Nationally Representative Individualized Risk Estimation Combining Individual Data from Epidemiologic Studies and Representative Surveys with Summary Statistics from Disease Registries

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ABSTRACT (198 words)

Estimating individualized absolute risks is fundamental to clinical decision-making but are often based on data that does not represent the target population. Current methods improve external validity by including data from population registries but require transportability assumptions of model parameters (relative risks and/or population attributable risks) from epidemiologic studies to the population. We propose a two-step weighting procedure to estimate absolute risk of an event (in the absence of competing events) in the target population without transportability assumptions. The first step improves external-validity for the cohort by creating “pseudoweights” for the cohort using a scaled propensity-based kernel-weighting method, which fractionally distributes sample weights from external probability reference survey units to cohort units, according to their kernel smoothed distance in propensity score. The second step poststratifies the pseudoweighted events in the cohort to a population disease registry by variables available in the registry. Our approach produces design-consistent absolute risks under correct specification of the propensity model. Poststratification improves efficiency and further reduces bias of risk estimates overall and by demographic variables available in the registry when the true propensity model is unknown. We apply our methods to develop a nationally representative all-cause mortality risk model for potential clinical use.

Keywords: risk prediction model, risk assessment, nonprobability cohort, finite population inference, propensity score weighting, Taylor series linearization variance
1 INTRODUCTION

Individualized absolute risks play an increasingly important role in clinical practice and planning public health programs. (Adams and Leveson 2012) Such applications require that the absolute risk models are unbiased for a target population. For example, Graubard et al. (2010) estimated the number of women with high risk of breast cancer in the US to plan magnetic resonance imaging (MRI) breast-cancer screening programs. Similarly, Katki et al. (2016) calculated the distribution of individualized lung cancer risk in the US to project the performance of potential lung-cancer screening programs.

We are motivated by the need to obtain unbiased individualized absolute risk estimation for all-cause mortality, which is critical for clinical decision-making for older patients. (Gill, 2012) Multiple indices of all-cause mortality exist, but all have problems related to bias, accuracy, and generalizability. (Yourman et al., 2012) There is a need to obtain unbiased estimates of absolute risks from an easily implemented model with a few crucial, easily elicited, risk factors. (Gill, 2012) The risk estimation would orient a clinician to use their experience to qualitatively judge whether a patient might live longer or shorter than the prediction (Schoenborn et al., 2021).

Estimating absolute risks requires large datasets, such as research cohorts, electronic health records, surveys, or disease registries. Data sources have strengths/weaknesses: cohorts have all the needed information but are not usually representative of the target population (Pinsky et al., 2007; Fry et al., 2017), surveys are representative but lack some risk factors and may have few (if any) outcomes, and disease registries are a census of outcomes but only summary statistics are available within a few demographic variables. Because usually no single dataset is the best to inform about each model parameter, there has been much recent statistical research on combining data sources, including individual-level data sources and summary statistics from large databases.
(Qin et al., 2015; Chatterjee et al., 2016; Zheng et al., 2021). Most of these existing methods are “model-based” that aim to build the risk model, under which, the model parameters are assumed to be transportable between data sources and the underlying target population, or between data sources within the same population. However, the transportability assumption can be violated if the risk model is misspecified or the data sources are not target-population representative.

For example, the Population Attributable Risk (PAR) method (Gail et al., 1989; Chen et al., 2006) is a model-based method that transports hazard ratio (HR) and PAR estimates from the cohort to the target population, and estimates the baseline cumulative hazard by borrowing composite event rates from a population disease registry. However, HRs estimated from the cohort can be biased from the population HRs of the same fitted risk model if cohort participation is “informative”, (i.e., cohort participation depends on the outcome given covariates), and therefore are not transportable (Binder 1992). Furthermore, PAR in the cohort is unlikely to be transportable because the PAR depends on the covariate distribution, which is generally not equal in the cohort and the target population.

A different approach is the burgeoning survey sampling literature on “design-based” propensity-score (PS)-based methods to improve representativeness of nonprobability samples. Design-based methods assume an implicit “sample inclusion” mechanism for nonprobability cohorts and estimate “pseudoweights” (i.e., inverse of the estimated sample inclusion probabilities) for cohort units, using probability survey samples as external references (Valliant & Dever, 2011; Elliott & Valliant, 2017; Wang et al., 2020, 2021a, b). In this paper, we propose a two-step pseudoweighting method to estimate absolute risks in the target finite population (FP), using survival data, that also includes summary statistics from a national registry. The first step creates initial pseudoweights for cohort participants by fractionally distributing sample weights
from external probability reference survey units to cohort units, according to their kernel smoothed distance in propensity score (“KW.S”). To further improve representativeness of the cohort and reduce variance, in the second step, we poststratify the KW.S weighted set of individuals with events in the cohort to the population registry by demographic variables (“post-KW.S”). We use Taylor series linearization variance estimation to incorporate all the sources of variability: pseudoweight estimation (including estimating the propensity model), complex design of the reference survey sample, and poststratification. Through simulations, we investigate how the cohort selection mechanism can lead to biased risk estimates from the PAR method and demonstrate that the proposed post-KW.S help reduce bias of the PAR risk estimates.

Post-KW.S has two advantages over model-based methods. First, under the design-based framework, post-KW.S does not require transportability assumptions because pseudoweights and poststratification ensure target-population representativeness when the propensity model is correctly specified. Second, the post-KW.S estimator of absolute risk is design-consistent for absolute risks estimated from the chosen absolute risk model for the target population, regardless of whether the chosen risk model is the true data-generating mechanism. However, post-KW.S requires a correct propensity model for generating pseudoweights for the cohort. We examine lack of fit of the propensity model in our example. Note that poststratification mitigates lack of fit for the demographic variables available in the registry.

We apply the proposed method to develop an individualized absolute risk model of all-cause mortality for the general US population. All-cause mortality usually has substantial “healthy volunteer” bias: for example, UK Biobank participants have half the all-cause mortality rate of the UK population (Fry et al., 2017). We will build the model by developing pseudoweights for the
NIH-AARP cohort study using the National Health Interview Survey (NHIS) as the reference survey, and poststratify to CDC population mortality rates by age/race/sex cells.

2 BASIC SURVIVAL MODEL, POPULATIONS, AND SAMPLING

Absolute risk is the probability of the event of interest occurring by time \( t \): \( r(t) = P(T \leq t) = 1 - S(t) \), where \( T \) is the time to the event. The survival function \( S(t) = \exp\{-\Lambda(t)\} \), with \( \Lambda(t) \) being the cumulative hazard function for \( T \) that is absolutely continuous and differentiable, and

\[
\Lambda(t) = \int_0^t \lambda(\tau) d\tau \quad \text{where} \quad \lambda(t) = \lim_{\epsilon \to 0^+} P(t \leq T < t + \epsilon \mid T \geq t) / \epsilon \quad \text{is the hazard at time} \ t. \]

Under a Cox regression model (Cox 1972), the hazard function is \( \lambda(t \mid z) = \lambda_0(t) \exp(\beta^T z) \), where \( z \) is a vector of non-time dependent covariates, \( \lambda_0(t) \) is the baseline hazard, and \( \beta \) is a vector of the log hazard-ratios.

2.1 Finite Population

The target finite population (FP) consists of \( M \) individuals indexed by \( i \in \{1, \ldots, M\} \). Each individual \( i \) has a vector of non-time dependent covariates \( z_i \), a potential event time \( T_i \) or independent censoring time \( C_i \), and the observed time \( X_i = \min(T_i, C_i) \). Denote the event counting process \( N_i(t) \), \( (N_i(t) = 1 \text{ if } T_i < t, \text{ and } T_i \leq C_i; \text{ and } N_i(t) = 0 \text{ otherwise}) \), and the at-risk process, \( Y_i(t) \), \( (Y_i(t) = 1 \text{ if } X_i \leq t; \text{ and } Y_i(t) = 0 \text{ otherwise}) \). The time metric is follow-up time with a maximum of \( t_0 \). The event status for each individual \( i \) during a given follow-up period is \( D_i \), \( (D_i = 1 \text{ if } T_i \leq t_0, \text{ and } D_i = 0 \text{ otherwise}) \). The diseased and non-diseased populations are \( FP_1 = \{i \mid D_i = 1, i \in FP\} \), with size \( M_1 \), \( FP_0 = \{i \mid D_i = 0, i \in FP\} \), with size \( M_0 \), respectively. The event proportion during the follow-up is \( M_1 / M \).

