



Harrison Healthcare's Coronary Heart Disease Risk Calculator Accurately Replicates the Framingham 10-Year Risk Score in a Simulated Dataset

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Introduction

Coronary heart disease (CHD) remains a leading global cause of morbidity and mortality. Despite CHD being largely preventable, with 80% of cases attributable to modifiable factors, accurate 10-year risk prediction remains a cornerstone of preventive care (World Health Organization, 2021; British Heart Foundation, 2025; Arnett et al., 2019).

The Framingham Risk Score (FRS; D’Agostino et al., 2008) is a widely used reference model for estimating an individual’s 10-year risk of developing CHD, including myocardial infarction and coronary death. Developed from a homogeneous cohort in mid-20th-century Massachusetts, the FRS calculates CHD risk by applying cohort-derived weights to traditional clinical variables such as age, cholesterol levels, systolic blood pressure, smoking status, and diabetes. While foundational, the model’s fixed structure limits its adaptability to evolving demographics, secular trends, and emerging risk factors (See [Appendix A1](#) for the FRS equations and a worked example).

In contrast, Harrison Healthcare’s CHD (HH-CHD) risk calculator uses a modular, literature-based method initially developed by Colditz et al. (2000), formalized by Shrier et al. (2018), and later enhanced by Saffer (2024). For each risk factor, an individual’s relative risk (RR) is standardized against the population average risk and multiplied with other standardized RRs to yield a combined score. This score is then log-transformed and scaled to produce an absolute 10-year CHD risk estimate. This modular design supports easy updates to risk weights and prevalence data as new evidence emerges and allows for the seamless addition or removal of risk factors, making it adaptable across diverse patient populations (See [Appendix A2](#) for HH-CHD equations and a worked example).

Study Objective

The objective of this study is to determine whether the HH-CHD risk calculator methodology can reproduce 10-year risk estimates generated by the Framingham Risk Score (FRS) when supplied with identical inputs. Establishing convergence under these serves as an important methodological validation step, demonstrating that the underlying methodology of HH-CHD yields outputs comparable to a gold-standard model when based on shared assumptions. This comparison helps rule out concerns around structural bias in the HH-CHD algorithm and clarifies that any future divergence in risk estimates reflects differences in epidemiological inputs rather than model design.

To test the convergence between the two risk calculators, we applied the original Framingham inputs to the HH-CHD model using a synthetic dataset constructed to match the published Framingham parameters and examined the degree of convergence between

the two calculators. We then updated the HH-CHD with contemporary values to observe how risk estimates shift, providing insight into how closely the updated model aligns with FRS when applied to the same synthetic dataset.

Methods

A synthetic sample of 10,000 adults (48% male; age range: 30-74 years) was generated to replicate the clinical characteristics and variable interrelationships observed in the original Framingham Heart Study Cohort. The dataset included key cardiovascular risk factors used in the Framingham Risk Score (FRS) calculations: systolic and diastolic blood pressure, total cholesterol (TC), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), diabetes status, and smoking status. Further details about synthetic cohort generation are provided in [Appendix A3](#).

Two calibration approaches were used to test the HH-CHD risk calculator. In the “*Framingham inputs*” condition, the model was supplied with the original relative risks and prevalence values used in the FRS, including both TC- and LDL-based cholesterol FRS models to reflect clinical variation. In the “*Contemporary inputs*” condition, the model was populated with updated relative risks and prevalence values derived from studies conducted over the past two decades, incorporating more recent evidence and population trends.

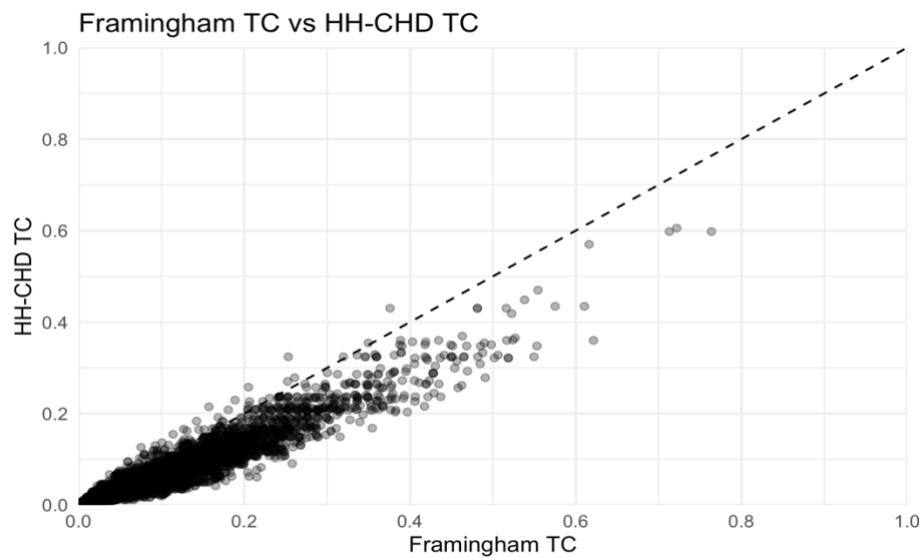
To assess the degree of agreement between HH-CHD and FRS risk estimates, several statistical methods were applied: Pearson and Spearman correlation coefficients to assess linear and rank-order association; a two-way absolute-agreement intraclass correlation coefficient (ICC) to evaluate consistency; and Bland–Altman analysis to quantify bias and limits of agreement. Results were stratified by sex and age group. Additionally, a Type II ANCOVA was conducted to identify covariates contributing to any systematic differences.

Main Results

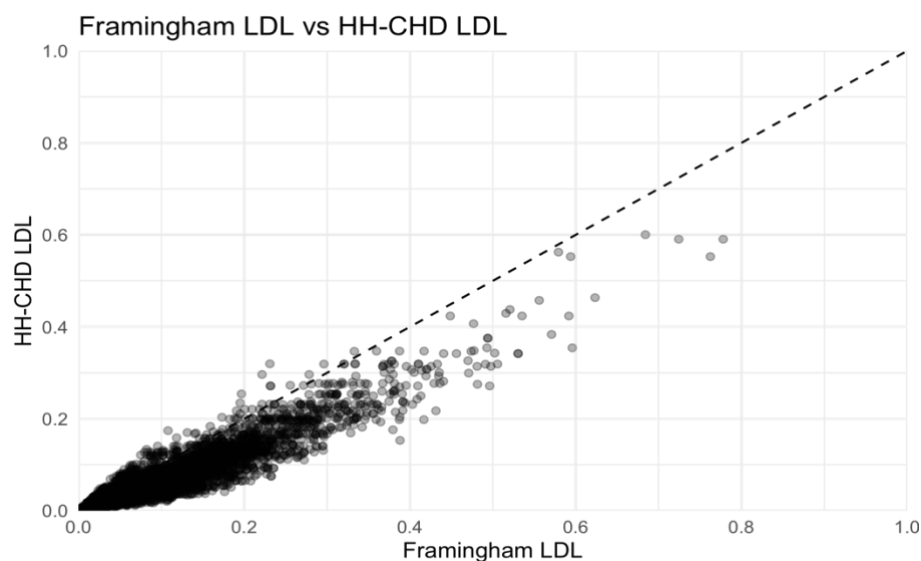
The HH-CHD risk calculator demonstrated strong convergence with the Framingham Risk Score (FRS) in estimating 10-year coronary heart disease (CHD). Using Framingham inputs, correlations between HH-CHD and FRS estimates were high for both the Total Cholesterol (TC) and low-density lipoprotein (LDL) models ($r = 0.95$ and $r = 0.94$, respectively). On average, HH-CHD estimates differed from FRS by approximately 3%, with 95% of scores falling within 7–9 percentage points of each other.

