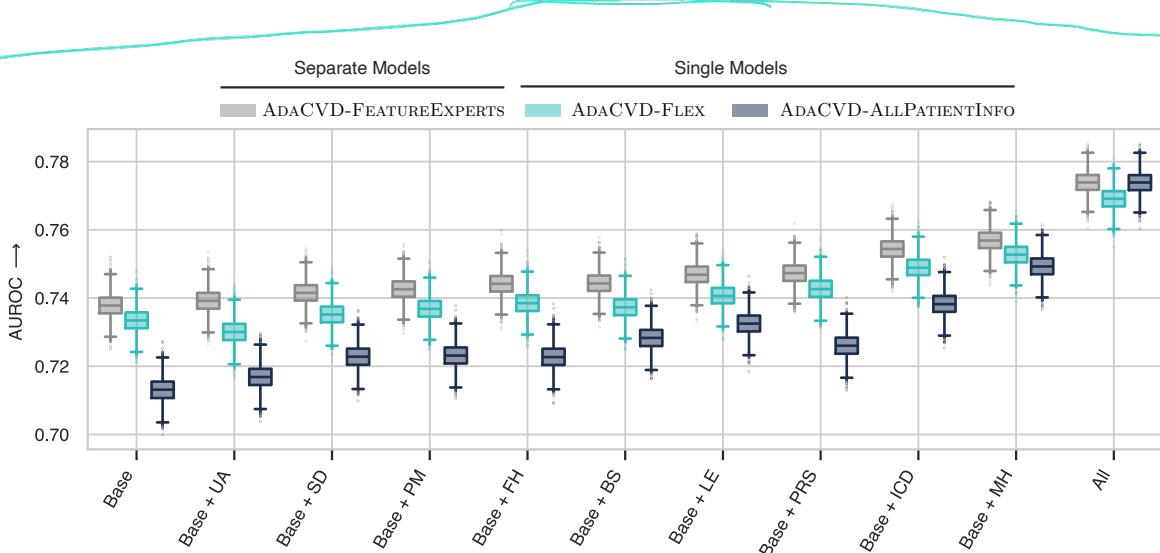
<sup>1</sup>A token refers to a unit of text used by language models during processing, which typically corresponds to a word or subword (e.g., common word fragments, punctuation marks, or individual characters in rare cases).



**Figure 4: Stratified evaluation across subgroups.** Evaluation of model performance (AUROC; y-axis) across (a, b) demographic, (c-e) clinical, and (f-i) socioeconomic subgroups. Each panel compares the Framingham Risk Score, PREVENT Risk Score, and five variants of ADACVD, from using only base risk factors to incorporating all available patient information. Across all subgroups, performance improves with the inclusion of additional patient information. The largest gains are observed for elderly individuals (+7.55%; b), those without higher education (+7.50%; i), current smokers (+7.45%; e), and individuals with diabetes (+7.21%; c). Despite subgroup variation, the relative ranking of feature groups remains largely consistent.

risk prediction models in practice is their ability to handle *varying* patient data at inference time—that is, to make predictions based on whatever information is available for a given patient. A key advantage of using LLM-based models is their flexibility in handling such variability: Patient information can be represented as free-text descriptions, allowing the model to process diverse and non-standardized inputs without relying on fixed feature sets and imputation of missing values. To evaluate whether a single model can flexibly handle varying levels of patient information at inference time, we compared three approaches. As a performance upper bound, we used the 11 expert models, each trained on a specific feature group. Next, we evaluated the model trained on all available features (ADACVD-ALLPATIENTINFO), testing its robustness when given incomplete information at inference. While this model maintained reasonable performance under missing input conditions, its accuracy was noticeably reduced (Fig. 5).

To improve robustness, we leveraged the model’s adaptability by further fine-tuning it on patient descriptions with varying levels of detail. In each training instance, only a random subset of features was included. This adaptation yielded a flexible version of the model, ADACVD-FLEX, capable of making accurate predictions from any available information. While its performance remains slightly below that of the specialized expert models trained on fixed feature subsets, the difference is small (Fig. 5). Crucially, the slight reduction



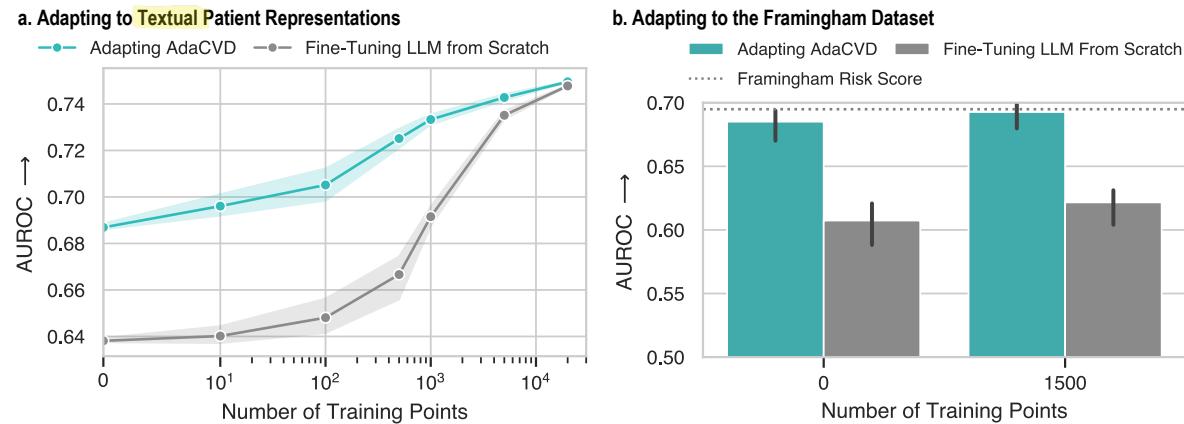
**Figure 5: Evaluation of ADACVD and ADACVD-FLEX when dealing with varying patient information.** Evaluation of model performance (y-axis; AUROC) when different amounts of patient information are available at inference time (x-axis; feature groups). The grey boxes (ADACVD-FEATUREEXPERTS) represent the performance of feature-specific expert models trained separately for each feature group, serving as an upper bound. The dark blue boxes (ADACVD-ALLPATIENTINFO) show the performance of the model trained on all features (single model) when evaluated on partial inputs. The turquoise boxes show the performance of ADACVD-FLEX, a version of the model further fine-tuned on patient representations with varying subsets of information. While slightly below the expert upper bound, ADACVD-FLEX provides robust and accurate predictions across all input conditions, enabling flexible deployment in real-world settings with variable and incomplete data.

in predictive accuracy is outweighed by the significant clinical advantage of having a *single* model that can seamlessly handle varying amounts of patient information.

## 2.6 Adapting to Textual Patient Representations

Textual representations of patients—such as those found in clinical notes, discharge reports, or physician summaries—are among the most common data modalities in clinical settings but cannot be processed directly by conventional risk scores or machine learning models. Such texts are diverse and significantly less structured than the prompts we used above (UKB-structured) to train ADACVD. We evaluated our model’s ability to adapt to these unstructured representations using the generated free-text patient descriptions UKB-notes. While these LLM-generated summaries mostly preserved key clinical information, they often expressed it in a more abstract or inferred form. For example, exact BMI values were sometimes replaced with phrases such as “*the patient is obese*”, and detailed physical activity metrics were summarized as “*the patient is very active*.” The focus of this work does not lie in evaluating these summaries. Instead, we treat them as given and assess how efficiently our model trained on structured representations could adapt to this unstructured input format.