We are interested in estimating the absolute risk at time \( t \) under the Cox regression model (Cox 1972) for an individual with covariate \( z \) in \( FP \),
\[ r^{FP}(t, z, \beta_{FP}, \Lambda_{0}^{FP}) = 1 - \exp\{-\Lambda_{0}^{FP}(t, \beta_{FP}) \cdot \exp(\beta_{FP}^T z)\}, \]  

(2.1)

where \( \beta_{FP} \) is a vector of FP log hazard-ratios obtained from a Cox regression model, and \( \Lambda_{0}^{FP}(t, \beta_{FP}) \) is the baseline cumulative hazard at time \( t \). Throughout this paper, by “absolute risk” we mean the probability of the event in the absence of competing events.

### 2.2 Cohort and Survey Sample Selection

Let \( s_c \subset FP \) denote a cohort with \( n_c \) individuals. Similarly to (Chen et al., 2020), we define a random indicator variable \( \delta_i^{(c)} (= 1 \text{ if } i \in s_c; 0 \text{ otherwise}) \) that specifies which individuals in FP participate in \( s_c \). Note that FP and \( s_c \) are also used to denote sets of indices for the target FP and the cohort, respectively. The underlying cohort participation rate for each \( i \in s_c \) is

\[ \pi_i^{(c)} \equiv P(i \in s_c \mid FP) = E_c\left( \delta_i^{(c)} \mid FP \right), \]

where the expectation \( E_c \) is with respect to the unknown random cohort sample participation process from FP. The corresponding cohort implicit (unknown) sample weight is \( w_i^{(c)} = 1/\pi_i^{(c)} \) for \( i \in s_c \). We require the following standard assumptions for cohort participation

**A1.** The cohort participation indicator \( \delta_i^{(c)} \) is independent of the observed time \( x \) given the covariates \( z \), i.e., \( \Pr(\delta_i^{(c)} = 1 \mid x, z) = \Pr(\delta_i^{(c)} = 1 \mid z) \).

**A2.** All FP individuals have a positive participation rate, i.e., \( \pi_i^{(c)} > 0 \) for \( i \in FP \).

In addition, we assume that there is a reference survey sample \( s_s \) that denotes the subset of indices for \( n_s \) individuals in the survey sample that are randomly sampled from the FP. The sample inclusion indicator, inclusion probability, and corresponding sample weights are defined by \( \delta_i^{(s)} (= 1 \text{ if } i \in s_s; 0 \text{ otherwise}), \pi_i^{(s)} = E_s\left( \delta_i^{(s)} \mid FP \right), \text{ and } w_i^{(s)} = 1/\pi_i^{(s)} \), respectively, where \( E_s \) is the expectation over all possible random samples according to the survey sample design. In practice, we assume the inclusion probabilities and sample weights include adjustments...
for nonresponse and calibration for $FP$ quantities, e.g., population totals by age, race/ethnicity and sex categories. We assume that all $FP$ members have positive survey sample selection probability, i.e., $\pi_i^{(s)} > 0$ for $i \in FP$.

3 ESTIMATING THE INDIVIDUALIZED ABSOLUTE RISK MODEL

3.1 Two-Step Pseudoweighting Method

Pseudoweights are not formal sampling weights but can improve representativeness of the cohort, $s_c$ (Valliant & Dever, 2011; Elliott & Valliant, 2017; Wang et al., 2020; 2021a, b). We propose a two-step pseudoweighting method. The first step computes pseudoweights for the cohort, $\{\hat{\omega}_i, i \in s_c\}$, using a scaled propensity-score-based kernel-weighting (KW.S) method in which an external survey sample, $s_s$ is used as a reference sample for the target $FP$. The KW.S weights are constructed based on covariates $z^*$ that are available in both $s_c$ and $s_s$. The second step poststratifies the pseudoweighted distribution of covariates $z_0^*$, which is usually a subset of covariates $z^*$ (e.g. demographic variables such as age, sex, race/ethnicity), among the cohort individuals with the event, i.e., $\{i, D_i = 1, i \in s_c\}$, to the distribution of $z_0^*$ among the events in the disease registry of the target population (i.e., $FP_1$). Note that if the distribution of $z_0^*$ is also available in $FP$ then the non-events in the cohort, i.e., $\{i, D_i = 0, i \in s_c\}$, can be poststratified to $FP_0$ (i.e., $FP - FP_1$) by $z_0^*$ at the second step as well (Section C of the supplementary materials).

3.1.1 First Step: Compute Pseudoweights for Cohort Using Propensity-Score-Based Kernel-Weighting Method

We fit a logistic propensity model in the combined cohort and weighted survey sample

$$\log \left( \frac{P(R_i = 1)}{1 - P(R_i = 1)} \right) = \gamma^T z_i^*, \text{for } i \in s_c \cup s_s, \quad (3.1)$$

(Wang et al., 2021a) where $R_i$ indicates being in the cohort or survey ($R_i = 1$ if $i \in s_c$, 0 if $i \in s_s$), $z_i^*$ is a vector of covariates available in both cohort and survey sample, and $\gamma$ is a vector of
unknown parameters. Notice that \( z^* \) and \( z \) in risk model (2.1) have common covariates but can be different from each other. For example, \( z^* \) can include important predictors in cohorts that are not collected in the survey (e.g., biomarkers). Denote \( y_{FP} \) as the value of \( y \) for the FP, which can be estimated from the scaled weighted estimating equation (Wang et al., 2021a)

\[
\psi^*(y) = \sum_{i \in s_c \cup s_s} w_i^*(R_i - p_i)z_i^* = 0, \tag{3.2}
\]

Where \( w_i^* = 1 \) for \( i \in s_c \) (i.e., \( R_i = 1 \) ), \( w_i^* = a \cdot w_i^{(s)} \) for \( i \in s_s \) (i.e., \( R_i = 0 \) ), \( a \in (0,1) \) is a scaling factor, and \( p_i = \expit(y^Tz_i^*) \) is the propensity score. Denote \( \hat{y} \) as the solution of (3.2). Note that \( E(\hat{y}) = y_{FP} + (\log a, 0, \cdots, 0)^T \) ensures that we can properly estimate the intercept accounting for the scaling. The scaling \( a \) is set to be sample fraction \( n_s/M \) to reduce the variation of the weights in the combined sample and thereby improves the efficiency of \( \hat{y} \) (Scott & Wild, 1986; Li et al., 2011; Landsman & Graubard, 2013; Wang et al., 2021a, b).

To construct pseudoweights \( \{ \hat{w}_i, i \in s_c \} \), each survey member first assigns a fraction of its sample weight to all cohort members proportionally to the kernel distance, measured by propensity scores, so that most of its sample weight is assigned to those cohort members with similar propensity scores. The assigned portions of the weight from each survey member are then summed up to form pseudoweights for cohort members. The details are as follows:

\[
\hat{w}_i = \sum_j \frac{K\left\{ (q_i^c - q_j^{(s)})/h \right\}}{\sum_{i \in s_c} K\left\{ (q_i^c - q_j^{(s)})/h \right\}} \cdot w_j^{(s)},
\]

where \( q_i^c = y^Tz_i^* \) and \( q_j^{(s)} = y^Tz_j^* \) for \( i \in s_c \) and \( j \in s_s \) respectively, with \( y \) estimated from equation (3.2), \( K(\cdot) \) is the kernel function where we use standard normal density function, and \( h = 0.9 \min(\hat{\sigma}, IQR/1.34) \cdot n_c^{-1/5} \) is the bandwidth selected by Silverman’s rule of thumb method.
(Silverman 1986), with $\hat{\sigma}$ and IQR being the standard deviation and interquartile range of \(\{q_i^{(c)}; i \in s_c\}\) respectively.