Figure 1. Scatterplots of HH-CHD vs. FRS estimates using Framingham inputs

A) Total Cholesterol (TC) Estimate



B) Low-Density Lipoprotein (LDL) Estimate



When populated with contemporary relative risks and prevalence figures, the HH-CHD calculator continued to show strong convergence with FRS estimates ($r = .87$ for TC; $r = .85$ for LDL). HH-CHD estimates were on average 2% lower, and 95% of estimates fell within 10% of the corresponding FRS estimates. Scatterplots illustrating this comparison are provided in [Appendix A9](#).

We also examined whether convergence varied by participant sex or age.

Sex

When stratified by sex, HH-CHD predictions differed from FRS by an average of 2-3% in women and 3% in men. Limits of agreement were narrower among women ($\pm 5\%$) than men ($\pm 6\%$), indicating that individual-level differences were more tightly clustered. While both sexes showed minimal systematic bias, agreement was slightly stronger in women.

Age

Risk estimate differences between HH-CHD and FRS increased slightly with age, by approximately 2% in individuals under 50 to 5% in those over age 70. This corresponds to an increase of 0.1% per year, or $\sim 1\%$ per decade. Among individuals over age 70, 90% of HH-CHD scores still fell within $\pm 9\%$ of FRS estimates, indicating stable convergence across age groups.

Sex–Age interaction

A small interaction effect between sex and age was observed in predicting differences between the HH-CHD and FRS estimates. However, this interaction explained less than 2% of the total variance, suggesting minimal practical impact.

Detailed results for all subgroup and interaction analyses are provided in [Appendix A6-A12](#).

Limitations & Next Steps

Several limitations should be considered when interpreting the results of this study.

1. Use of Synthetic Data

These analyses relied on a synthetic dataset constructed to mirror the distributions and covariances of the original Framingham cohort. While this allowed for precise control over model inputs and direct comparison of outputs, it lacks the real-world complexity of clinical data. Factors such as missing values, incomplete records, and more nuanced variable interdependencies were therefore not represented. Future research using actual clinical datasets will be necessary to confirm model performance.

2. Absence of CHD Outcome Data

The study was designed to evaluate analytic convergence, not predictive validity. Since the synthetic dataset did not include CHD outcomes, the analyses cannot evaluate the real-world accuracy of either model in forecasting CHD events. Prospective validation efforts are currently underway using longitudinal clinical datasets, allowing for both

HH-CHD and FRS to be tested against real-world CHD outcomes.

3. Restricted Variables

Although the HH-CHD model is designed to incorporate a larger number and broader range of risk factors (including biomarkers, medications, and lifestyle variables) this study was restricted to the six variables used to calculate the FRS (age, cholesterol [TC and LDL], blood pressure, smoking, and diabetes). This constraint ensured a valid one-to-one comparison between estimates but did not permit evaluation of the extended capabilities of HH-CHD. Future work will examine the additive contribution of these additional HH-CHD variables.

4. Use of a Single Baseline Survival Curve

To convert relative risk into absolute 10-year risk, a fixed, sex-specific baseline survival curve derived from the Framingham cohort was applied. While this maintained consistency with the original FRS methodology, it may limit generalizability to populations with different baseline event rates. Upcoming analyses will incorporate alternative survival curves (e.g., from ARIC or MESA) to test calibration across more diverse populations.

Conclusion

The HH-CHD risk calculator achieved its analytic objective: it successfully replicated the 10-year coronary heart disease (CHD) risk estimates produced by the Framingham Risk Score (FRS) when provided with identical inputs. This high level of convergence, reflected in the near-identical estimates across the risk spectrum, demonstrates that the modular, literature-derived methodology used by the HH-CHD can emulate the output of a long-established, cohort-derived model with near-perfect fidelity.

When updated with contemporary relative risks and prevalence estimates, HH-CHD continued to produce results that closely tracked with FRS, while also reflecting modern epidemiologic data. Its structure allows individual risk factors to be added, removed, or recalibrated without reengineering the entire model—offering transparency, flexibility, and adaptability as new evidence emerges.

These findings represent an important foundational step in evaluating HH-CHD as a modern alternative to legacy risk calculator tools. While outcome-based validation in real-world populations remains essential and is currently underway, this analytic comparison provides strong preliminary support for HH-CHD's methodological soundness and clinical

potential. The model is well-positioned for continued development and future clinical integration.

References

- Arnett, D. K., Blumenthal, R. S., Albert, M. A., Buroker, A. B., Goldberger, Z. D., Hahn, E. J., Ziaeian, B. (2019). 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease. *Circulation*, 140(11), e596–e646.
<https://doi.org/10.1161/CIR.0000000000000678>
- British Heart Foundation. (2025). Global heart & circulatory diseases factsheet.
<https://www.bhf.org.uk/-/media/files/for-professionals/research/heart-statistics/bhf-cvd-statistics-global-factsheet.pdf>
- Colditz, G. A., Atwood, K. A., Emmons, K., Monson, R. R., Willett, W. C., Trichopoulos, D., & Hunter, D. J. (2000). Harvard report on cancer prevention volume 4: Harvard Cancer Risk Index. Risk Index Working Group, Harvard Center for Cancer Prevention. *Cancer causes & control : CCC*, 11(6), 477–488.
<https://doi.org/10.1023/a:1008984432272>
- D’Agostino, R. B., Vasan, R. S., Pencina, M. J., Wolf, P. A., Cobain, M., Massaro, J. M., & Kannel, W. B. (2008). General cardiovascular risk profile for use in primary care: The Framingham Heart Study. *Circulation*, 117(6), 743–753.
<https://doi.org/10.1161/CIRCULATIONAHA.107.699579>
- Després, J. P., Moorjani, S., Lupien, P. J., Tremblay, A., Nadeau, A., & Bouchard, C. (1990). Regional distribution of body fat, plasma lipoproteins, and cardiovascular disease. *Arteriosclerosis*, 10(4), 497–511. <https://doi.org/10.1161/01.ATV.10.4.497>
- Franklin, S. S., Gustin, W., Wong, N. D., Larson, M. G., Weber, M. A., Kannel, W. B., & Levy, D. (1997). Hemodynamic patterns of age-related changes in blood pressure: The Framingham Heart Study. *Circulation*, 96(1), 308–315.
<https://doi.org/10.1161/01.CIR.96.1.308>
- Lauer, M. S., Anderson, K. M., Levy, D., & Wilson, P. W. F. (1994). The impact of obesity on left ventricular mass and geometry: The Framingham Heart Study. *JAMA*, 271(6), 456–460. <https://doi.org/10.1001/jama.1994.03510300040029>
- Saffer, B. Y. (2024). *Accounting for mediation effects in risk prediction calculators* (White paper). Harrison Healthcare.

<https://docs.google.com/document/d/1E6MgIISETNYOmSLrnpDGtUup9AD9wNRZrqEHakVIFJk/edit?usp=sharing>

Shrier, I., Colditz, G. A., & Steele, R. J. (2018). Synthesizing risk from summary evidence across multiple risk factors. *Epidemiology (Cambridge, Mass.)*, 29(4), 533–535.

<https://doi.org/10.1097/EDE.0000000000000820>

Wilson, P. W. F., D’Agostino, R. B., Levy, D., Belanger, A. M., Silbershatz, H., & Kannel, W. B. (1998). Prediction of coronary heart disease using risk factor categories.