We compared two strategies: (i) fine-tuning an LLM from scratch on the free-text representations and (ii) continuing fine-tuning our structured-data model ADACVD, resulting in an adapted version ADACVD-TEXT. Figure 6a shows the AUROC as a function of the number of training examples. The adapted model ADACVD-TEXT consistently outperformed the model fine-tuned from scratch, particularly in low-data regimes. Even without any data from the target domain, it performed well (AUROC 0.685), and with just 10 examples, it reached an AUROC of 0.697. In contrast, fine-tuning an LLM from scratch required 100 times more data ( $> 1000$  points) to achieve similar results.



**Figure 6: Data-efficient adaptation of ADACVD to new input formats and populations.** **a.** Adaptation to unstructured, textual patient representations. The turquoise curve shows the performance of **ADA**CVD-TEXT, adapted from a model trained on structured inputs, while the grey curve represents a model fine-tuned from scratch. **ADA**CVD-TEXT consistently outperforms the model trained from scratch, especially in low-data regimes. **b.** Adaptation to a shifted target population (Framingham cohort). In both the zero-shot and few-shot settings (1500 training examples), the adapted **ADA**CVD model (turquoise bars) outperforms the baseline LLM fine-tuned from scratch (grey bars), and approaches the performance of the original Framingham Risk Score (dotted line).

## 2.7 Adapting to Distribution Shifts

Beyond changes in patient representation, another critical challenge for deploying risk prediction models in practice is adapting to distribution shifts. Such shifts can arise, for example, when applying models across different hospitals or geographic regions.

To assess the adaptability of LLMs in this scenario, we used a publicly available subset from the original Framingham Heart Study [19, 26], conducted in the 1960s in Framingham, USA. Figure 12 in the Supplementary Material compares the distribution of the base risk factors and disease outcomes between the two cohorts. The marginal distributions of these two datasets differ, likely for two main reasons. First, geographical differences between the US and the UK contribute to variations in risk factors. Second, temporal differences play a significant role: the Framingham study was the first landmark investigation that identified major CVD risk factors, which influenced both patient outcomes and preventive care strategies over time.

We evaluate **ADA**CVD in a zero-shot setting and after further fine-tuning it on a small dataset from the target domain ( $n = 1500$ ). For comparison, we also assess the base LLM, both zero-shot and after fine-tuning on the same limited dataset. Figure 6b shows the AUROC computed on a validation set of the Framingham dataset. When applied zero-shot, **ADA**CVD already achieved strong performance (AUROC 0.687). Similar to the findings above, the model is able to adapt quickly and data-efficiently to this new patient cohort, ultimately reaching the performance of the original Framingham risk score (AUROC 0.693), which was derived from a larger version of this dataset. In contrast, the base LLM performed poorly in both the zero-shot (AUROC 0.614) and fine-tuned setting (AUROC 0.625).

## 3 Discussion

Cardiovascular disease risk estimation is a critical task in preventive healthcare, yet the tools that clinicians rely on often fall short when confronted with the complexities of real-world clinical settings. To address these limitations, we developed **ADA**CVD, an adaptable risk prediction model based on a large language model (LLM) fine-tuned on diverse patient data from the UK Biobank. **ADA**CVD moves beyond the rigidity of existing approaches and is designed to be robust to the diverse, dynamic, and often imperfect nature of

clinical data.

Key findings and their implications should be emphasized. First, in a benchmark setting with structured, complete, and consistent data, ADACVD achieved state-of-the-art performance in 10-year CVD risk prediction. It outperformed established medical risk scores and matched the performance of specialized tabular machine learning models that are specifically optimized for this setting. However, such idealized data conditions rarely occur in practice. Clinical data is often incomplete, heterogeneous, and inconsistently formatted. Especially when considering comprehensive patient information—which we have shown to be highly relevant—consistency is difficult to ensure. In these more realistic scenarios, we showed that ADACVD maintained robust predictive performance, due to its ability to handle free-text inputs and variable formats. Existing approaches typically fail under these conditions for their reliance on fixed input formats and assumptions of data completeness. Our stratified analyses further demonstrated that this flexibility of integrating comprehensive patient information benefits underrepresented groups, including elderly individuals, smokers, individuals with diabetes, and individuals without higher education. Across all groups, we observed clear benefits from the inclusion of detailed health-related information, showing that this does not come at the expense of specific subpopulations.

Second, this work also highlights the untapped potential of using clinical notes for ML-based decision support. Free-text documentation is ubiquitous in the clinic and captures rich, context-specific insights about a patient’s condition that are often lost in rigid tabular representations. We demonstrated that ADACVD can reason effectively over such unstructured input and that fine-tuning the model on structured data facilitates this capability. This finding opens up exciting possibilities for applying similar methods to other conditions beyond cardiovascular disease, potentially enabling opportunistic screening and decision support without the need for costly, time-consuming data preprocessing or manual feature engineering.

Third, a key strength of ADACVD is its adaptability across three critical dimensions: input content, input format (structured data vs. free-text), and population distribution. Our results show that the adaptation of ADACVD along these axes is data-efficient, requiring up to 100 times fewer labeled examples to adapt to new settings compared to models trained from scratch. This capability is highly relevant for real-world applicability, where large, labeled datasets from the target setting may be unavailable or costly to obtain. We have explicitly disentangled these three axes to understand their individual effects on model performance. While real-world clinical deployments will likely involve simultaneous shifts across multiple dimensions, we believe our findings generalize well to these combined scenarios.

Finally, our study emphasizes the importance of task-specific fine-tuning for achieving high performance on complex clinical decision-making tasks. While general-purpose LLMs have demonstrated impressive capabilities in medical question answering [16, 27] and summarization [18], we observed that open-access models of small and medium size performed poorly in CVD risk prediction when applied zero-shot. This underscores the need for targeted fine-tuning using task-specific data. Although prior work [28] has shown that ChatGPT-4, a significantly larger model, performs comparably to the Framingham risk score for CVD risk prediction in zero-shot settings, our domain-specific fine-tuning approach achieved higher accuracy using significantly smaller models (with approximately 300 times fewer parameters), which can be run on modest hardware. Moreover, our model can be deployed locally without relying on external APIs, and thereby ensures that patient data remains private and compliant with regulatory standards.

This study has limitations. First, model training was conducted exclusively on data from the UK Biobank, which may not fully represent the diversity of the global population. Although we included evaluation on the Framingham cohort, further validation across different countries and healthcare systems is necessary. Second, there is a lack of real-world datasets that pair textual patient representations, such as clinical notes and physician reports, with subsequent disease outcomes. To address this gap, we synthetically generated free-text patient descriptions to simulate clinical notes using structured real-world inputs. While previous work has demonstrated that such synthetic summaries can be both accurate and clinically relevant [17, 18], we emphasize the need for the creation of publicly available, high-quality datasets containing real clinical text. Ideally, these notes should be collected longitudinally to support research on disease progression and long-term outcomes.

In summary, our work presents a compelling new pathway for CVD risk prediction, showing that large

language models, when fine-tuned on population-scale clinical data, can effectively support clinical decision-making and address the complexities of real-world healthcare. By enabling flexible integration of diverse patient information and robust adaptation to new settings, this framework offers a promising route toward increased interoperability and knowledge transfer across heterogeneous clinical environments.



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## 4 Methods

Real-world clinical settings pose challenges to CVD risk prediction models, requiring them to handle diverse input information in varying formats and to adapt quickly to different healthcare environments. To address these requirements, we adopt the paradigm of task-specific fine-tuning of a pre-trained, general-purpose large language model (LLM). This paradigm has demonstrated key properties relevant to our setting: (i) transformer-based architectures enable flexible input representations via text prompts and depart from fixed, pre-defined input features; (ii) strong language understanding capabilities allow the incorporation of textual information; and (iii) efficient adaptation capabilities, e.g., through few-shot learning or fine-tuning, support robustness to domain shifts.