### 3.1.2 Second step: Poststratification of the Event Weights in the Cohort to the Population Disease Registry

After obtaining the KW.S pseudoweights, we post-stratify the KW.S pseudoweighted distribution of a subset of the covariates, \(z_0^c\), among the events in the cohort, denoted as \(s_{c,1}\), to that in the population registry, \(FP_1\). We form \(G\) post-strata by \(z_0^c\) in \(s_{c,1}\) and \(FP_1\). The post-stratification factor for \(i \in s_c\) is

\[
 f_i = \begin{cases} 
 1, & \text{for } i \in s_{c,0} \\
 \frac{M_{1,g}}{\sum_{j \in s_{c,1}^{(g)}} \hat{w}_j}, & \text{for } i \in s_{c,1}^{(g)} 
\end{cases} 
\]

where \(s_{c,0}\) is the set of non-events in the cohort, \(g = 1, \ldots, G\) is the \(g^{th}\) post-strata, \(M_{1,g}\) is the size for the \(g^{th}\) post-strata in \(FP_1\), and \(s_{c,1}^{(g)}\) is the \(g^{th}\) post-strata in \(s_{c,1}\). The final post-KW.S pseudoweights for the cohort from the two step approach are \(\{\hat{w}_i = f_i \cdot \hat{w}_i, i \in s_c\}\).

If distribution of \(z_0^c\) is also available in \(FP\), the poststratification can be similarly done for the non-events in the cohort using \(f_i = \left(\sum_{j \in s_{c,0}^{(g)}} \hat{w}_j\right)^{-1} M_{0,g}\) for \(i \in s_{c,0}\), where \(M_{0,g}\) is the size for the \(g^{th}\) post-strata in \(FP_0\), and \(s_{c,0}^{(g)}\) is the \(g^{th}\) post-strata in \(s_{c,0}\).

### 3.2 Cohort Estimates of the Absolute Risk

We estimate the log hazard-ratio \(\beta\) from the post-KW.S weighted estimating equation in the cohort

\[
 \bar{U}(\beta) = \sum_{i \in s_c} \int_0^\infty \hat{w}_i \left\{z_i - \hat{S}^{(0)}(\tau, \beta)^{-1} \hat{S}^{(1)}(\tau, \beta)\right\} dN_i(\tau) = 0, 
\]

where \(\hat{w}_i\) is the post-KW.S weight for cohort unit \(i\) proposed in Section 3.2, \(\hat{S}^{(u)}(\tau, \beta) = M^{-1} \sum_{j \in s_c} \hat{w}_j Y_j(\tau) \exp(\beta^T z_j) \cdot z_j^{\otimes u}\), with \(z_j^{\otimes 0} = 1, z_j^{\otimes 1} = z_j\), and \(dN_i(\tau) = N_i(\tau) - N_i(\tau -)\) is
the increment of \( N_t \) at time \( \tau \), with \( N_t(\tau - \varepsilon) = \lim_{\varepsilon \to 0^+} N_t(\tau - \varepsilon) \). Denote the solution of (3.4) as \( \hat{\beta}_{\omega} \).

Then we have the following result, proved in section A.2 of the supplementary materials:

**Theorem** Under conditions A1, A2 in Section 2.2 and C1-C6 in the supplementary materials A.1 and assuming the logistic regression model (3.1) is correctly specified for the propensity scores, \( \hat{\beta}_{\omega} \) is a consistent estimator of the finite population parameter \( \beta_{FP} \), i.e., \( \hat{\beta}_{\omega} = \beta_{FP} + O_p(n^{-1/2}) \).

The post-KW.S weighted Breslow baseline cumulative hazard estimator (Breslow, 1972) is

\[
\hat{\Lambda}_0^B(t, \hat{\beta}_{\omega}) = \int_0^t \frac{d\tilde{N}(\tau)}{S^{(0)}(\tau, \hat{\beta}_{\omega})},
\]

where \( d\tilde{N}(\tau) = M^{-1} \sum_{i \in \omega} \tilde{w}_i dN_i(\tau) \). In contrast, the PAR method (Gail et al., 1989; Chen et al., 2006) provides an alternative to the Breslow estimator that includes composite disease rates from a registry. The post-KW.S weighted PAR estimator is

\[
\hat{\Lambda}_0^p(t, \hat{\beta}_{\omega}) = \int_0^t \{1 - \hat{A}R(t, \hat{\beta}_{\omega})\} \cdot \lambda^*(\tau) d\tau,
\]

where \( \hat{A}R(t, \hat{\beta}_{\omega}) = 1 - \hat{S}^{(0)}(t, \hat{\beta}_{\omega})^{-1} \hat{S}^{(0)}(t) \) is the post-KW.S weighted cohort estimator of the “population attributable risk” (Pfeiffer and Gail, 2017), with \( \hat{S}^{(0)}(t) = M^{-1} \sum_{i \in \omega} \tilde{w}_i Y_i(t) \), and \( \lambda^*(t) = dN(t)/S^{(0)}(t) \), with \( dN(t) = M^{-1} \sum_{i \in FP} dN_i(t) \) is the composite incidence rate obtained from an external registry. We have the following result, proved in section A.3 of the supplementary materials:

**Corollary** Under C7 and C8 in the supplementary materials A.1 and conditions required by Theorem, \( \hat{\Lambda}_0^p(t, \hat{\beta}_{\omega}) \) and \( \hat{\Lambda}_0^B(t, \hat{\beta}_{\omega}) \) are consistent estimators of the finite population parameters \( \Lambda_0^{FP}(t, \beta) \), i.e., \( \hat{\Lambda}_0^p(t, \hat{\beta}_{\omega}) = \Lambda_0^{FP}(t, \beta_{FP}) + O_p(n^{-1/2}) \); \( \hat{\Lambda}_0^B(t, \hat{\beta}_{\omega}) = \Lambda_0^{FP}(t, \beta_{FP}) + O_p(n^{-1/2}) \) uniformly at time \( t \).

Finally, the absolute risk estimators for a specific risk factor value \( z \) at time \( t \) are
\[
\hat{r}^B(t, z, \hat{\beta}_\omega, \hat{\Lambda}_0^B) = 1 - \exp\{-\hat{\Lambda}_0^B(t) \cdot \hat{r}\}, \\
\hat{r}^P(t, z, \hat{\beta}_\omega, \hat{\Lambda}_0^P) = 1 - \exp\{-\hat{\Lambda}_0^P(t) \cdot \hat{r}\},
\]
(3.5)

by using the post-KW.S weighted Breslow’s and PAR’s estimator of cumulative baseline hazard respectively, where \(\hat{r}\) = \(\exp(\hat{\beta}_\omega^T \cdot z)\) is the post-KW.S estimator of the relative risk (i.e. hazard ratio). Since \(\hat{r}^B\) and \(\hat{r}^P\) are continuous functions of \(\hat{\Lambda}_0^B(t), \hat{\Lambda}_0^P(t)\), and \(\hat{\beta}_\omega\), which are design-consistent, \(\hat{r}^B\) and \(\hat{r}^P\) are also consistent estimators of \(r^{FP}(t, z, \beta_{FP}, \Lambda_0^{FP})\) in formula (2.1). We note that the design consistency of \(\hat{r}\) holds for any FP risk model specified in formula (2.1).

### 3.3 Variance Estimation and Taylor Deviates

To account for all sources of variability due to implicit cohort selection, propensity estimation, and poststratification, we use a Taylor linearization method to estimate the variance of the post-KW.S cohort estimator of the absolute risk.

#### 3.3.1 Taylor deviates for the absolute risk estimator

Taylor deviates are widely used for simplifying the variance estimator of risks under complex sample designs. (Mark & Katki, 2006; Graubard & Fears, 2005; Kovalchik & Pfeiffer, 2014; (Shin et al., 2020) First, define \(w_i\) as the sample weight in the combined sample of \(s_c \cup s_s\) \((w_i = 1\) for \(i \in s_c\), and \(w_i = w_i^{(s)}\) for \(i \in s_s\), i.e. cohort members get weight of 1, while survey members get their survey sampling weight. Then the influence function operator \(\Delta_i(\cdot)\) for post-KW.S estimators of absolute risks is

\[
\Delta_i(\hat{r}) = w_i \frac{\partial \hat{r}}{\partial w_i} = -\exp\{-\hat{\Lambda}_0(t, \hat{\beta}_\omega) \cdot \hat{r}\} \cdot \hat{r} \left[ z^T \Delta_i(\hat{\beta}_\omega) \hat{\Lambda}_0(t, \hat{\beta}_\omega) + \Delta_i(\hat{\Lambda}_0(t, \hat{\beta}_\omega)) \right],
\]
(3.6)

for \(i \in s_c \cup s_s\), where \(\hat{r}\) can be \(\hat{r}^B\) or \(\hat{r}^P\), depending on the choice of baseline cumulative hazard estimator \(\hat{\Lambda}_0(t, \hat{\beta}_\omega) = \hat{\Lambda}_0^B(t, \hat{\beta}_\omega)\) or \(\hat{\Lambda}_0^P(t, \hat{\beta}_\omega)\) respectively, \(\Delta_i(\hat{\beta}_\omega) = w_i \cdot \frac{\partial \hat{\beta}_\omega}{\partial w_i}\) and
\( \Delta_i \{ \hat{\lambda}_0(t, \hat{\beta}_w) \} = w_i \cdot \partial \hat{\lambda}_0(t, \hat{\beta}_w) / \partial w_i \) are the influence functions for the log-odds ratio and cumulative baseline hazard respectively. The post-KW.S weights are functions of the original weights so that the randomness due to KW.S weight assignment and poststratification can be considered in the variance estimation. See section B of the supplementary materials for derivation of \( \Delta_i \{ \hat{\beta}_w \} \) and \( \Delta_i \{ \hat{\lambda}_0(t, \hat{\beta}_w) \} \).