Circulation, 97(18), 1837–1847. <https://doi.org/10.1161/01.CIR.97.18.1837>

World Health Organization. (2021, June 11). Cardiovascular diseases (CVDs) fact sheet.

[https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds))

Appendix — Supplementary Methods, Equations, and Full Result Tables

A1 Framingham 10-Year Risk: Full Computational Workflow

Step	Formula
Linear predictor (L)	$L_{total} = \beta_{age} \times (Age) + \beta_{chol} \times (chol\ category) + \dots$
Cohort mean (L_{mean})	$L_{mean} = (\beta_{age} \times Mean_{Age}) + (\beta_{chol} \times Mean_{chol}) + \dots + (\beta_{smoker} \times Mean_{smoker})$
A	$A = L_{total} - L_{mean}$ $L_{mean} = TC = 3.0975 \text{ for men, } 9.92545 \text{ for women}$ $L_{mean} = LDL = 3.00069 \text{ for men, } 9.914136 \text{ for women}$
B	$B = e^A$
10-year survival	$S_{abs}(10) = S_0^B = \exp(B \ln S_0)$
10-year risk	$R(10) = 1 - S_{abs}(10) = 1 - \exp(B \ln S_0)$ <p>TC: $S_0men = 0.90015$, $S_0women = 0.96246$</p> <p>LDL: $S_0men = 0.90017$, $S_0women = 0.9628$</p>

Framingham LDL Worked Example:

Consider a 65-year-old man with LDL of 165 mg/dL (4.27 mmol/L), HDL of 35 mg/dL (1.01 mmol/L), blood pressure (146/88 mm Hg) that falls into stage I hypertension, and no diabetes, who is a smoker.

$$L_{mean} = LDL = 3.00069 \text{ (for men)}$$

$$L_{total} = 65 \times 0.04826 + 0.26755 + 0.21643 + 0.55714 + 0.54377 + (0.42146 \times 0) \\ = 4.7099$$

$$A = 4.7099 - 3.00069 = 1.7092$$

$$B = e^{1.7092} = 5.525$$

$$R(10) = 1 - 0.90017^{5.525} = 1 - 0.615 = 0.385$$

Result: This individual's FRS estimated **10-year risk of developing CHD is 39%.**

A2 HH-CHD Calculation: Modular, Log-Sum Framework

Step	Formula
Factor-level prevalence-weighted relative risk (WPR)	$WPR_f = \sum_i P_{f,i} RR_{f,i/r}$
Overall population relative risk (PR)	$\ln(PR) = \sum_f \ln(WPR_f)$
Cumulative Incidence Rate (CIR)	$\ln(CIR) = \sum_f \ln(RR_{f,i/r})$
Centered log-ratio	$\Delta = \ln(CIR) - \ln(PR)$ <p>(For numerical stability compute log transformed)</p>
R-ratio	$R = e^{\Delta}$
Survival-power scaling, 10-y risk	$Risk_{10} = 1 - S_0^R = 1 - \exp(\Delta \ln S_0)$ <p>TC: $S_{0men} = 0.90015$, $S_{0women} = 0.96246$</p> <p>LDL: $S_{0men} = 0.90017$, $S_{0women} = 0.9628$</p>

Framingham Inputs HH-CHD LDL Worked Example:

In this example we refer to the original FRS relative risk and prevalence values not the contemporary inputs of the HH-CHD risk calculator. Contemporary relative risk and prevalence values are available upon demand.

Consider a 65-year-old man with LDL of 165 mg/dL (4.27 mmol/L), HDL of 35 mg/dL (1.01 mmol/L), blood pressure (146/88 mm Hg) that falls into stage I hypertension, and no diabetes, who is a smoker.

Factor	RR	WPR
Age	2.62	1.4147
LDL	1.74	1.3622
HDL	1.00	1.0915
Systolic blood pressure (SBP)	1.73	1.3303
Diabetes	1.00	1.0255
Smoking	1.71	1.2847

$$\ln(PR) = 1.4247 \times 2.3622 \times 1.0915 \times 1.3303 \times 1.0255 \times 1.2847 = 3.6865 = \ln(3.6865) \approx 1.3059$$

$$\ln(CIR) = 2.62 \times 1.74 \times 1.0 \times 1.73 \times 1.0 \times 1.71 = 13.4652 = \ln(13.4652) \approx 2.5985$$

$$\Delta = 2.5985 - 1.3059 = 1.2926$$

$$R = e^{\Delta} = e^{1.2926} = 3.6526$$

$$Risk_{10} = 1 - \exp(3.6526 \times \ln(0.90017)) = 1 - 0.90017^{3.6526} \approx 0.319$$

Result: This individual's HH-CHD estimated **10-year risk of developing CHD is 32%**

A3 Synthetic Cohort Generation

A synthetic dataset of $N = 10,000$ adults (48% male) was generated to reflect the distributional characteristics of the original Framingham Heart Study (FHS). Seven continuous variables—age, systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), total cholesterol (TC), low-density lipoprotein cholesterol (LDL), and high-density lipoprotein cholesterol (HDL)—were sampled from a multivariate normal distribution. Means and standard deviations were derived from Wilson et al. (1998), and a 7×7 correlation matrix was applied to impose realistic inter-variable relationships: SBP–DBP ($r \approx 0.68$) from Franklin et al. (1997), TC–LDL ($r \approx 0.80$) from Lauer et al. (1994), BMI–TC and BMI–HDL ($r \approx 0.32$, $r \approx -0.29$) from D’Agostino et al. (2008) and Després et al. (1990), and age–lipids ($r \approx 0.20$) from Wilson et al. (1998).

This approach ensured that the simulated dataset preserved not only the individual distributions of variables but also their joint covariance structure, mirroring the characteristics observed in large epidemiologic cohorts.

Blood pressure was discretized into Joint National Committee (JNC-V) blood-pressure categories (Normal, High-Normal, Stage I, Stage II–IV). Binary flags for diabetes, smoking, and antihypertensive use were simulated based on prevalence rates conditional on SBP category. Age effects were modeled in 10-year bins (30–39 ... 70–74) with the 40–49 bin normalized to a relative risk of 1.0 to align with FRS and HH-CHD specifications.

A4 Statistical Software and Packages

All analyses were executed in R 4.3 (R Foundation, 2025): dplyr 1.1, irr 0.84, ggplot2 3.5, car 3.1, emmeans 1.10, psych 2.3, writexl 1.5. Model comparisons were conducted using Pearson and Spearman correlations, intraclass correlation coefficients (ICC) for absolute agreement, Bland–Altman analyses to assess bias and limits of agreement, and Type II ANCOVA to explore age and sex effects.