With ADACVD, we present an approach to employ this paradigm for CVD risk prediction. We use a pre-trained LLM as a starting point and adjust it to the task of CVD risk prediction via supervised, parameter-efficient fine-tuning on real-world data.

### 4.1 Model Architecture and Fine-Tuning

Given a patient with individual-specific information, our model predicts the risk of developing CVD within the next 10 years. To achieve this, we fine-tuned LLMs for this specific task in a supervised manner using real-world data. This involves several key components: the choice of base LLM (see Section 4.1.1), the construction of patient prompts (see Section 4.1.2), the extraction of risk predictions (see Section 4.1.3), and the supervised training process using parameter-efficient fine-tuning (see Section 4.1.4).

#### 4.1.1 Selecting Pre-Trained LLMs as Strong Starting Points

The LLMs we used are all autoregressive, decoder-only transformer models. We concentrated on open-access LLMs that we can deploy and fine-tune locally to ensure that no sensitive patient data leaves our servers. We focused on two classes of leading open-access LLMs for their balance between performance and computational efficiency during fine-tuning: small models (2-3 billion parameters) and medium-sized models (7-8 billion parameters). Specifically, we used `Mistral` (7B) [21], `Llama` (3B, 8B) [29], `Phi` (3B) [30], and `Gemma` (2B) [31]. We use the instruction-tuned versions of these models. Since we observed similar performance after fine-tuning within each model class (see Fig. 9a in Supplementary Material A.3), we used `Mistral-7B-Instruct` as the starting point to develop our main model ADACVD.

#### 4.1.2 Generating Patient Representations

We create two different types of natural language prompts for describing patients: a highly structured one (for UKB-structured and Fram) and an unstructured text that simulates clinical notes (for UKB-notes). Here, we describe how we generated the prompts that we used as input to our model. The data sources used for this process are described in Section 4.3.

**Structured Representations** To create structured text representations, we serialize data on patients into a detailed textual description, as shown below.

```
Structured patient representations
Patient description:
Gender: Male;
Age: 41 years;
<Feature Name>: <Feature Value>;
...
```

For all features, we use descriptive and precise names. Depending on the type of feature, the value can be a number (rounded to 1 digit), a short text snippet derived from questionnaire-type information, or a list thereof for questions that allow multiple answers.

**Textual Representations** In the absence of real-world datasets containing unstructured textual descriptions of patients with corresponding 10-year CVD outcomes, we leveraged LLMs to generate patient descriptions that mimic realistic clinical notes. For this, we followed prior work demonstrating LLMs' effectiveness in generating realistic medical summaries [17, 18]. We used structured patient information as the input and instructed the model to produce a free-text summary of each patient. For the generation, we used two different system prompts, shown below:

Prompt I for generating patient summaries

You are a medical doctor writing detailed clinical notes.

Patient description:

<Feature Name>: <Feature Value>;  
...

Based on this information, generate a concise and natural clinical summary describing the patient in a few sentences.

Prompt II for generating patient summaries

You are a medical doctor writing detailed clinical notes.

Patient description:

<Feature Name>: <Feature Value>;  
...

Based on this information, generate a brief summary of the patient with an emphasis on relevant cardiovascular-related information. Do not provide risk evaluation or any clinical judgment.

#### 4.1.3 Binary Classification in the Token Space

To fine-tune LLMs for CVD risk prediction, we framed the problem as a binary classification task in the token space (similar to [32, 33]). Instead of producing a numeric risk prediction in text form, we retrieved the likelihood of the model answering *Yes* or *No* to a question posed in binary form: *Will this patient experience a major cardiovascular event in the next ten years?* We extracted the logits and subsequently normalized them to generate the final CVD risk prediction. During training, we completed the prompt with a binary label based on the true observed 10-year CVD outcome of each patient and learned the parameters to minimize the cross-entropy loss between predicted probabilities and observed outcomes.

#### 4.1.4 Efficient Fine-Tuning via Low-Rank Adaptation (LoRA)

Given the high computational cost of fully training such large models, we employed parameter-efficient fine-tuning (PEFT; [34]), namely Low-Rank Adaptation (LoRA; [22]). LoRA introduces lightweight adapter modules to the attention blocks of the transformer model while keeping the original pre-trained parameters frozen. Specifically, we targeted the query, key, and value projection layers, with a rank value of 16. With this approach, we updated only around 0.13% of the model parameters during fine-tuning and thereby

significantly reduced computational demands. The training was done on a cluster of NVIDIA H100 and A100 GPUs. We provide further details on the training process for all models in Table 1.

**Table 1:** Details on model training and adaptation

Model	Initialization	Dataset (size)	#Epochs
ADACVD	Mistral-7B-Instruct	UKB-structured (467k)	2
ADACVD-FLEX	ADACVD	UKB-structured (467k)	1
ADACVD-TEXT	ADACVD	UKB-notes (20k)	5
ADACVD-SHIFT	ADACVD	Fram (3k)	10

## 4.2 Base Model and Model Adaptation

Using the training procedure described in Section 4.1, we developed a strong base model, AdaCVD, which we further adapted into three directions. We trained the base model in a setting with complete, structured, and identically distributed data, which is commonly assumed when developing machine learning models. While this setting allows for rigorous evaluation against standard benchmarks, it does not fully reflect the complexities of real-world clinical data. In the clinic, data is often incomplete, unstructured, and subject to distribution shifts across populations (e.g., in different geographic regions). These challenges represent domain shifts. In the following sections, we describe how we developed the base model (Section 4.2.1) and how we effectively and data-efficiently adapted the base model AdaCVD to handle such shifts (Sections 4.2.2 to 4.2.4).

### 4.2.1 Training the Core ADACVD Model

Following the fine-tuning process outlined in Section 4.1.4, we developed our base model ADACVD using structured representations of patients from the UK Biobank (UKB-structured). We train the model for two epochs on all patients from the training dataset ( $n = 467k$ ), using mini-batches of size 8-16<sup>2</sup>. We provide further technical details on the training process in Table 1. The hyperparameters were chosen based on the model’s performance on the validation set.

To assess the importance of different patient information for risk assessment, we trained expert models for each of the 10 information groups defined below (see Section 4.3 for details), each focusing on a different aspect of health-related patient information. For this, we generated patient descriptions solely using the information contained in the specific feature group and the base risk factors. Hence, this process resulted in 11 different expert models: BASE, using only the base risk factors; BASE+X for the 9 different feature groups; and ALLPATIENTINFO, which uses information from all feature groups simultaneously. Each model was specifically designed to deal with a fixed feature group at inference time.

### 4.2.2 Adapting to Incomplete and Variable Patient Information

Instead of having to deal with 11 different models, depending on what patient information is provided, we aimed to have a single model that could deal with varying information from all feature groups at the same time. For this, we compared two approaches. A straightforward approach is to use ALLPATIENTINFO, i.e., the model trained on complete information of all feature groups, and to simply provide incomplete information during inference. Hereby, we assess the models’ ability to deal with missing information. Note, however, that missing values are not explicit null values that require imputation, e.g., with the population median. Instead, incomplete information is only implicit and is simply left out of the patient descriptions. In a second approach, we made use of the model’s adaptability. We adapted the model ALLPATIENTINFO by continuing fine-tuning on patients with varying information. For each patient, we randomly sampled a subset of features during training and generated a patient description using only these features. This way,

<sup>2</sup>The batch size varied depending on the length of the patient descriptions across different settings.

the model learns to deal more effectively with incomplete information. We refer to the resulting model as **ADACVD-FLEX**. The performance of the 11 feature expert models provides an upper bound per feature group.