3.3.2 Variance estimation for the estimated absolute risk

The finite population variance of an estimator, \( \hat{\theta} \), can be approximated by the variance of the sum of the influence operators, \( \Delta_i(\hat{\theta}) \), i.e., \( \text{var}(\hat{\theta}) \approx \text{var}\{\sum_{i=1}^{n} \Delta_i(\hat{\theta})\} \) for simple random samples (Vaart, 1998, Chapter 20). We consider a general case where the survey sample is selected under a stratified multistage cluster samples with \( H \) sampling strata and \( u_h \) primary sample units (PSUs) in stratum \( h \). The Taylor linearization estimator, \( \text{var}(\hat{r}) \), can be obtained by

\[
\text{var}(\hat{r}) = \text{var}\left\{ \sum_{i \in s_c \cup s_s} \Delta_i(\hat{r}) \right\} = \sum_{h=1}^{H+1} \frac{u_h}{u_h - 1} \sum_{i=1}^{u_h} (v_{hi} - \bar{v}_h)^2, \tag{3.7}
\]

where cohort \( s_c \) is treated as stratum, \( H + 1 \) independent from \( s_s \), in the combined sample \( s_c \cup s_s \) (under condition C9 in section A of the supplementary materials, assuming the cohort and the survey sample selection are independent), \( v_{hi} = \sum_{j=1}^{u_{hi}} \Delta_{hij}(\hat{r}) \) is the sample total of the influence operator for cluster \( hi \), and \( \bar{v}_h = (u_h)^{-1} \sum_{i=1}^{u_h} v_{hi} \). Independent cohort individuals are treated as clusters, i.e., \( u_{H+1} = n_c \), although (3.5) also allows clustering or stratification.

4 SIMULATION STUDIES

4.1 Finite population generation

We generated a finite population \( FP \) of size \( M = 200,000 \) with three covariates \( z_1 \sim N(0, 4) \), \( z_2 \sim N(0, 1.5) \), and \( z_3 \sim N(0, 1) \). We generated time to event data using a \( \text{Weibull}(\theta, \alpha) \) so that the survival function is \( S(t; z) = \exp\{- (\theta t)^{\alpha}\} \), with \( \theta^{\alpha} = \exp(\beta_0 + \beta^T z) \), where \( \beta = \)
(\beta_1, \beta_2, \beta_3)^T$, and \(z = (z_1, z_2, z_3)^T\). The hazard function is \(\lambda(t; z) = at^{a-1} \exp(\beta_0) \exp(\beta^T z)\), with the baseline hazard \(\lambda_0(t) = at^{a-1} \exp(\beta_0)\). The absolute risk is

\[
r(t; z) = 1 - \exp \left\{ - \int_0^t \alpha t^{\alpha-1} \exp(\beta_0) \exp(\beta^T z) \right\}.
\]

We set \(\alpha = 1\) for a time-invariant hazard, \(\beta_0 = \log(-\log 0.95)/15\) for a 95% 15-year survival rate at the referent level \(z = 0\), and \(\beta = (0.25, 0.4, 0.15)\). We allowed subjects to randomly enter the study in the first year, \(T_0 \sim U(0, 1)\). We set administrative censoring at 15 years after start of the study and \(C_1 = 15 - T_0\) is time from entry to administrative censoring. Also, we considered censoring from death due to other causes, \(C_2 \sim Weibull(\theta = -(\log 0.9)/15, \alpha = 1)\), for an expected 10% of subjects of deaths from other causes by \(t = 15\). We define event times \(X = \min(T, C_1, C_2)\), where \(T \sim Weibull(\theta, \alpha = 1)\), and \(D\) indicates the event of interest, \(D = I\{T \leq \min(C_1, C_2)\}\).

### 4.2 Registry, cohort and survey sample

The registry is the event set in the population, i.e., \(FP_1 = \{i \mid D_i = 1, i \in FP\}\), with size \(M_1\). The event rate in the population is \(M_1/M = 8.12\%\). We assumed that only the categorized covariate \(z_2, z_2^* (z_2^* = 1\text{ if }z_{2,i} < 0; z_{2,i}^* = 2\text{ otherwise})\), was available in the registry for post-stratification.

A cohort of \(n_c = 5,000\) was randomly selected using Probability Proportional to Size (PPS) sampling with the size defined by \(\exp(\gamma_1 z_1 + \gamma_2 z_2 + \gamma_d D + \gamma_{2,d} z_2 D)\). We varied values of \(\gamma_d\), and \(\gamma_{2,d}\) under four scenarios (Table 1) to investigate how the unrepresentativeness of the cohort affects the hazard ratio, baseline hazard, and absolute risk. Scenario 1 sampled the cohort depending on covariates \(z_1\) and \(z_2\) only. Scenario 2 oversampled the event set (i.e. \(D = 1\)) in addition to the sample design of Scenario 1, without changing the \(z\) distribution of Scenario 1. In Scenarios 3 and 4, the cohort selection depended on the event status \(D\) conditional on the covariate
Scenario 4 oversampled the event set while Scenario 3 under sampled the event set conditional on \( z_2 \). These four scenarios correspond to four combinations of (un)biased naïve cohort estimates of log hazard-ratio (\( \beta \)), and baseline cumulative hazard (\( \Lambda_0 \)). All of \( z_1, z_2, \) and \( z_3 \) were assumed available in the cohort.

A survey of size \( n_s = 3,000 \) was also randomly selected using PPS sampling with selection probability \( \exp(0.07z_1 + 0.1z_2) \) in all four scenarios. Only \( z_1 \) and \( z_2 \) were available in the survey.

We compared the post-KW.S weighted estimators with the KW.S (Wang et al., 2021a), the naïve cohort, and sample-weighted survey estimators of log hazard-ratio (\( \beta \)), Breslow (\( \Lambda_0^\beta \)) or PAR method (\( \Lambda_0^\beta \)) baseline cumulative hazard, and absolute risks for low- (\( \eta_{low} \)), medium- (\( \eta_{med} \)), and high-risk (\( \eta_{high} \)) groups. The three risk groups were set by the values of \( z \) corresponding to their 25%, 50%, and 75% percentiles, respectively. In simulations, the post-KW.S method only poststratified events in the cohort (\( s_{c,1} \)) to the disease registry (\( FP_1 \)) following formula (3.3). Since the event rate in the population was low (\( \sim 8\% \)), poststratifying the non-events in the cohort would not provide much efficiency gain.

### 4.3 Simulation results

Results for the four scenarios are shown in Table 1, Figure D.1-Figure D.3 in the supplementary materials, and Table 2. Sample-weighted survey estimates of log hazard-ratios \( \beta_1, \beta_2 \) were unbiased. However, due to missing predictor \( z_3 \), \( \widehat{\Lambda}_0 \) was slightly biased by 1% (Figure D.1) and \( \hat{r} \) were +12% and -8% biased for the low- and high-risk groups respectively (Table 2).