A5 Overall Agreement - Framingham Inputs

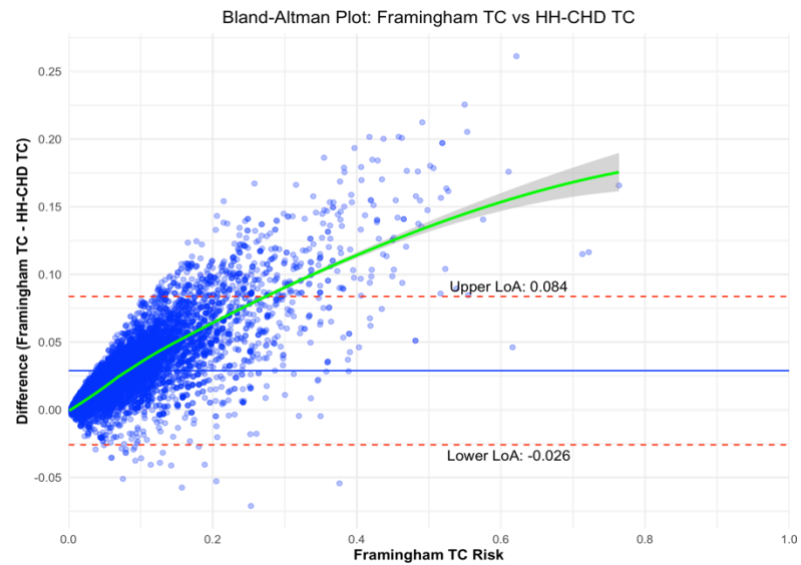
Table 1. Agreement and Correlation Metrics for Framingham vs HH-CHD Risk Scores

Metric	Framingham TC vs HH-CHD TC	Framingham LDL vs HH-CHD LDL
Pearson r	0.950	0.939
Spearman ρ	0.937	0.923
ICC	0.825	0.805
Mean difference (Framingham – HH-CHD)	0.029	0.030
95 % LoA (± 1.96 SD)	–0.026 to +0.084	–0.027 to +0.087

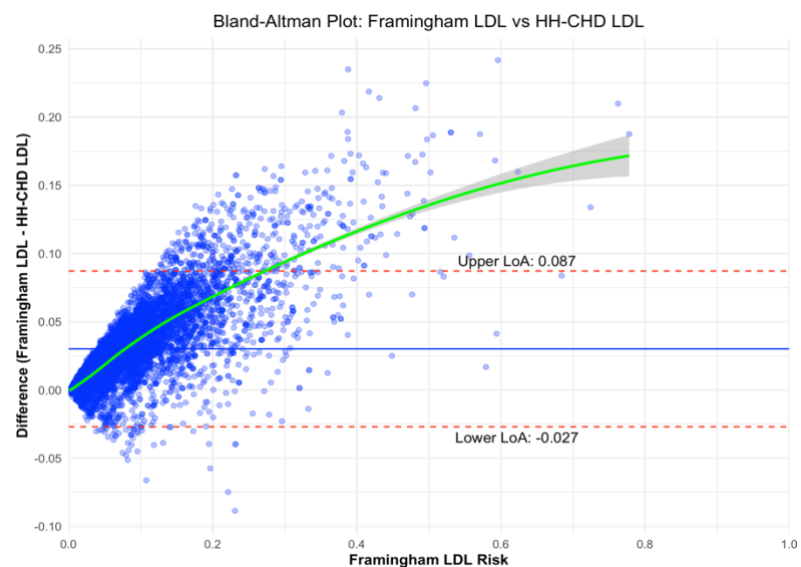
Abbreviations: TC, total cholesterol; LDL, low-density lipoprotein cholesterol; HH-CHD, Harrison Healthcare coronary heart disease risk calculator; ICC, intraclass correlation coefficient; LoA, limits of agreement.

Figure 2. Bland–Altman Plots Comparing Framingham and HH-CHD Risk Calculators

A) TC Estimate



B) LDL Estimate



Abbreviations: LDL, low-density lipoprotein cholesterol; TC, total cholesterol; LoA, limits of agreement.

A6 Subgroup Bland–Altman Statistics (Sex and Age) - Framingham Inputs

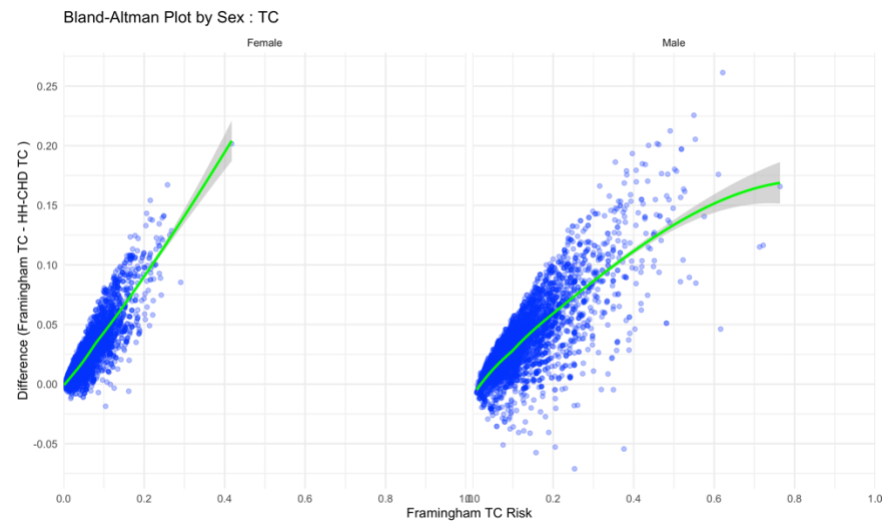
Table 2. Age- and Sex-Stratified Bland-Altman Statistic Comparing Framingham vs HH-CHD

Model	Group	Bias	LoA	Pearson	Spearman
TC	Female	0.024	0.045	0.901	0.915
TC	Male	0.034	0.062	0.952	0.946
TC	<50	0.019	0.037	0.918	0.920
TC	50-70	0.041	0.060	0.934	0.909
TC	>70	0.047	0.088	0.971	0.953
LDL	Female	0.028	0.049	0.912	0.923
LDL	Male	0.033	0.064	0.943	0.929
LDL	<50	0.019	0.039	0.903	0.904
LDL	50-70	0.043	0.062	0.920	0.890
LDL	>70	0.049	0.086	0.968	0.949

Abbreviations: TC, total cholesterol; LDL, low-density lipoprotein cholesterol; LoA, limits of agreement.

Figure 3. Bland–Altman Plots Comparing Framingham and HH-CHD Risk Calculators, Stratified by Sex