#### 4.2.3 Adapting to Textual Patient Representations

Our initial model, ADACVD, was fine-tuned at scale on structured patient representations. Even though these representations were encoded in text format, they followed a highly standardized and consistent structure. In contrast, real-world clinical settings rarely provide such uniformity. Patient information is often documented in unstructured formats, such as clinical notes, physician reports, or discharge summaries, making free-text one of the most prevalent data modalities in practice. A key challenge for CVD risk prediction models is thus the ability to process and reason over unstructured text inputs. Therefore, we conducted an experiment in which we evaluate how well ADACVD, trained exclusively on structured inputs, generalizes to unstructured text representations in a zero-shot setting. Additionally, we examine how efficiently it can be adapted to this new input format via further fine-tuning, resulting in a variant we refer to as **ADACVD-NOTES**. For comparison, we also fine-tune the base LLM directly on the textual patient descriptions *from scratch*, without any prior fine-tuning on structured data.

We perform this experiment on our generated dataset of clinical notes (**UKB-notes**). For some prompts, we provided only the base risk factors as inputs (using Prompt I), and for others, we provided more detailed patient information (all feature groups except lab values, i.e., UA and BS; using Prompt II). We generate this dataset for a subset ( $n = 40\,000$ ) of the UK Biobank cohort. Importantly, we use data from patients not seen during the first fine-tuning stage. To assess the data efficiency, we randomly select subsets for training using different random seeds.

The generated patient summaries averaged 135 tokens with base risk factors and 248 tokens with additional patient information. We capped the lengths at 200 tokens (cropping 3% of cases) for base summaries and 400 tokens (cropping 11% of cases) for detailed ones.

Manual inspection of a subset of the generated summaries confirmed that relevant clinical information was generally preserved, though often rephrased. For example, numerical values were replaced with qualitative descriptors (e.g., *elevated cholesterol levels*), and some features were inferred indirectly (e.g., mentioning obesity instead of stating the BMI value). Summaries based on base risk factors retained nearly all original information, while those including more granular inputs (e.g., physical activity broken down by type and duration) tended to be abstracted (e.g., *the patient is very active*). Our focus in this work does not lie in evaluating these summaries. Instead, we treat them as given and examine how effectively LLMs can learn from such text-based inputs and how efficiently a model trained on structured data adapts to this unstructured format. Examples of such patient summaries can be found in Supplementary Material A.2.

#### 4.2.4 Adapting to Distribution Shifts

Distribution shifts are a critical challenge when deploying machine learning models in practice. In clinical decision-making tasks such shifts can occur when applying models across different hospitals, different geographic regions, or temporal contexts. To evaluate how well our model is able to adapt to such shifts, we use data from the Framingham Heart Study. This cohort differs from the UK Biobank in both the time of data collection (Framingham: starting 1948; UKB: starting 2016) and the location (Framingham: US; UKB: UK). We first evaluate how well the base model ADACVD, trained on UKB data, generalizes to the Framingham dataset without any additional fine-tuning. Then, to assess adaptability, we perform further fine-tuning of ADACVD using the Framingham data (ADACVD-SHIFT). We compare this to fine-tuning the pre-trained LLM *from scratch* only on the Framingham data. To robustly compute metrics, we perform cross-validation using five different random 50-50 train-test splits ( $n = 1\,507$  each) and report the median performance. We compare this to the performance of the Framingham risk score, which was derived from a larger cohort of the same study.

## 4.3 Data Sources and Cohort Descriptions

We use two primary data sources in this study: the UK Biobank [20, 35] ( $n = 467\,063$ ) and the Framingham Heart Study [19] ( $n = 3\,014$ ). The UK Biobank (in various formats, as described above) serves as the main dataset for training, adaptation, and evaluation. Data from the Framingham Heart Study is used for adaptation and evaluation.

### 4.3.1 UK Biobank

The UK Biobank is a large-scale longitudinal biomedical database containing detailed health information of over approximately half a million individuals across the UK. It offers a comprehensive repository of patient characteristics, encompassing sociodemographic information, physical measures, lab values, genetic data, lifestyle factors, medical history, and more. Information was collected at a baseline assessment, and after that, disease outcomes and mortality were continuously recorded in a follow-up period of up to 19 years.

**Task & Outcome Definition** We define our task as predicting the risk of developing a fatal or non-fatal CVD event within 10 years of the baseline assessment. Hereby, a CVD event is defined as the first occurrence of any of the following ICD-9 and ICD-10 diagnosis codes:

- **ICD-9:** 410–414 (ischemic heart diseases), 430–434 (hemorrhagic and ischemic stroke), and 436–438 (cerebrovascular diseases)
- **ICD-10:** F01 (vascular dementia), I20–I25 (ischemic heart diseases), I50 (heart failure), and I60–I69 (cerebrovascular diseases)

This aligns with definitions used in prior studies [6, 36]. We combined information from three sources: hospital in-patient admissions, self-reported data, and death registries. Participants with a history of CVD prior to the baseline assessment ( $n = 35\,070$ ) were excluded, applying the same definition for CVD as used for the outcome variable.

**Cohort** The final cohort comprised 467 063 participants aged 37–73 years at baseline. The cohort was randomly split into a training (75%), test (20%), and validation set (5%). All reported results are computed on the test set unless stated otherwise. Over the 10-year follow-up period, 7.5% ( $n = 34\,983$ ) of the participants developed CVD. Table 3 in Supplementary Material A.1 shows the baseline characteristics of the study population.

**Comprehensive Health Information** We incorporate comprehensive health-related information on individuals and have defined ten distinct information categories designed to reflect realistic clinical scenarios.

- **Base Risk Factors (Base):** This set of features is commonly used by established CVD risk scores. It consists of age, gender, smoking status, diabetes, total cholesterol, HDL cholesterol, cholesterol medication use, blood pressure, blood pressure medication use, body mass index (BMI), ethnic background, and estimated glomerular filtration rate (eGFR).
- **Polygenic Risk Scores (PRS):** These values quantify the genetic susceptibility of an individual to a broad range of diseases and traits by aggregating the effects of multiple genetic variants. It covers conditions such as cardiovascular diseases, different cancer types, autoimmune disorders, metabolic traits, and neurological and psychiatric disorders. We include 36 scores.
- **Medical History (MH):** Self-reported health information collected through questionnaires, encompassing diagnosed conditions with the individual's age at diagnosis, past medical procedures, medication use, and screening history.
- **Blood Samples (BS):** 43 laboratory-analyzed biomarkers measured in the blood sample collected at recruitment, including 26 biochemistry markers and 17 haematological assays.

- **Family History (FH)**: Questionnaire-based information on health conditions of biological and adopted family members, offering insights into hereditary health risks.
- **Lifestyle and Environment (LE)**: Self-reported data on physical activity, sleep habits, smoking behavior, and alcohol consumption, providing a comprehensive view of daily routines, health behaviors, and environmental exposures.
- **Physical Measures (PM)**: Measurements of body size, body composition by impedance, electrocardiogram (ECG) during exercise, arterial stiffness, and spirometry.
- **Sociodemographics (SD)**: Information on living arrangements, household composition, income, education level, employment status, and work conditions.
- **Urine Assays**: Biochemical measurements of urinary components, including creatinine, microalbumin, potassium, and sodium.
- **ICD Codes (ICD)**: A record of all past diagnoses using ICD-9 and ICD-10 codes.