The bias of naïve cohort estimates varied in the four scenarios with different sample selection mechanisms. In scenario 1, the cohort selection depended on covariates only. Hence, the naïve cohort estimates of \( \beta \) and \( \Lambda_0^\beta \) were approximately unbiased leading to unbiased \( \hat{r}^B \) (Table 2). In scenario 2, besides oversampling higher values of \( z_1 \) and \( z_2 \), the cohort marginally
oversampled the event set. The event rate in the cohort was 36.5% higher than in the population. This sampling slightly biased $\mathbf{b}$, but substantially increased bias in $\hat{\Lambda}_0^B$ by $\sim$30% over follow-up. The $n_{\text{low}}$, $n_{\text{med}}$, and $n_{\text{high}}$ were overestimated by 36.9%, 29.5%, and 22.7% respectively. Scenario 3 under sampled the event set conditionally on covariate $z_2$ for the cohort, resulting in -19.3% bias in $\hat{\beta}_2$. The naïve cohort $\hat{r}$ was biased ranging from -11.1% to 1.8% for the three groups. In scenario 4, both cohort naïve $\hat{\beta}_2$ and $\hat{\Lambda}_0^B$ were biased because marginal and joint distribution of $\mathbf{z}$ and $D$ were all different in the cohort from those in the $FP$. As a result, the naïve cohort $\hat{r}$ in scenario 4 had worst bias among all the scenarios.

The naïve cohort estimate using the PAR method baseline cumulative hazard, $\hat{\Lambda}_0^P$, was biased by -35% in all scenarios (Table 2; Figure D.1 in the supplementary materials). This is because the $AR$ itself was biased due to different covariate distributions in the cohort from the population. However, $\hat{\Lambda}_0^P$, by incorporating composite rate from the $FP$, was more efficient than $\hat{\Lambda}_0^B$ in all scenarios and yielded smaller mean-squared error (MSE) in scenarios 2 and 4 (Figure D.2 and Figure D.3 in the supplementary materials). Furthermore, unlike $\hat{\Lambda}_0^B$, $\hat{\Lambda}_0^P$ was not sensitive to the biased event rate. We varied the event rate in the cohort by changing $\gamma_d$ in the cohort selection propensity model in more scenarios. The relative bias of $\hat{\Lambda}_0^B$ jumped from 0% to 60% as the event rate increased from 11.5% to 18.5% in the cohort, while the relative bias of $\hat{\Lambda}_0^P$ remained -35% (Figure D.4 in the supplementary materials).

The KW.S method yielded approximately unbiased estimates for $\mathbf{b}$, $\Lambda_0$, and $r$ for the 3 risk groups (Table 1 and Table 2). The KW.S weighted PAR estimator (details in section B of the supplementary materials) sharply reduced the variance of $\hat{\Lambda}_0$, leading to a large reductions in MSE of $\hat{r}$. By poststratifying the distribution of $z_2$ in the event set of the KW.S weighted cohort to the registry, the post-KW.S weighted estimator using the PAR method most reduced the variances of
\[ \hat{\beta}_2, \hat{\lambda}_0, \text{ and } \hat{r}, \] without increasing bias, minimizing MSE in all scenarios. The TL variance estimates were close to the empirical variances. We also varied the correlation among \( z_1, z_2, \) and \( z_3. \) The pattern of bias in the naïve estimates of log-hazard ratios, baseline cumulative hazards, and absolute risks were similar. Tables D.1-D.3 shows the results when \( \rho(z_1, z_3) = \rho(z_2, z_3) = 0.6. \)

5 DEVELOPING A NATIONALLY REPRESENTATIVE INDIVIDUALIZED ALL-CAUSE MORTALITY RISK MODEL

We develop an individualized absolute risk model for all-cause mortality using the NIH-AARP Diet and Health Study, which recruited \( n_c = 567,169 \) AARP members among 8 states from 1995-1996, ages 50 to 71 years (NIH-AARP, 2006). For the reference survey, we used the NHIS, a cross-sectional household interview survey of the civilian noninstitutionalized US population. To make the two samples as contemporaneous as possible, we chose the 1997 NHIS respondents aged 50 to 71 years (\( n_s = 9,306 \) participants). The 1997 NHIS has a multistage stratified cluster sample design with 339 strata with each consisting of two sampled PSUs. Both NIH-AARP and NHIS were linked to National Death Index (NDI) for ten-year follow-up mortality information (NCHS 2009; NCHS 2013). NHIS estimates serve as a low-bias high-variance “gold standard”, allowing us to examine how much bias in the NIH-AARP estimates can be corrected by pseudo-weighting, and how much variance in NHIS estimates can be reduced. Finally, we used CDC mortality rates 1999-2009 (CDC, 2021) as population composite mortality rates in the PAR method baseline cumulative hazard and for the population joint distribution of age, sex, race/ethnicity, and mortality, which is used for poststratification. The NIH-AARP cohort has substantially lower mortality than CDC rates in all age groups (“healthy volunteer effect”) (Figure 1). The NHIS estimates appear unbiased relative to CDC rates, but with considerable variance.
The all-cause mortality risk model included key easily-elicited covariates. We included age, sex, race/ethnicity and 3 lifestyle factors: smoking in 4 categories, physical activity (dichotomized at <3 times/week), and body mass index [BMI]. We also included self-reported health status, a key highly predictive factor for mortality yet easily elicited (Gill 2012), as a five-level linear trend variable with scores (Excellent=0, very good=1, good=2, fair=3, poor=4).

We first create the KW.S weights by fitting the propensity models to the combined NIH-AARP and weighted NHIS 1997 (with the weights being the scaled NHIS sample weights \( \{a \cdot w_i^{(s)}, i \in \text{NHIS}\} \), where \( a = n_{s}/\left(\sum_{i=1}^{n_{s}} w_i^{(s)}\right) \)), that included all mortality model covariates, as well as education and marital status (which were excluded from the mortality model as being improper for clinicians to ask patients). The propensity model parameters (Table 3) show that, in AARP, women, minorities, and people with “poor” health status are greatly underrepresented. By assigning pseudoweights, KW.S nearly equalized the covariate distribution in the AARP to the weighted NHIS (Table D.1 in the supplementary materials). However, KW.S underestimated the population mortality rate and failed to match the joint distribution of covariates and mortality status in AARP to CDC (Table D.2 in the supplementary materials), suggesting lack-of-fit of the propensity model. As CDC provided joint distribution of mortality and age, sex and race/ethnicity in the U.S. (i.e., the target population), the KW.S weights can be poststratified to counts of both deaths as well as alive individuals in the CDC population, denoted by “post-KW.S (POP)” (Section C in the supplement materials). Poststratification increased the weighted sum of deaths and corrected the covariate distributions by mortality status, especially for minorities such as non-Hispanic Black. For comparison, we also considered “post-KW.S (RG)” that only poststratified KW.S weights to counts of deaths, following formula (3.3), to reflect practical situations when the covariate distribution is only available in the event registry.
Table 4 shows the HRs from NHIS, naïve AARP, KW.S, and post-KW.S methods. Pseudoweighting and poststratification were most important for race/ethnicity. For non-Hispanic Blacks, the AARP had an implausible HR=1.03 but was HR=1.26 using post-KW.S(POP) and HR=1.29 using post-KW.S(RG). For non-Hispanic-other (mostly Asian-American), the AARP had an implausible HR=1.01, and even the NHIS had an implausible HR=0.95, but HR’s using the post-KW.S(RG) and post-KW.S(POP) dropped to HR=0.66 and 0.65, respectively.

We estimated the absolute risks of 10-year mortality for three risk groups (Table 5). The NHIS-PAR estimates were treated as “unbiased”, with 10-year risks of mortality of 0.05, 0.13, and 0.87 for low-, medium-, and high-risk groups respectively. However, they were variable due to the small sample size. The naïve AARP-Breslow estimates were substantially biased for all three groups due to the biased HRs and baseline cumulative hazards (Figure 5 in the supplementary materials). The naïve AARP-PAR and the KW.S-PAR methods reduced the bias by 36%-54% for low- and high-risk groups. However, they increased the bias for the medium-risk group because of biased HR estimates. In contrast, the post-KW.S(POP) PAR method removed almost all the bias for the three groups, and further improved efficiency of the KW.S method by poststratification, yielding the smallest MSE among all methods considered, followed by the post-KW.S(RG) Breslow method. Absolute risks of mortality for years before year ten had a consistent pattern with Table 5 (Figure D.6 in the supplementary materials). Table 6 shows the ratio of expected 10-year mortality risk (calculated by the (weighted) sample mean of estimated absolute risks) to observed 10-year mortality in CDC in the post-strata. The naïve AARP-Breslow substantially underestimated the risk of mortality in nearly all post-strata, but the naïve AARP-PAR and pseudoweighting provided successive improvements. The Post-KW.S(POP) PAR method generally yielded the closest average risk to CDC mortality (although not exactly the same) among
all methods, including the NHIS, especially for minority groups, followed by the post-KW.S(RG) method.