A) TC Estimate



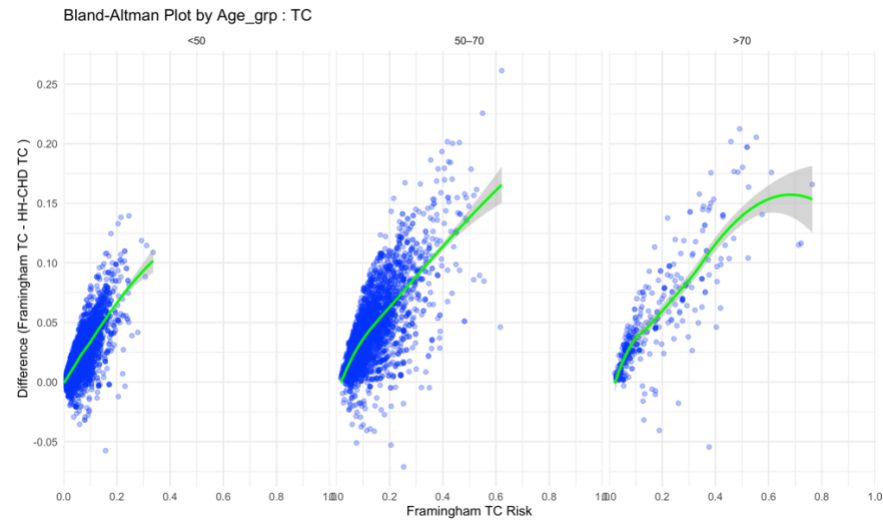
B) LDL Estimate



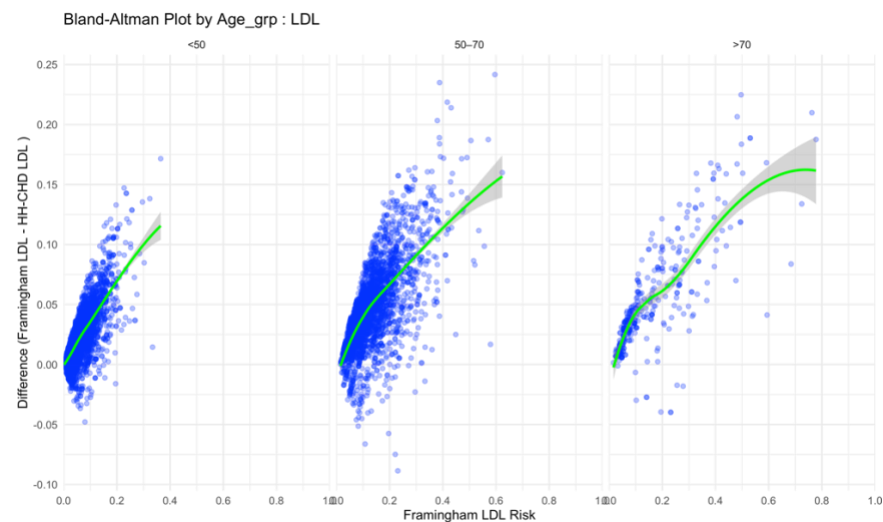
Abbreviations: LDL, low-density lipoprotein cholesterol; TC, total cholesterol.

Figure 4. Bland–Altman Plots Comparing Framingham and HH-CHD Risk Calculators, Stratified by Age

A) TC Estimate



B) LDL Estimate



Abbreviations: LDL, low-density lipoprotein cholesterol; TC, total cholesterol; grp, group.

A7 ANCOVA: Type II Tests of Bias - Framingham Inputs

Table 3. Type II ANCOVA of Bias Framingham vs HH-CHD

Model	Term	Sum Sq	Df	F value	Pr(>F)	MS	Partial η^2
TC	Mean TC Risk	1.7634	1	4853.80	<.0001	1.7634	0.3269
TC	Sex	0.0902	1	248.40	<.0001	0.0902	0.0242
TC	Age	0.0590	1	162.35	<.0001	0.0590	0.0160
TC	Sex × Age	0.0248	1	68.30	<.0001	0.0248	0.0068
TC	Residuals	3.6313	9995	—	—	0.0004	0.5000
LDL	Mean LDL Risk	2.1717	1	5452.90	<.0001	2.1717	0.3530
LDL	Sex	0.2722	1	683.39	<.0001	0.2722	0.0640
LDL	Age	0.0755	1	189.69	<.0001	0.0755	0.0186
LDL	Sex × Age	0.0871	1	218.65	<.0001	0.0871	0.0214
LDL	Residuals	3.9807	9995	—	—	0.0004	0.5000

Abbreviations: TC, total cholesterol; LDL, low-density lipoprotein cholesterol; Sum Sq, sum of squares; Df, degrees of freedom; F value, F-statistic; Pr(>F), probability (p-value) that the observed F exceeds the critical value under the null hypothesis; MS, mean square; partial η^2 , partial eta-squared.

A8 Simple-Slope & Adjusted-Mean Results - Framingham Inputs

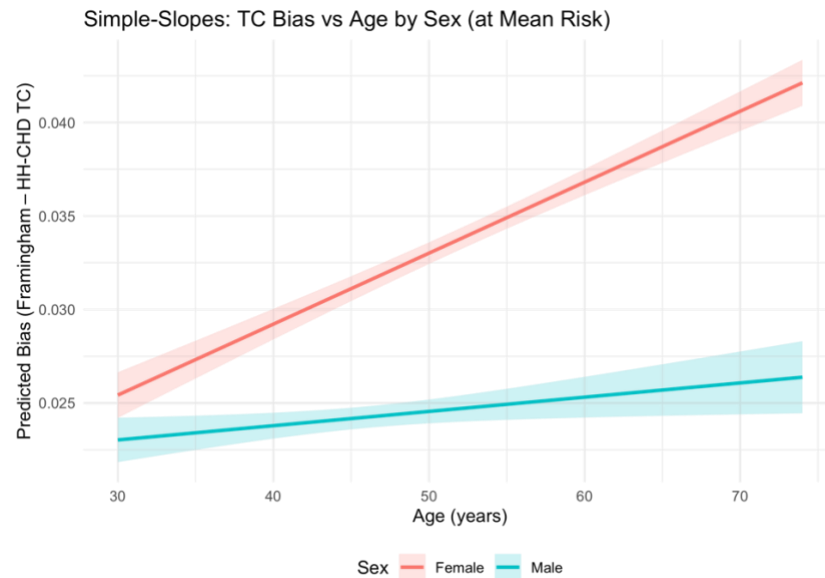
Table 4. Simple Slopes & Adjusted Means Framingham vs HH-CHD

Model	Sex	Age Slope (SE)	t (df)	p	Adj. Mean Bias (95 % CI)	Female–Male Contrast (95 % CI)	p
TC	Female	0.0004 (0.0001)	15.13 (9995)	< .001	0.033 (0.032, 0.033)	0.008 (0.007, 0.009)	< .001
TC	Male	0.0001 (0.0001)	2.28 (9995)	.022	0.025 (0.024, 0.025)	—	—
LDL	Female	0.0005 (0.0000)	19.26 (9995)	< .001	0.037 (0.036, 0.037)	0.014 (0.013, 0.015)	< .001
LDL	Male	-0.0001 (0.0000)	-1.74 (9995)	.081	0.023 (0.022, 0.023)	—	—

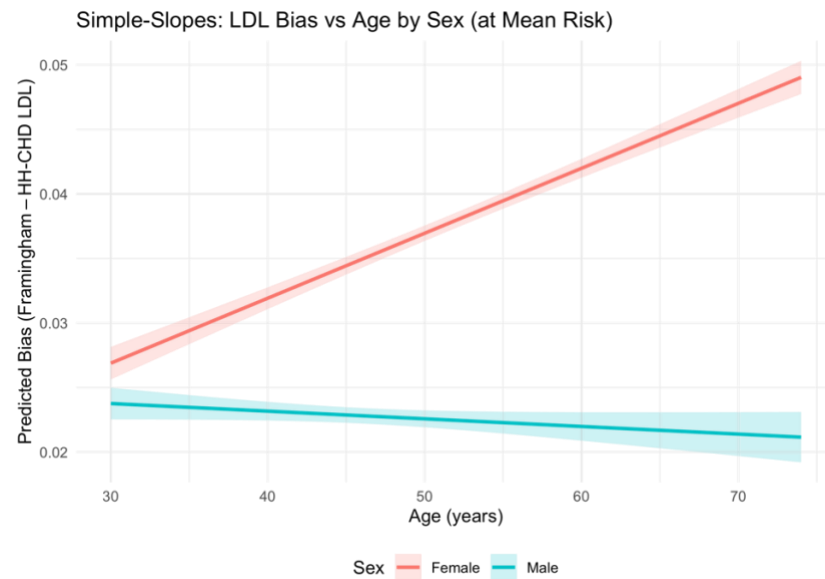
Abbreviations: TC, total cholesterol; LDL, low-density lipoprotein cholesterol; SE, standard error; *t*, *t*-statistic; *df*, degrees of freedom; *p*, two-tailed probability value; Adj., adjusted; CI, confidence interval.