We provide the exact list of field IDs and features used per category in Table 4 in Supplementary Material A.1.

### 4.3.2 Framingham Heart Study

The Framingham Heart Study is a cohort study that focused on cardiovascular disease. It began in 1948 in Framingham, US. The study was instrumental in identifying major CVD risk factors such as hypertension, high cholesterol, smoking, and obesity, and remains one of the most influential epidemiological studies in cardiovascular research. We use the publicly available, de-identified subset of this dataset [26]. For each participant, we are given the following information at baseline: Gender, age, total cholesterol, HDL cholesterol, systolic blood pressure, blood pressure medication, diabetes, smoking states, and BMI. We use data from the third period, because previous periods were missing information on HDL cholesterol. We only used participants with complete information. We combine the following three variables as our target: CVD, STROKE, MI\_FCHD. We exclude participants with previous CVD, using the same definition as for the outcome. The final cohort comprised  $n = 3014$  individuals.

## 4.4 Evaluation

### 4.4.1 Metrics

We evaluated the models using standard metrics suitable for unbalanced binary classification tasks. Specifically, we used the area under the receiver operator curve (AUROC) to assess the model's ability to differentiate between individuals who develop the disease and those who do not. Additionally, we used the C-Index to compare the ranking of predictions with the observed time of CVD events. To assess calibration, we used the Brier Score. For all metrics, we report the median value and their 95% spread across 5000 bootstrapping rounds. The observed large spreads are a result of high sample dependence, which is likely due to class imbalance. We decided not to measure randomness across different training runs (e.g., different seeds or initialization parameters) due to the high computational cost. However, we observed very stable results with respect to such randomness.

### 4.4.2 Comparisons & Baselines

For all experiments using tabular input features, we compared our method with various baseline methods, including medical risk scores, standard machine learning methods, and LLMs (zero-shot).

**Medical Risk Scores** We implemented medical risk scores derived from different geographic cohorts. We list all risk scores, geographic regions, and the exact sets of input features in Table 2.

**Table 2:** Medical Risk Scores

Risk Score	Derivation Cohort	Input Features
Framingham [6]	US	Age, sex, total cholesterol, HDL cholesterol, systolic BP, BP medication, smoking status, diabetes
PREVENT [23]	US	Age, sex, total cholesterol, HDL cholesterol, systolic BP, BP medication, smoking status, diabetes, eGFR, cholesterol medication, BMI
ASCVD (AHA/ACC) [25]	US	Age, sex, total cholesterol, HDL cholesterol, systolic BP, BP medication, smoking status, diabetes, ethnicity
SCORE2 [37]	Europe	Age, sex, total cholesterol, HDL cholesterol, systolic BP, smoking status, diabetes
QRISK [24]	UK	Age, sex, total cholesterol, HDL cholesterol, systolic BP, BP medication, smoking status, diabetes, townsend deprivation index <sup>3</sup> , family history of premature CVD, BMI

**Machine Learning Baselines** The second group of baseline models comprises standard supervised machine learning methods, including the Cox Proportional Hazards model, logistic regression, and gradient-boosted trees. We used the following software packages for the implementations: lifelines for the Cox PH model, sklearn for logistic regression, and lightgbm for gradient-boosted trees.

**LLMs (Zero-Shot)** To assess the zero-shot predictions of different pre-trained LLMs, we provided a patient description, gave precise instructions, and extracted the prediction from the response, similar to [28]. We instructed the models to utilize a JSON format within their responses to ensure straightforward extraction of the numeric risk prediction. Specifically, our instruction was: *Based on the provided patient description, what is the estimated 10-year risk of cardiovascular disease (CVD)? Please provide your answer solely as a numeric percentage in a machine-readable JSON format.* We generated 100 new tokens and extracted the risk prediction from the response. If no valid JSON was provided, we set the prediction to nan. When a model did not comply with the instructions, all predictions were invalid and hence, we were not able to compute any evaluation metrics.

## Code Availability

The source code for AdACVD is available at <https://github.com/FrederikeLuebeck/adacvd>.

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## Author contributions

F.T. and S.G. initiated and conceived the study; F.L., J.W., F.T., S.G., A.K., and B.S. contributed to the refinement of the research question; F.L., J.W., and F.T. devised the model architecture and evaluation framework; F.L. and S.G. performed the dataset curation and data analysis; F.L. performed data processing, model training, evaluation, and all experiments; M.M. reviewed the code; F.L., J.W., F.T., S.G., A.K., and B.S. wrote the manuscript; All authors approved the final version of the manuscript.

## **Declaration of interests**

The authors declare no competing financial interests.



## A Supplementary Material

### A.1 UK Biobank

**Table 3:** Characteristics of the UK Biobank Cohort, excluding participants with CVD prior to the baseline assessment. We report median values and their standard deviation.

	Female (n = 261 030)	Male (n = 206 033)
Age (years)	57.00 (7.99)	57.00 (8.21)
BMI (kg/m <sup>2</sup> )	26.03 (5.14)	27.18 (4.17)
Total Cholesterol	225.99 (43.09)	214.66 (42.13)
HDL Cholesterol	60.33 (14.58)	48.26 (12.03)
Systolic Blood Pressure	133.00 (19.23)	139.50 (17.38)
Blood Pressure Medication	15.80%	19.76%
eGFR	97.60 (13.01)	97.53 (12.69)
Smoker	8.78%	12.39%
Diabetic	3.37%	5.74%

**Table 4:** List of field IDs used for the information categories in the UK Biobank. IDs marked with an asterisk are further processed into features. Information on the field can be found on the UK Biobank Showcase Webpage [38].

Field IDs	
<b>Base</b>	31, 93, 2443, 4080, 6153*, 6177*, 20116, 21000, 21001, 21003, 30690, 30700*, 30760
<b>PRS</b>	26202, 26204, 26206, 26210, 26212, 26214, 26216, 26218, 26220, 26223, 26225, 26227, 26229, 26232, 26234, 26238, 26240, 26242, 26244, 26246, 26248, 26250, 26252, 26254, 26258, 26260, 26265, 26267, 26269, 26273, 26275, 26278, 26283, 26285, 26287, 26289
<b>MH</b>	2178, 2188, 2296, 2306, 2316, 2345, 2355, 2365, 2415, 2443, 2453, 2463, 2473, 2492, 2844, 2966, 2976, 3005, 3761, 3786, 3809, 3992, 4012, 4022, 4041, 4717, 6150, 6151, 6152, 6153, 6154, 6155, 6177, 6179
<b>BS</b>	23000, 30000, 30010, 30020, 30030, 30040, 30050, 30060, 30070, 30080, 30090, 30100, 30110, 30120, 30130, 30140, 30150, 30160, 30600, 30610, 30620, 30630, 30640, 30650, 30660, 30670, 30680, 30690, 30700, 30710, 30720, 30730, 30740, 30750, 30760, 30770, 30780, 30790, 30810, 30840, 30860, 30870, 30880, 30890
<b>ICD</b>	41280*, 41270*, 41281*, 41271*
<b>FH</b>	1807, 1845, 3526, 4501, 20107, 20110, 20111, 20112, 20113, 20114
<b>SD</b>	670, 709, 728, 738, 767, 777, 796, 806, 816, 826, 845, 3426, 4674, 6138*, 6143, 20119
<b>LE</b>	864, 874, 884, 894, 904, 914, 924, 943, 971, 981, 991, 1001, 1011, 1021, 1070, 1080, 1090, 1160, 1190, 1200, 1210, 1220, 1239, 1249, 1259, 1269, 1279, 1558, 1568, 1578, 1588, 1598, 1608, 1618, 1628, 2624, 2634, 3637, 3647, 20116, 20117, 20160, 20161, 20162, 22035, 22036, 22037, 22038, 22039
<b>PM</b>	3062, 3063, 3064, 4194, 4195, 4196, 4198, 4199, 4200, 4204, 4207, 5983, 6015, 6016, 6017, 6032, 6033, 6034, 6039, 20150, 20151, 20256, 20257, 20258, 21001, 21021, 23098, 23099, 23100, 23101, 23102
<b>UA</b>	30500, 30505, 30510, 30520, 30525, 30530, 30535

## A.2 Examples of textual patient representations

The patient is a 41-year-old non-smoking, non-diabetic female of white ethnicity with a BMI of 23.1 Kg/m<sup>2</sup>. She has a cholesterol level of 4.9 mmol/L and an HDL cholesterol level of 1.9 mmol/L. Her blood pressure, as measured automatically, is 108.5 mmHg. She is not currently taking any cholesterol-lowering medication or blood pressure medication. Her eGFR is 120.37, indicating normal kidney function.