6 DISCUSSION

We proposed individualized absolute risk estimators by using data from nationally representative surveys to create pseudoweights for an epidemiologic cohort, then post-stratifying the pseudoweighted event set (and non-event set) in the cohort to the population registry. This approach accounts for typical strengths/weaknesses of the data sources: cohorts are large and have rich covariate and outcome information but are nonrepresentative, surveys are representative but lack some risk factors and may have few (if any) outcomes, and disease registries are a census of outcomes but provide only summary statistics for a few demographic variables. In contrast to “model-based” methods, our proposed post-KW.S PAR method is a design-based method that does not require transportability assumptions of naïve parameter estimates between data sources within target population, although does require that the propensity model used to calculate pseudoweights is correctly specified. Poststratification is important to further reduce bias when the propensity model is misspecified and to improve efficiency of absolute risk estimation when using KW.S.

In simulations, as expected, the naïve Breslow estimate of risk, using only the cohort data, is biased, except when the cohort participation is non-informative (Scenario 1). The naïve PAR method for absolute risks is generally biased, even if the cohort participation only depends on covariates of the Cox model, because the attributable risks, which the method transports from the cohort, are not population-representative. The best method in all scenarios was the post-KW.S weighted PAR method, which reduces bias of the naïve PAR estimates of $\beta$ and PAR by incorporating the post-KW.S weights, and borrowing composite event rates from the registry.
For developing an individualized model of all-cause mortality, the HRs estimated from the naïve AARP cohort are close to those estimated from NHIS (except for race/ethnicity), but underestimated the baseline cumulative hazard, as expected, due to the “healthy volunteer effect”. The KW.S method greatly reduced bias in absolute risk estimates, except for race/ethnicity, which required poststratifying (post-KW.S) to get sensible HRs and unbiased absolute risks. The post-KW.S method reduced the most bias and provided approximately unbiased estimates of absolute covariate-specific risk with the smallest MSE among all methods considered.

As shown in the application, we recommend the post-KW.S(POP) PAR method that poststratifies both events and non-events in the cohort. However, in practice, the composite event rate, or the joint distribution of the covariates and event status in the target population, may not be available. For example, in the CDC registry, the joint distribution of age in years, sex and race is not available for some cause-specific mortality. Therefore, if only the distribution of the covariates in the registry is available, then we recommend the post-KW.S(RG) Breslow method, otherwise if only the composite event rate is available, then we recommend the KW.S PAR method.

Our approach could potentially be easily automated by software. Individual researchers need not fit new propensity models for each application. Only one set of KW.S pseudoweights needs to be attached to the cohort and reused for building each risk model. Registry outcome rates need to be input to poststratify the outcome of interest, but software could automatically include population rates for commonly used outcomes, such as mortality or cancer incidence.

Our key modeling assumption, correct specification of the propensity model, can be violated due to missing covariates or incorrect functional form of the model. One can examine covariate distributions between the pseudoweighted cohort and weighted survey sample, but this is limited to common covariates in the two samples. We have previously shown, for estimating
means, the consistency of the KW.S estimator requires only a weak exchangeability assumption (WEA). (Wang et al., 2021a), and extending this result to absolute risks is an area of future research. In our example, KW.S did not obtain realistic HRs for minorities, suggesting lack of fit of the propensity model for minorities, and that the HRs for minorities were not transportable, which would be a problem for methods requiring transportability. A key value of poststratification is to ameliorate issues with the propensity model. However, poststratification is limited to the variables available in the registry. Much research is being conducted on improving propensity models, such as using machine learning. (Lee et al., 2010; Westreich et al., 2010) More research on propensity model diagnostics is crucial for evaluating the performance of the proposed post-KW.S method in practice.

Before clinical use can be considered for our individualized all-cause mortality model, it requires external validation and studies to examine the best way to communicate life-expectancy to patients for medical decision making. Although we have kept the model covariates simple to facilitate potential clinical use, future all-cause mortality models could be made more powerful by accounting for the severity of comorbidities and for geriatric ‘frailty’. (Schoenborn et al., 2021)

In addition to developing more realistic propensity models and model diagnostics, other topics need further research. The proposed two-step weighting procedure could be extended to other epidemiologic study designs, such as case-cohort, nested case-control, and case-control studies, which are examples of multi-phase sampling designs (Smoot and Haneuse 2015). For example, the NCI Breast Cancer Risk Assessment Tool estimates relative risks from a case-control study rather than a cohort. Also, our methods can be extended to also apply to account for competing risks.
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Figure 1 Log-Mortality rates over time by age groups in the CDC registry, 1997 NHIS, and NIH-AARP

Table 1. Estimates of Log-Relative Risk ($\beta$) in Four Scenarios of Simulations

| Scenarios & Methods | Relative Bias $^1$ (%) | Empirical Variance $^2$ ($\times 10^4$) | MSE $^3$ ($\times 10^4$) |
|---------------------|------------------------|----------------------------------------|------------------------|
| Survey              | $\beta_1$ | $\beta_2$ | $\beta_3$ | $\beta_1$ | $\beta_2$ | $\beta_3$ | $\beta_1$ | $\beta_2$ | $\beta_3$ |
| Scenario 1          | -0.02     | 0.05      | N/A       | 2.49      | 15.11     | 2.49      | 15.11     |
| Naïve               | -0.11     | -0.55     | -0.56     | 1.16      | 7.29      | 16.39     | 1.16      | 7.34      | 16.39     |
| KW.S                | 0.18      | 0.09      | 0.35      | 1.61      | 8.63      | 18.93     | 1.61      | 8.63      | 18.93     |
| Post-KW.S           | 0.22      | 0.17      | 0.29      | 1.51      | 4.49      | 18.96     | 1.51      | 4.50      | 18.96     |
| Scenario 2          | -4.37     | -4.31     | -4.75     | 0.86      | 5.71      | 12.53     | 2.05      | 8.78      | 12.97     |
| Naïve               | -4.45     | 0.17      | 0.04      | 1.30      | 7.31      | 15.45     | 1.31      | 7.31      | 15.45     |
| KW.S                | -0.43     | 0.29      | 0.01      | 1.25      | 4.02      | 15.45     | 1.26      | 4.03      | 15.45     |
| Post-KW.S           | -0.43     | 0.26      | -0.19     | 1.62      | 6.03      | 20.19     | 1.64      | 6.04      | 20.20     |
| Scenario 3          | 1.05      | -19.29    | 0.28      | 1.25      | 8.46      | 17.91     | 1.32      | 69.98     | 17.91     |
| Naïve               | 0.50      | 0.46      | -0.16     | 1.67      | 13.78     | 20.25     | 1.68      | 13.81     | 20.25     |
| KW.S                | 0.54      | 0.26      | -0.19     | 1.62      | 6.03      | 20.19     | 1.64      | 6.04      | 20.20     |
| Post-KW.S           | -2.84     | -21.94    | -3.74     | 0.92      | 6.23      | 13.27     | 1.42      | 85.89     | 13.54     |
| Scenario 4          | -0.35     | 0.55      | -0.38     | 1.36      | 13.87     | 16.23     | 1.37      | 13.92     | 16.23     |
| Naïve               | -0.34     | 0.30      | -0.38     | 1.30      | 5.58      | 16.16     | 1.31      | 5.60      | 16.16     |

$^1$Relative bias $RB\% = B^{-1} \sum_{b=1}^{B} (\hat{\beta}^{(b)} - \beta_{FP}) / \beta_{FP} \times 100\%$, where $B = 10,000$ is the number of simulations, $\hat{\beta}^{(b)}$ is the estimate of $\beta_{FP}$ obtained from the $b$-th simulated samples.

$^2$Empirical variance $V = (B - 1)^{-1} \sum_{b=1}^{B} (\hat{\beta}^{(b)} - B^{-1} \sum_{b=1}^{B} \hat{\beta}^{(b)})^2$.

$^3$Mean squared error $MSE = B^{-1} \sum_{b=1}^{B} (\hat{\beta}^{(b)} - \beta_{FP})^2$. 