Figure 5. Simple Slopes Bias vs Age by Sex

A) TC Estimate

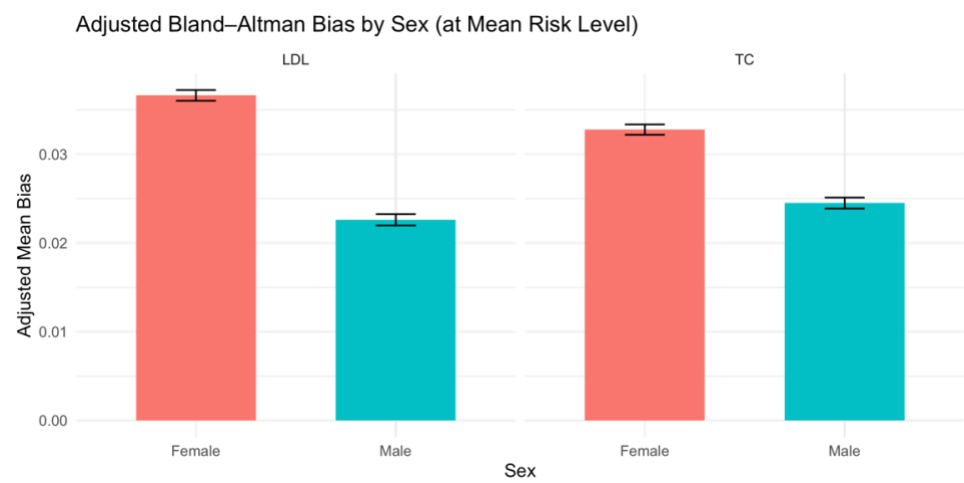


B) LDL Estimate



Abbreviations: LDL, low-density lipoprotein cholesterol; TC, total cholesterol; HH, Harrison Healthcare risk calculator.

Figure 6. Adjusted Mean Bias



Abbreviations: LDL, low-density lipoprotein cholesterol; TC, total cholesterol.

A9 Overall Agreement – Contemporary Inputs

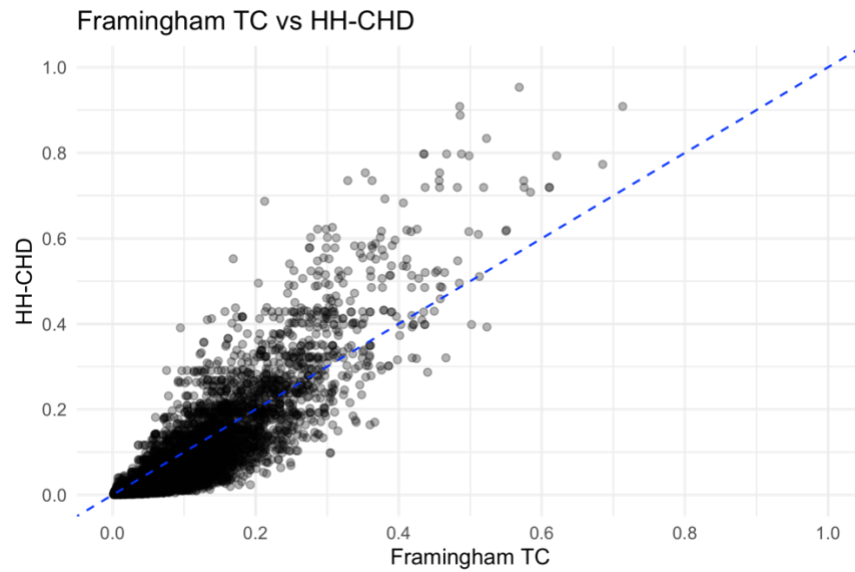
Table 5. Agreement and Correlation Metrics for Framingham vs HH-CHD Risk Scores

Metric	Framingham TC vs HH-CHD	Framingham LDL vs HH-CHD
Pearson correlation (r)	0.865	0.854
Spearman correlation (ρ)	0.860	0.855
ICC	0.811	0.802
Mean difference (Framingham – HH)	0.020	0.018
95 % LoA (±1.96 SD)	± 0.097	± 0.101

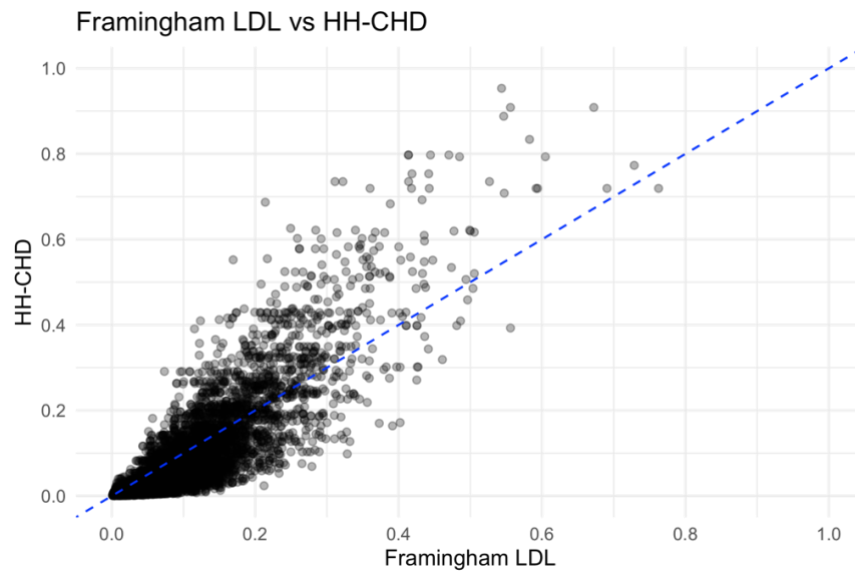
Abbreviations: TC, total cholesterol; LDL, low-density lipoprotein cholesterol; HH-CHD, Harrison Healthcare coronary heart disease risk calculator; ICC, intraclass correlation coefficient; LoA, limits of agreement.