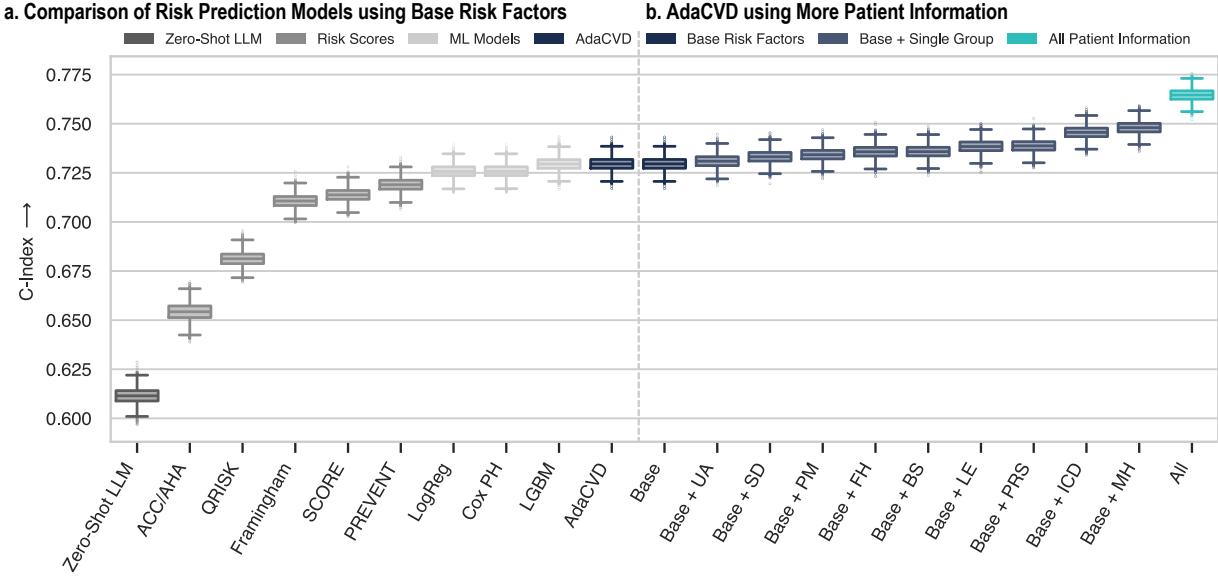
The patient is a 61-year-old male with a BMI of 24.9 Kg/m<sup>2</sup>, previously a smoker but not currently. He has a cholesterol level of 4.8 mmol/L and a low HDL cholesterol level of 1.1 mmol/L. His systolic blood pressure is 133 mmHg. He does not have diabetes, is not on blood pressure medication, and does not take cholesterol-lowering medication. His estimated glomerular filtration rate (eGFR) is 77.55, indicating good kidney function.

The patient is a 48-year-old non-smoking, non-diabetic female of white ethnicity with a normal body mass index (BMI) of 21.9 Kg/m<sup>2</sup>. She has a borderline high cholesterol level, with a low HDL cholesterol level. Her blood pressure, as measured automatically, is slightly elevated at 134.5 mmHg. She is not currently on any cholesterol-lowering medication or blood pressure medication. Her estimated glomerular filtration rate (eGFR) is within the normal range at 96.05.

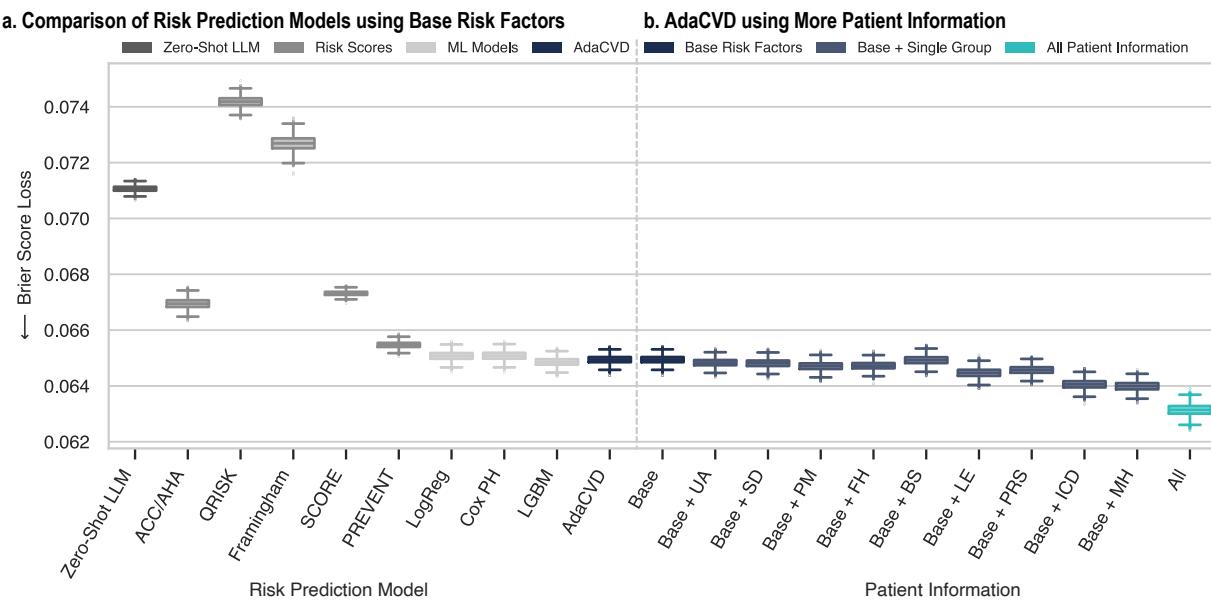
The patient is a 41-year-old female with a BMI of 23.1 Kg/m<sup>2</sup>, who has never smoked and has no history of diabetes or hypertension. Her cholesterol level is 4.9 mmol/L, with an HDL cholesterol of 1.9 mmol/L. She is currently not on any cholesterol-lowering medication. Her systolic blood pressure, as measured automatically, is 108.5 mmHg. She has a family history of non-accidental death in close genetic family members. Her PRS for cardiovascular disease (CVD) is 2.3 relative risk, and her PRS for venous thromboembolic disease (VTE) is 2.2 relative risk. She engages in regular walking and light DIY, and her sleep duration is 8 hours/day. She consumes alcohol three or four times a week, with an average weekly spirits intake of 4 measures. Her maximum workload during a fitness test was 80 Watts, and her maximum heart rate during the test was 139 bpm. She lives in a house or bungalow with 2 people and has a college or university degree as her highest qualification.