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Table continues...
Table 2. Estimates of Absolute Risks for three risk groups in Four Scenarios of Simulations

| Method         | Relative Bias (%) | Empirical Variance ($\times 10^6$) | Variance Ratio² | MSE ($\times 10^6$) |
|----------------|-------------------|-------------------------------------|-----------------|---------------------|
|                | $\hat{\eta}_{low}$ | $\hat{\eta}_{med}$ | $\hat{\eta}_{high}$ | $\hat{\eta}_{low}$ | $\hat{\eta}_{med}$ | $\hat{\eta}_{high}$ | $\eta_{low}$ | $\eta_{med}$ | $\eta_{high}$ | $\eta_{low}$ | $\eta_{med}$ | $\eta_{high}$ |
| Survey (B)     | 11.96             | 1.14                             | -8.23            | 0.83                | 5.40                | 38.88               | 1.03          | 1.02          | 1.02          | 0.99         | 5.41        | 47.01         |
| Survey (P)     | 11.88             | 1.17                             | -8.09            | 0.25                | 0.69                | 0.91                | 1.00          | 0.99          | 0.99          | 0.40         | 0.71        | 8.77          |
| **Scenario 1** | Size for PPS sampling: exp(0.1$x_1$ + 0.05$x_2$) | | | | | | |
| Naïve (B)      | -0.16             | -0.93                           | -1.44            | 0.34                | 2.62                | 23.09               | 1.06          | 1.06          | 1.06          | 1.06         | 1.04        | 1.04          |
| Naïve (P)      | -34.43            | -34.89                          | -35.13           | 0.06                | 0.23                | 0.90                | 1.01          | 1.01          | 1.00          | 1.01         | 1.44        | 1.44          |
| KW.S (B)       | 0.04              | -0.29                           | -0.32            | 0.42                | 3.21                | 28.39               | 1.01          | 1.00          | 1.00          | 1.04         | 3.21        | 28.40         |
| KW.S (P)       | 0.47              | 0.22                            | 0.28             | 0.14                | 0.45                | 1.58                | 1.03          | 0.97          | 0.88          | 0.14         | 0.45        | 1.59          |
| Post-KW.S (B)  | -0.12             | -0.25                           | -0.14            | 0.35                | 2.82                | 26.55               | 1.10          | 1.09          | 1.07          | 0.35         | 2.82        | 26.55         |
| Post-KW.S (P)  | 0.25              | 0.13                            | 0.27             | 0.12                | 0.39                | 1.60                | 1.01          | 0.93          | 0.87          | 0.12         | 0.39        | 1.61          |
| **Scenario 2** | Size for PPS sampling: exp(0.1$x_1$ + 0.05$x_2$ + 0.3$D$) | | | | | | |
| Naïve (B)      | 36.89             | 29.53                           | 22.74            | 0.51                | 3.53                | 28.19               | 1.04          | 1.04          | 1.05          | 1.98         | 13.50       | 90.32         |
| Naïve (P)      | -30.24            | -33.92                          | -37.23           | 0.05                | 0.18                | 0.69                | 1.02          | 1.01          | 0.98          | 1.04         | 13.33       | 167.23        |
| KW.S (B)       | 0.49              | -0.16                           | -0.55            | 0.35                | 2.64                | 23.47               | 1.02          | 1.00          | 0.98          | 0.35         | 2.64        | 23.51         |
| KW.S (P)       | 1.15              | 0.55                            | 0.21             | 0.12                | 0.37                | 1.38                | 1.05          | 1.00          | 0.87          | 0.12         | 0.38        | 1.38          |
| Post-KW.S (B)  | 0.47              | 0.00                            | -0.27            | 0.28                | 2.18                | 20.49               | 1.09          | 1.08          | 1.05          | 0.28         | 2.18        | 20.50         |
| Post-KW.S (P)  | 0.92              | 0.45                            | 0.20             | 0.10                | 0.32                | 1.38                | 1.07          | 1.04          | 1.00          | 0.10         | 0.32        | 1.39          |
| **Scenario 3** | Size for PPS sampling: exp(0.1$x_1$ + 0.05$x_2$ - 0.1$x_2$ · $D$) | | | | | | |
| Naïve (B)      | 1.76              | -5.06                           | -11.12           | 0.40                | 2.73                | 21.92               | 1.04          | 1.03          | 1.03          | 0.41         | 3.02        | 36.78         |
| Naïve (P)      | -24.58            | -29.61                          | -34.05           | 0.09                | 0.29                | 0.99                | 0.98          | 0.98          | 1.00          | 0.74         | 10.31       | 140.30        |
| KW.S (B)       | -1.27             | -1.12                           | -0.61            | 0.47                | 3.66                | 33.37               | 1.03          | 1.01          | 1.00          | 0.48         | 3.68        | 33.41         |
| KW.S (P)       | -1.03             | -0.81                           | -0.22            | 0.16                | 0.51                | 1.73                | 1.06          | 1.04          | 0.94          | 0.16         | 0.51        | 1.74          |
| Post-KW.S (B)  | -1.35             | -1.04                           | -0.45            | 0.38                | 3.15                | 30.49               | 1.13          | 1.10          | 1.06          | 0.39         | 3.16        | 30.51         |
| Post-KW.S (P)  | -1.03             | -0.73                           | -0.13            | 0.13                | 0.42                | 1.72                | 1.04          | 0.99          | 0.93          | 0.13         | 0.43        | 1.72          |
| **Scenario 4** | Size for PPS sampling: exp(0.1$x_1$ + 0.05$x_2$ + 0.3$D$ - 0.1$x_2$ · $D$) | | | | | | |
| Naïve (B)      | 46.02             | 29.98                           | 15.91            | 0.61                | 3.81                | 27.54               | 1.04          | 1.03          | 1.03          | 2.90         | 14.08       | 57.98         |
| Naïve (P)      | -19.93            | -28.67                          | -36.25           | 0.07                | 0.21                | 0.71                | 1.07          | 1.05          | 1.06          | 0.50         | 9.61        | 158.68        |
| KW.S (B)       | 0.36              | -0.22                           | -0.49            | 0.40                | 2.93                | 25.22               | 1.00          | 0.99          | 0.99          | 0.40         | 2.93        | 25.25         |
| KW.S (P)       | 0.66              | 0.16                            | -0.01            | 0.14                | 0.43                | 1.45                | 1.08          | 1.07          | 0.89          | 0.14         | 0.44        | 1.45          |
| Post-KW.S (B)  | 0.59              | 0.12                            | -0.12            | 0.30                | 2.42                | 22.68               | 1.09          | 1.07          | 1.04          | 0.31         | 2.42        | 22.68         |
| Post-KW.S (P)  | 0.76              | 0.29                            | 0.06             | 0.10                | 0.34                | 1.43                | 1.06          | 1.03          | 0.97          | 0.10         | 0.34        | 1.43          |

¹(B) and (P) represents Breslow’s and the PAR methods for cumulative baseline hazard estimation respectively.

²Variance ratio is the ratio of mean of Taylor variance estimates and variance of the risk estimates.
Table 3 Fitted Propensity Model in NIH-AARP Data Example

| Covariate                  | Estimate | Std. Err¹ |
|----------------------------|----------|-----------|
| (Intercept)                | -0.19    | 0.123     |
| Age group                  |          |           |
| Ref: 50-54                 |          |           |
| 55-59                      | 0.83     | 0.034     |
| 60-64                      | 1.18     | 0.035     |
| 65-69                      | 1.33     | 0.036     |
| 70-71                      | 0.06     | 0.049     |
| Sex Ref: Male              |          |           |
| Female                     | -0.42    | 0.029     |
| Race Ethnicity             |          |           |
| Ref: Non-Hispanic White    |          |           |
| Non-Hispanic Black         | -1.05    | 0.038     |
| Hispanic                   | -1.40    | 0.044     |
| Non-Hispanic Other         | -0.39    | 0.067     |
| Marital Status             |          |           |
| Ref: (Living as) Married   |          |           |
| Widowed                    | 0.49     | 0.040     |
| Divorced or Separated      | 0.58     | 0.034     |
| Never married              | 0.31     | 0.050     |
| Education Level            |          |           |
| Normal                     | 0.47     | 0.015     |
| BMI Ref: Underweight       |          |           |
| Normal                     | 0.38     | 0.108     |
| Overweight                 | 0.41     | 0.108     |
| Obese                      | 0.60     | 0.109     |
| Physical Activities        |          |           |
| >=3 times/week             |          |           |
| Very good                  | 0.68     | 0.034     |
| Good                       | 0.81     | 0.035     |
| Fair                       | 0.61     | 0.043     |
| Poor                       | -0.09    | 0.058     |