Figure 7. Scatterplots Framingham vs HH-CHD

A) TC Estimate



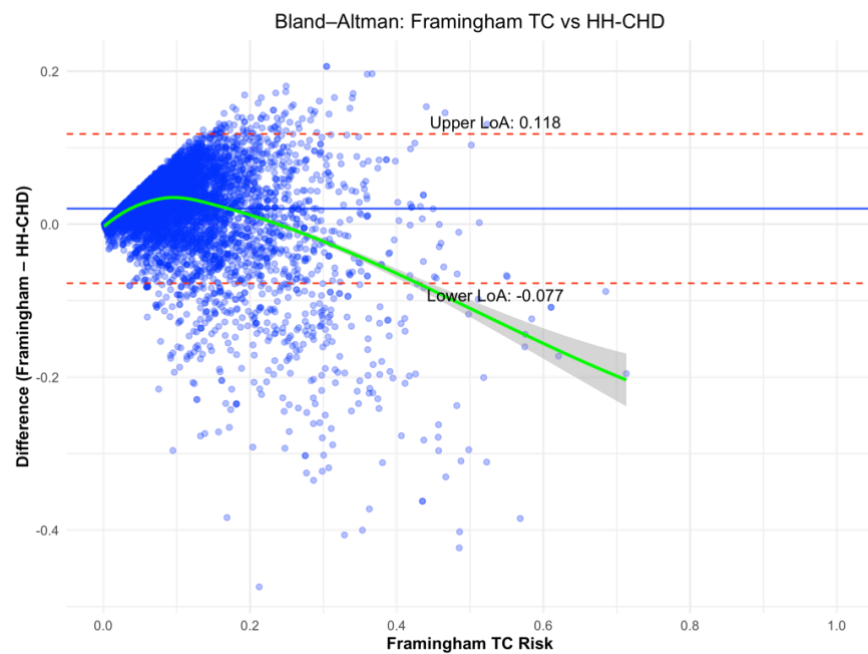
B) LDL Estimate



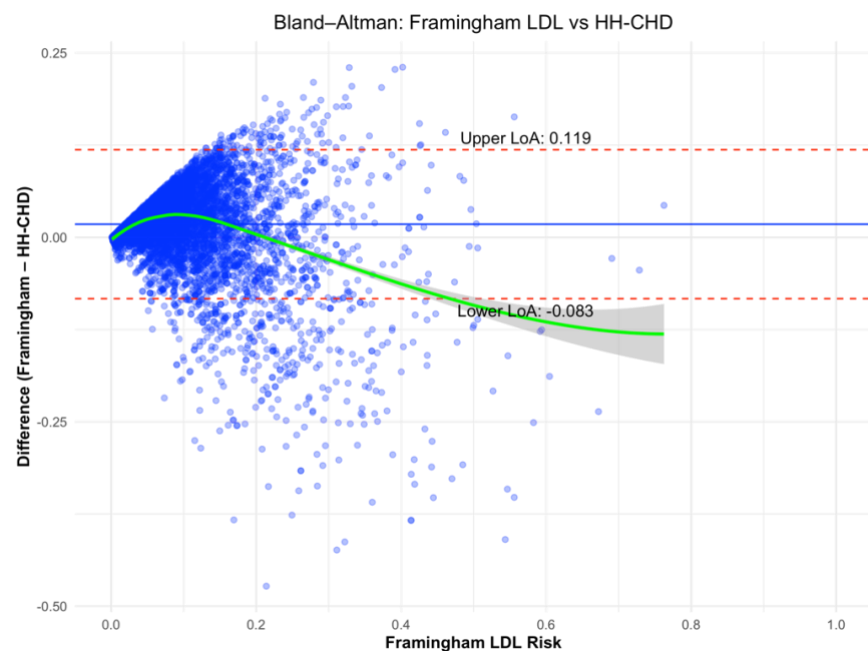
Abbreviations: LDL, low-density lipoprotein cholesterol; TC, total cholesterol; HH, Harrison Healthcare risk calculator.

Figure 8. Bland–Altman Plots Comparing Framingham and HH-CHD Risk Calculators

A) TC Estimate



B) LDL Estimate



Abbreviations: HH, Harrison Healthcare risk calculator; LDL, low-density lipoprotein cholesterol; TC, total cholesterol; LoA, limits of agreement.

A10 Subgroup Bland–Altman Statistics (Sex and Age) – Contemporary Inputs

Table 6. Age- and Sex-Stratified Bland-Altman Statistic Comparing Framingham vs HH-CHD

Model	Group	Bias	LoA	Pearson	Spearman
TC	Female	0.016	0.071	0.767	0.840
TC	Male	0.025	0.119	0.886	0.894
TC	<50	0.015	0.122	0.857	0.831
TC	50-70	0.028	0.053	0.754	0.765
TC	>70	-0.021	0.160	0.861	0.819
LDL	Female	0.016	0.071	0.765	0.840
LDL	Male	0.020	0.125	0.870	0.870
LDL	<50	0.011	0.128	0.840	0.816
LDL	50-70	0.026	0.053	0.750	0.764
LDL	>70	-0.024	0.157	0.867	0.831

Abbreviations: TC, total cholesterol; LDL, low-density lipoprotein cholesterol; LoA, limits of agreement.

Figure 9. Bland–Altman Plots Comparing Framingham and HH-CHD Risk Calculators, Stratified by Age

A) TC Estimate



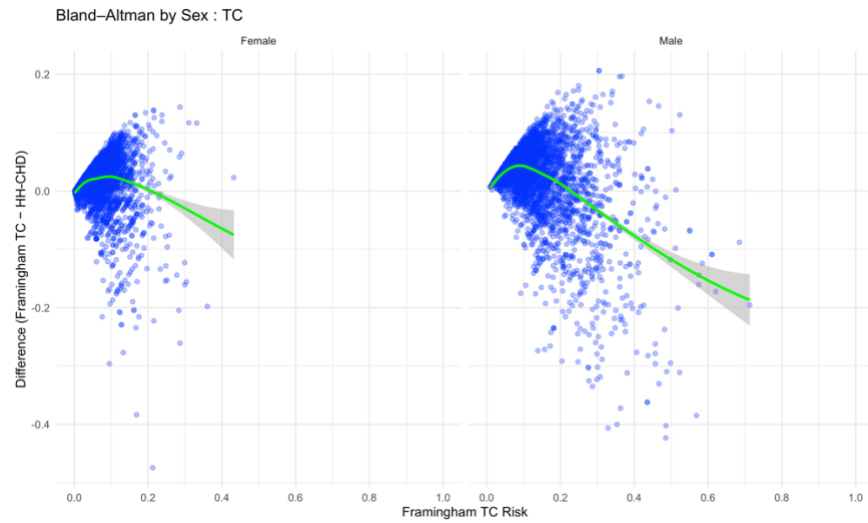
B) LDL Estimate



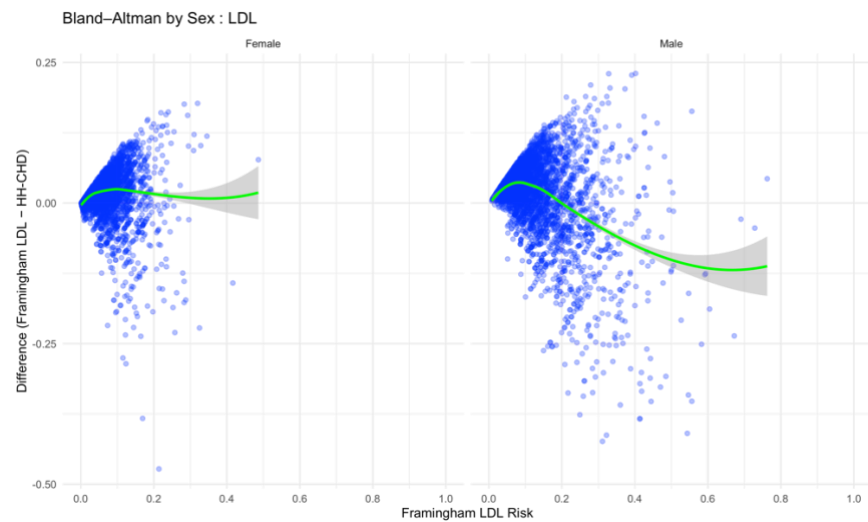
Abbreviations: HH, Harrison Healthcare risk calculator; LDL, low-density lipoprotein cholesterol; TC, total cholesterol; grp, group.

Figure 10. Bland–Altman Plots Comparing Framingham and HH-CHD Risk Calculators, Stratified by Sex

A) TC Estimate



B) LDL Estimate



Abbreviations: HH, Harrison Healthcare risk calculator; LDL, low-density lipoprotein cholesterol; TC, total cholesterol.