The patient is a 65-year-old female with a BMI of 22.9 Kg/m<sup>2</sup>. She is a current smoker and has a systolic blood pressure of 122 mmHg. Her cholesterol level is 6.1 mmol/L, with an HDL cholesterol of 1.3 mmol/L. She is not taking any cholesterol-lowering medication. Her estimated glomerular filtration rate (eGFR) is 89.92. She has a standard polygenic risk score (PRS) for coronary artery disease (CAD) of 1.1 relative risk. She has no history of diabetes, hypertension, or cardiovascular disease. She is physically active, walking 7 days a week and engaging in moderate physical activity for 300 minutes a day. She has no known vascular or heart problems diagnosed by a doctor. Her sleep duration is 6 hours a day, and she does not snore or daytime doze. She has a standard PRS for hypertension of 0.3 relative risk.

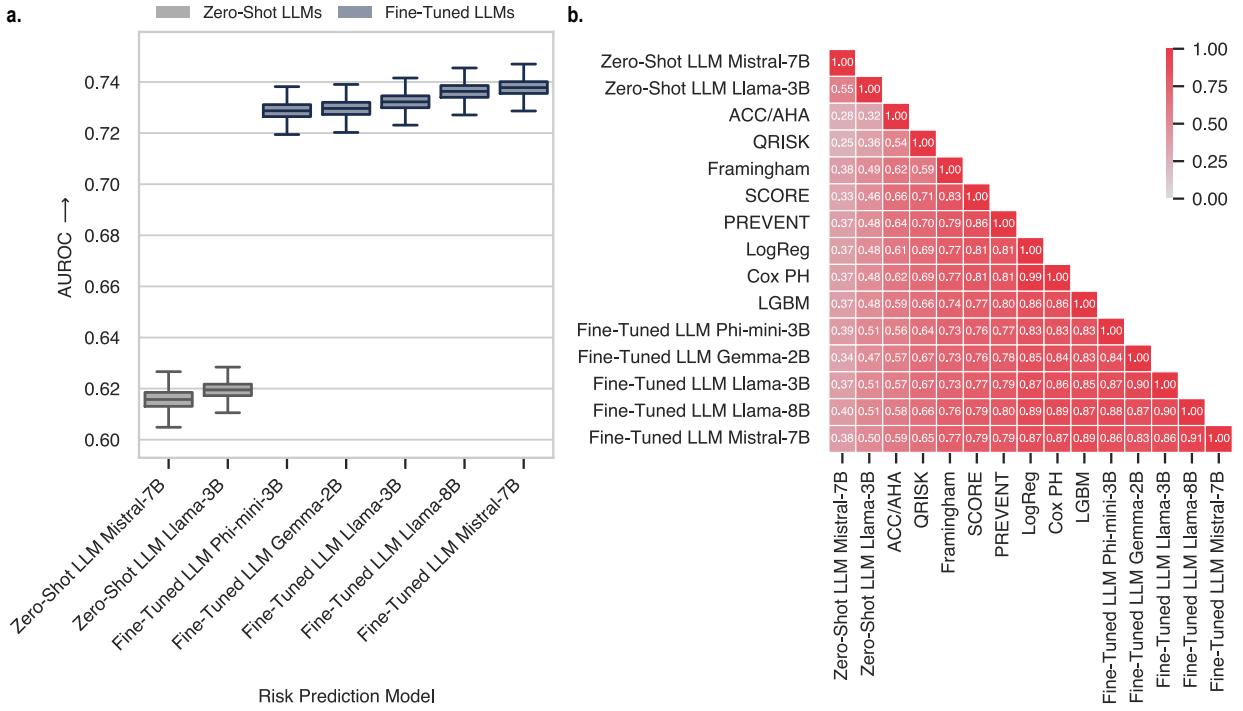
### A.3 Additional Results



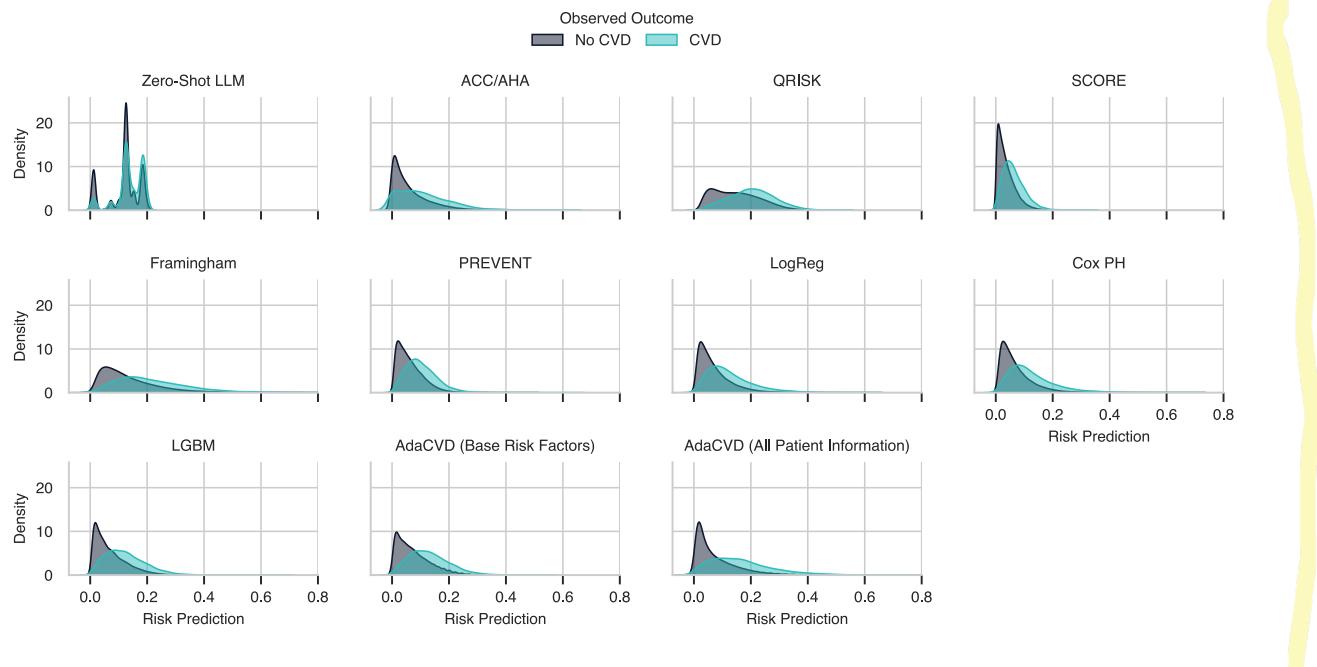
**Figure 7: Evaluation of predictive performance of different risk prediction models (C-Index).** **a.** Comparison of CVD risk prediction models using only a limited set of base risk factors. **b.** AdaCVD when additional patient information is incorporated. Acronyms: Urine Assays (UA), Sociodemographic factors (SD), Physical Measures (PM), Family History (FH), Blood Samples (BS), Lifestyle & Environment (LE), Polygenic Risk Scores (PRS), ICD Codes (ICD), and Medical History (MH). Each feature group includes the base risk factors. The *All Patient Information* setting integrates all feature categories.