¹Standard error estimates considers the complex multi-stage design of the NHIS sample, and treats the AARP sample as a stratum in the combined sample. All covariates have p-values smaller than 0.001.
|                          | NHIS 1997 | Naïve AARP | KW.S  | Post-KW.S (RG) | Post-KW.S (POP) |
|--------------------------|-----------|------------|-------|----------------|-----------------|
| **Age in years** (ref: 50 yrs) | 1.10 (1.08, 1.11) | 1.10 (1.10, 1.10) | 1.10 (1.09, 1.10) | 1.08 (1.08, 1.09) | 1.10 (1.09, 1.10) |
| **Sex (ref: Male)** | | | | | |
| Female | 0.63 (0.55, 0.72) | 0.67 (0.66, 0.68) | 0.66 (0.64, 0.68) | 0.66 (0.64, 0.69) | 0.64 (0.63, 0.65) |
| **Race ethnicity (ref: NH White)** | | | | | |
| NH Black | 1.34 (1.12, 1.61) | 1.03 (0.99, 1.07) | 1.01 (0.95, 1.07) | 1.29 (1.19, 1.40) | 1.26 (1.21, 1.32) |
| Hispanic | 0.99 (0.74, 1.27) | 0.82 (0.77, 0.87) | 0.77 (0.70, 0.84) | 0.80 (0.73, 0.88) | 0.83 (0.70, 0.86) |
| NH Other | 0.95 (0.68, 1.34) | 1.01 (0.97, 1.06) | 1.11 (1.04, 1.19) | 0.66 (0.58, 0.76) | 0.65 (0.63, 0.67) |
| **BMI (ref: normal weight)** | | | | | |
| Underweight | 1.37 (0.85, 2.22) | 1.62 (1.52, 1.72) | 1.67 (1.32, 2.12) | 1.67 (1.48, 1.87) | 1.67 (1.48, 1.87) |
| Overweight | 0.80 (0.70, 0.91) | 0.89 (0.87, 0.90) | 0.84 (0.66, 1.07) | 0.83 (0.80, 0.87) | 0.84 (0.80, 0.87) |
| Obese | 0.84 (0.72, 0.99) | 1.01 (0.99, 1.03) | 0.94 (0.74, 1.20) | 0.94 (0.89, 0.99) | 0.94 (0.90, 0.99) |
| **Smoking (ref: never smoking)** | | | | | |
| Former, quit ≥10 yrs | 1.06 (0.89, 1.26) | 1.31 (1.29, 1.34) | 1.32 (1.28, 1.37) | 1.28 (1.22, 1.34) | 1.29 (1.23, 1.35) |
| Former, quit <10 yrs | 1.97 (1.61, 2.40) | 2.04 (1.99, 2.09) | 2.02 (1.94, 2.09) | 1.95 (1.85, 2.06) | 1.95 (1.84, 2.06) |
| Current, <1pk/dy | 2.16 (1.83, 2.56) | 2.41 (2.35, 2.47) | 2.24 (2.15, 2.34) | 2.14 (2.01, 2.28) | 2.16 (2.02, 2.30) |
| Current, ≥1pk/dy | 2.70 (2.11, 3.44) | 3.00 (2.92, 3.09) | 2.82 (2.69, 2.95) | 2.70 (2.54, 2.86) | 2.70 (2.54, 2.87) |
| **Physical Activity (ref: < 3 times/week)** | | | | | |
| ≥3 times/week | 0.67 (0.55, 0.81) | 0.84 (0.82, 0.85) | 0.84 (0.82, 0.86) | 0.84 (0.81, 0.87) | 0.85 (0.82, 0.88) |
| **Health Status** (ref: Excellent) | | | | | |
| * | 1.58 (1.49, 1.67) | 1.66 (1.64, 1.67) | 1.74 (1.71, 1.76) | 1.71 (1.68, 1.75) | 1.71 (1.68, 1.75) |

*A five-level trend variable with scores (Excellent=0, very good=1, good=2, fair=3, poor=4)*
Table 5. Inference of absolute risk of mortality in ten years for three risk groups

| Risk Group | NHIS PAR | AARP Breslow | AARP PAR | KW.S PAR | Post-KW.S (RG) Breslow | Post-KW.S (POP) PAR |
|------------|----------|--------------|----------|----------|------------------------|---------------------|
| **Estimate (SE × 10^2)** | | | | | | |
| Low | 0.05 (1.47) | 0.04 (0.18) | 0.04 (0.20) | 0.05 (0.31) | 0.06 (0.46) | 0.05 (0.37) |
| Medium | 0.13 (3.04) | 0.20 (0.51) | 0.22 (0.55) | 0.22 (1.01) | 0.14 (1.05) | 0.13 (0.69) |
| High | 0.87 (4.07) | 0.77 (0.83) | 0.80 (0.77) | 0.81 (1.18) | 0.86 (1.28) | 0.87 (0.98) |
| **Bias Rdc. (%)** | | | | | | |
| Low | 100 | N/A | 40.71 | 53.92 | 151.7 | 102.98 |
| Medium | 100 | N/A | -33.29 | -39.99 | 93.55 | 97.26 |
| High | 100 | N/A | 35.66 | 41.21 | 89.2 | 99.45 |
| **MSE (× 10^4)** | | | | | | |
| Low | 2.16 | 1.37 | 0.51 | 0.38 | 0.57 | 0.14 |
| Medium | 9.25 | 41.70 | 73.93 | 82.23 | 1.27 | 0.51 |
| High | 16.59 | 116.95 | 48.72 | 41.58 | 2.99 | 0.96 |

1 The three risk groups are defined as (1) Low: 50-year-old, male, Hispanic, underweighted, former smoker (quit yrs<10), ≥3 times/week physical activities, excellent self-reported health status; (2) Medium-risk group: 60-year-old, female, Non-Hispanic other, obese, current smoker (<1 pack/day), ≥3 times/week physical activities, very good self-reported health status; and (3) High-risk group: 70-year-old, male, Non-Hispanic Black, overweight, current smoker (>1 pack/day), <3 times/week physical activities, fair self-reported health status.

2 Bias reduction is the percentage of the bias reduced from the naïve AARP Breslow estimate, by treating the NHIS PAR-method estimates as unbiased. 100% bias reduction means removing all the bias (i.e., unbiased NHIS estimates); bias reduction smaller than 0 or greater than 200% means increasing the bias.

3 Bias in MSE calculation assumes that the NHIS PAR-method estimates are unbiased.

Table 6. Ratio of (Weighted) Mean of 10-year Absolute Risk Estimates (Expected) and CDC Mortality Rates (Observed) by Demographic Variables available in CDC data.

| Post-Strata | NHIS PAR | AARP Breslow | AARP PAR | KW.S PAR | Post-KW.S (RG) Breslow | Post-KW.S (POP) PAR |
|-------------|----------|--------------|----------|----------|------------------------|---------------------|
| Overall | 0.98 | 0.88 | 0.97 | 0.96 | 1.03 | 0.97 |
| **Age** | | | | | | |
| 50-54 | 0.94 | 0.73 | 0.82 | 0.94 | 1.11 | 0.98 |
| 55-59 | 0.95 | 0.72 | 0.80 | 0.92 | 1.05 | 0.97 |
| 60-64 | 0.98 | 0.75 | 0.83 | 0.95 | 1.02 | 0.99 |
| 65-71 | 0.95 | 0.72 | 0.80 | 0.94 | 0.94 | 0.96 |
| **Sex** | | | | | | |
| Male | 0.98 | 0.84 | 0.93 | 0.98 | 1.03 | 0.97 |
| Female | 0.97 | 0.85 | 0.94 | 0.95 | 1.03 | 0.97 |
| **Race Ethnicity** | | | | | | |
| NH White | 0.94 | 0.89 | 0.98 | 0.98 | 1.03 | 0.98 |
| NH Black | 1.03 | 0.65 | 0.72 | 0.72 | 0.98 | 0.95 |
| Hispanic | 1.22 | 0.90 | 1.00 | 0.93 | 1.01 | 0.96 |
| NH Other | 1.35 | 1.43 | 1.58 | 1.75 | 1.12 | 0.97 |