A11 ANCOVA: Type II Tests of Bias – Contemporary Inputs

Table 7. Type II ANCOVA of Bias Framingham vs HH-CHD

Model	Term	Sum Sq	Df	F value	Pr(>F)	MS	Partial η^2
TC	Mean TC Risk	1.7634	1	4853.80	<0.0001	1.7634	0.3269
TC	Sex	0.0902	1	248.40	<0.0001	0.0902	0.0242
TC	Age	0.0590	1	162.35	<0.0001	0.0590	0.0160
TC	Sex × Age	0.0248	1	68.30	<0.0001	0.0248	0.0068
TC	Residuals	3.6313	9995	—	—	0.0004	0.5000
LDL	Mean LDL Risk	0.0906	1	114.53	<0.0001	0.0906	0.0114
LDL	Sex	2.0912	1	2643.24	<0.0001	2.0912	0.2095
LDL	Age	0.0207	1	26.19	<0.0001	0.0207	0.0026
LDL	Sex × Age	0.3816	1	482.30	<0.0001	0.3816	0.1530
LDL	Residuals	7.9075	9995	—	—	0.0008	0.5000

Abbreviations: TC, total cholesterol; LDL, low-density lipoprotein cholesterol; Sum Sq, sum of squares; Df, degrees of freedom; F value, F-statistic; Pr(>F), probability (p-value) that the observed F exceeds the critical value under the null hypothesis; MS, mean square; partial η^2 , partial eta-squared.

A12 Simple-Slope & Adjusted-Mean Results – Contemporary Inputs

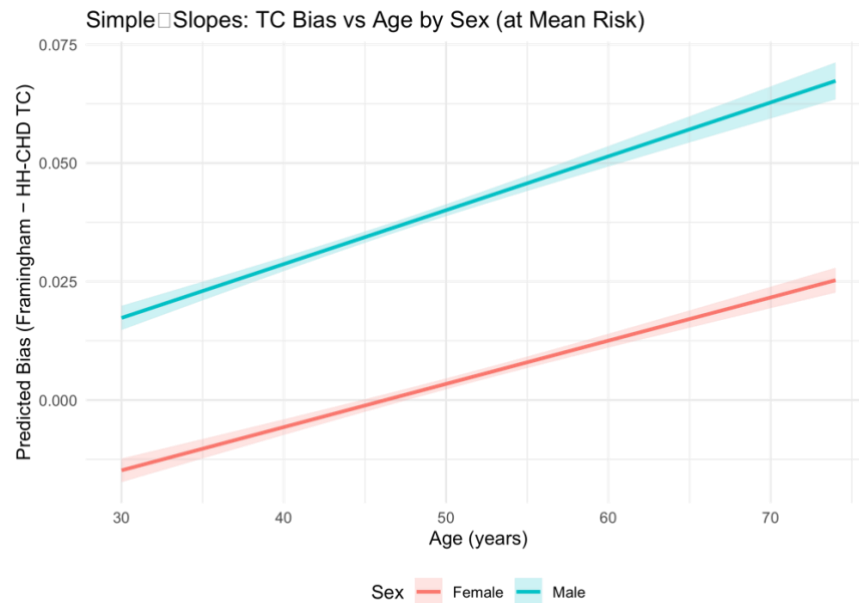
Table 8. Simple Slopes & Adjusted Means Framingham vs HH-CHD

Model	Sex	Age Slope (SE)	t (df)	p	Adj. Mean Bias (95 % CI)	Female – Male Contrast (95 % CI)	p
TC	Female	0.0009 (0.0001)	17.25 (9995)	< .001	0.003 (0.002, 0.004)	–0.037 (–0.038, – 0.035)	< .001
TC	Male	0.0011 (0.0001)	16.36 (9995)	< .001	0.039 (0.038, 0.041)	—	—
LDL	Female	0.0009 (0.0001)	15.62 (9995)	< .001	0.005 (0.003, 0.006)	–0.027 (–0.029, – 0.026)	< .001
LDL	Male	0.0006 (0.0001)	8.51 (9995)	< .001	0.032 (0.031, 0.033)	—	—

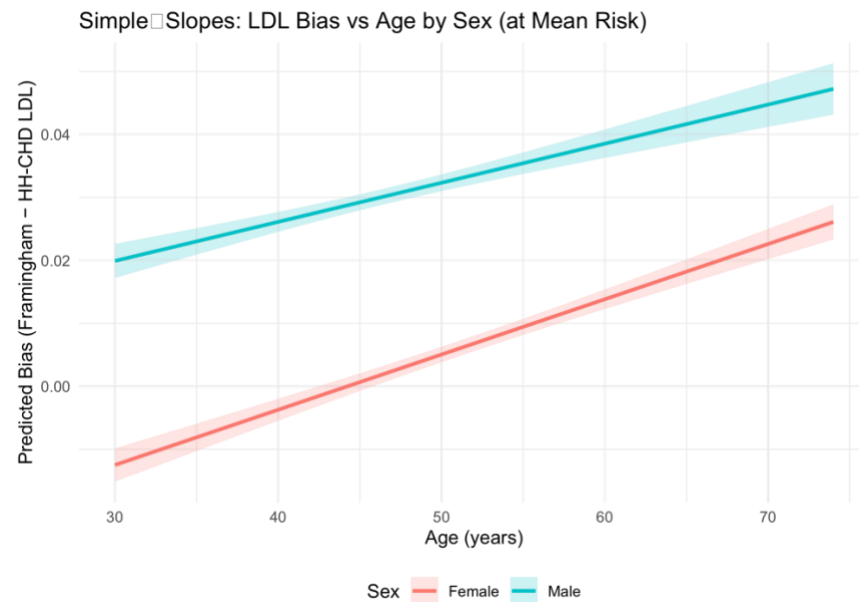
Abbreviations: TC, total cholesterol; LDL, low-density lipoprotein cholesterol; SE, standard error; *t*, *t*-statistic; *df*, degrees of freedom; *p*, two-tailed probability value; Adj., adjusted; CI, confidence interval.

Figure 11. Simple Slopes Bias vs Age by Sex

A) TC Estimate

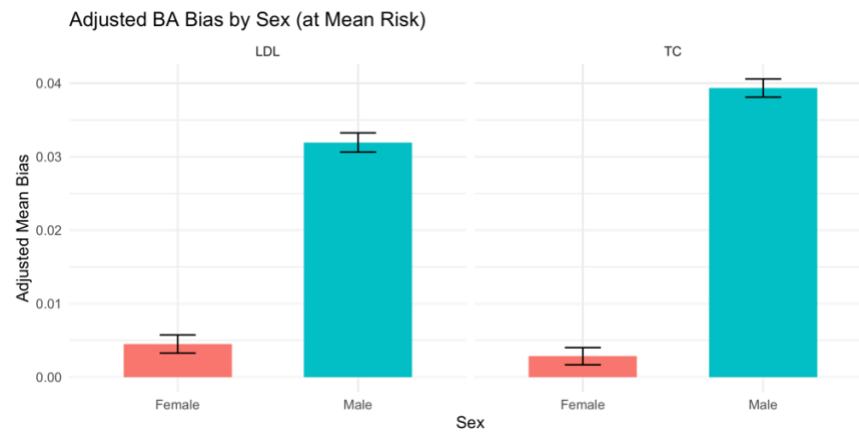


B) LDL Estimate



Abbreviations: HH, Harrison Healthcare risk calculator; LDL, low-density lipoprotein cholesterol; TC, total cholesterol.

Figure 12. Adjusted Mean Bias



Abbreviations: HH, Harrison Healthcare risk calculator; LDL, low-density lipoprotein cholesterol; TC, total cholesterol.

A13 Code Availability

All R scripts, and step-by-step analytical pipelines used in this study are openly available at GitHub (https://github.com/Harrison-Healthcare/Risk_Calculator).