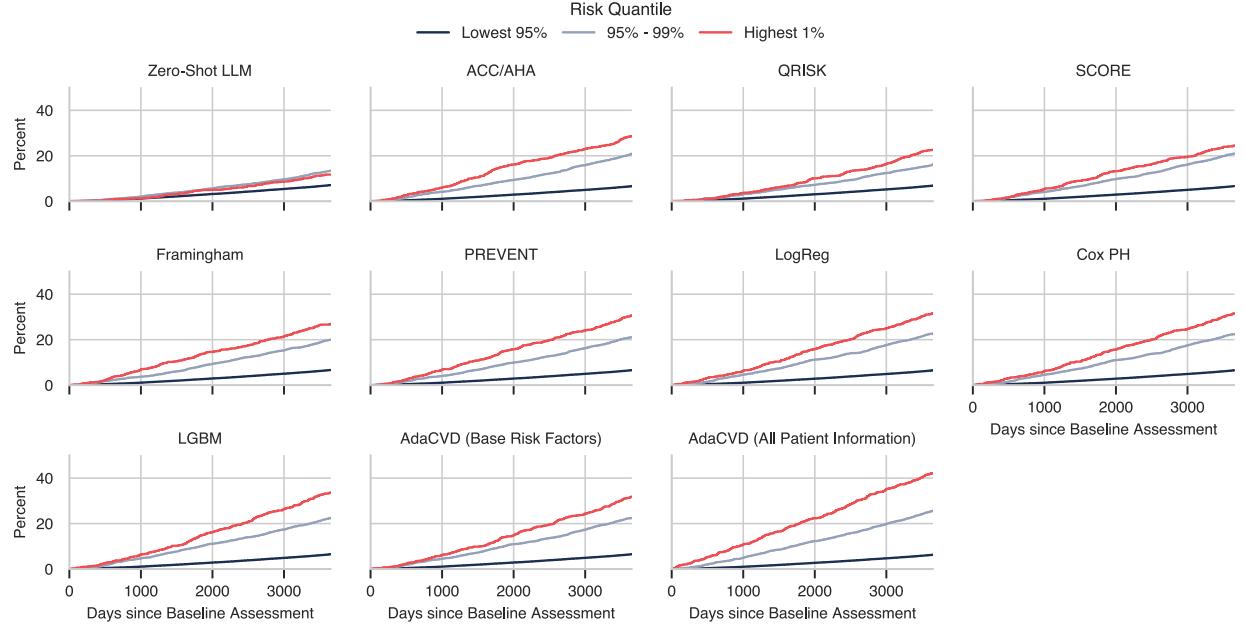
**Figure 8: Evaluation of calibration of different risk prediction models (Brier Score Loss).** **a.** Comparison of CVD risk prediction models using only a limited set of base risk factors. **b.** AdaCVD when additional patient information is incorporated. Acronyms: Urine Assays (UA), Sociodemographic factors (SD), Physical Measures (PM), Family History (FH), Blood Samples (BS), Lifestyle & Environment (LE), Polygenic Risk Scores (PRS), ICD Codes (ICD), and Medical History (MH). Each feature group includes the base risk factors. The *All Patient Information* setting integrates all feature categories.



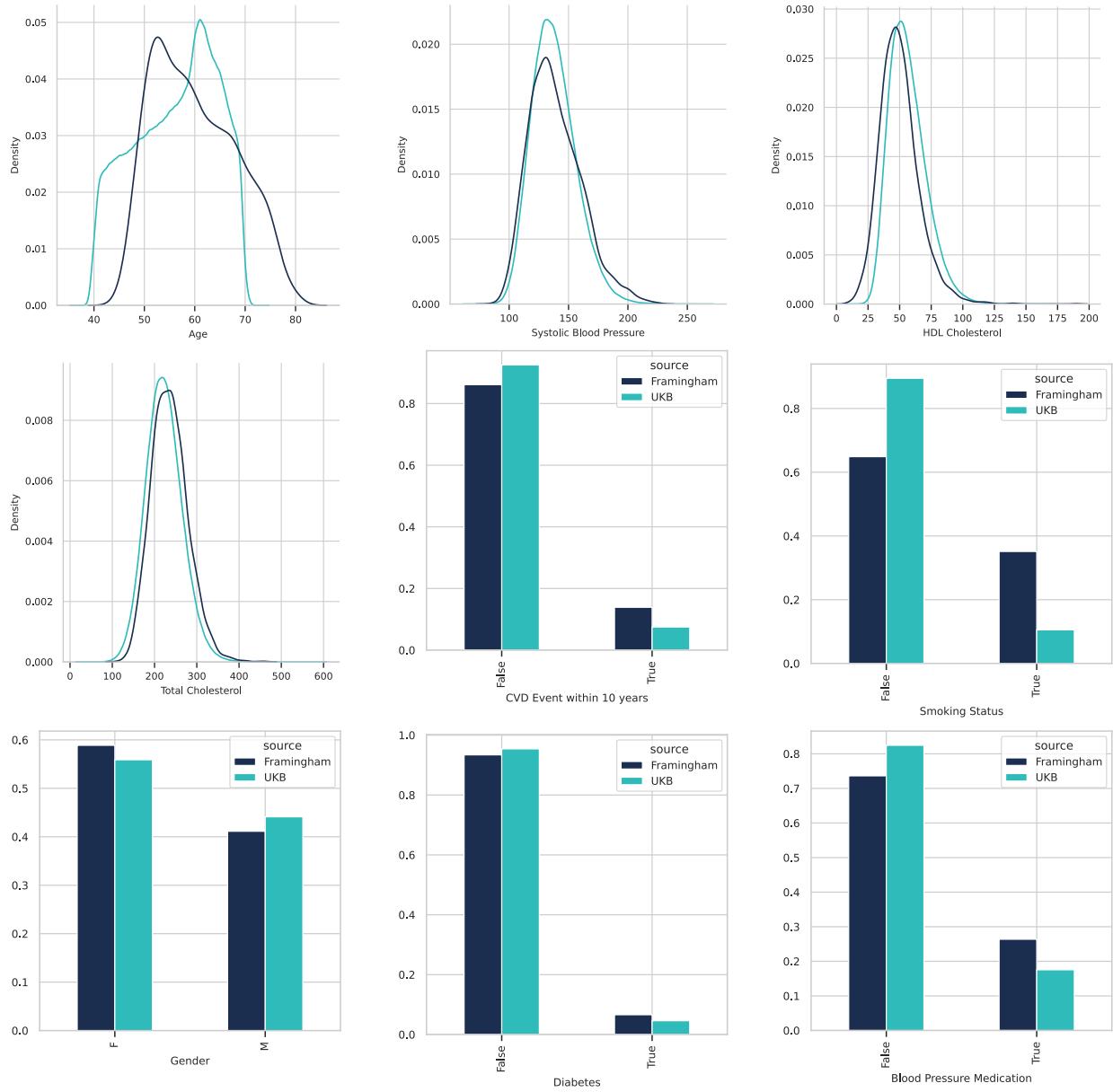
**Figure 9: Evaluation of risk prediction models using the base risk factors.** **a.** Comparison of different LLMs of small and medium size, both zero-shot and fine-tuned. LLMs not shown in the zero-shot group did not comply with the instructions. **b.** Correlation between predictions of different risk prediction models, as measured by the Kendall rank correlation coefficient.



**Figure 10: Distribution of risk predictions.** Risk prediction distributions for individuals that developed CVD vs. those who did not for different risk prediction models.



**Figure 11: Stratified event curves.** Event curves stratified by predicted risk percentiles (lowest 95%, 95 – 99%, and highest 1%) for different risk prediction models. The x-axis denotes the 10-year follow-up period (in days); The y-axis shows the observed incidence for each risk group up until that day; The rightmost points indicate the observed 10-year incidence rates for each risk group.



**Figure 12:** Comparison of the marginal distributions of the base risk factors between the UK Biobank and the Framingham Heart Study participants.