Active information, missing data and prevalence estimation

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Abstract

The topic of this paper is prevalence estimation from the perspective of active information. Prevalence among tested individuals has an upward bias under the assumption that individuals’ willingness to be tested for the disease increases with the strength of their symptoms. Active information due to testing bias quantifies the degree at which the willingness to be tested correlates with infection status. Interpreting incomplete testing as a missing data problem, the missingness mechanism impacts the degree at which the bias of the original prevalence estimate can be removed. The reduction in prevalence, when testing bias is adjusted for, translates into an active information due to bias correction, with opposite sign to active information due to testing bias. Prevalence and active information estimates are asymptotically normal, a behavior also illustrated through simulations.

Keywords: Active information; Asymptotic normality; Biased estimate; COVID-19. Missing data; Prevalence estimation.

1. Introduction

According to the No Free Lunch Theorems, in a search problem, on average, no search does better than blind (Wolpert and MacReady, 1997). Therefore, when for a particular case one search does different than a uniform search (better or worse), it is because the programmer used her knowledge (good or bad) either of the target or the structure of the space, or both. Active information was introduced to measure the amount of information a programmer infuses in a search to reach the target with different probability than through a blind search (Dembski and Marks II, 2009a,b). For a search space $\mathcal{X}$ and a target $A \subset \mathcal{X}$, active information is then naturally defined as $I^+ = \log(p/p_0)$, where $p$ is the probability of reaching $A$ under the algorithm devised by the programmer, and $p_0$ is the uniform probability of reaching $A$.
Another interpretation of active information will allow to see that a data set in \( \mathcal{X} \), whose distribution is consistent with a probability \( p \) of reaching \( A \), will have a local mode in the region \( A \) if \( I^+ > 0 \) (Díaz-Pachón et al., 2019; Liu et al., 2022). Montañéz and collaborators have also used active information to analyze intention perception (Hom et al., 2021). Hössjer and Díaz-Pachón (2022) have used active information to measure fine-tuning. And Díaz-Pachón and Marks II (2020) used it to compare non-neutral to neutral population genetics models.

In this paper active information is used to unify estimation and bias correction of the prevalence \( p_0 \) of a disease when data is missing. This corresponds to a setting where \( \mathcal{X} \) is a population of individuals whereas \( A \) is the subpopulation of affected individuals. It is assumed that such a prevalence estimate is computed from a subsample of tested individuals and that the data analyst does not control the sampling scheme, but rather that individuals voluntarily choose to be tested. Since individuals with stronger symptoms are more likely to have the disease and get tested, knowledge of these symptoms represents information that leads to an estimated prevalence with an upward bias \( p - p_0 \). This bias is quantified in terms of a positive active information \( I^+_T = \log(p/p_0) \) due to testing bias, since it quantifies the degree at which individuals’ willingness to be tested correlates with their symptoms.

Incomplete testing is regarded as a missing data problem (Little and Rubin, 2002), and various missingness mechanisms will be considered here. In particular, when data is missing at random (MAR), the bias of the prevalence estimate can be removed. This corresponds to a negative active information \( I^+_C \) due to bias correction. Under ideal MAR conditions, when the bias correction is successful, the total active information \( I^+ = I^+_T + I^+_C \), after bias correction, is zero.

2. Active information due to testing bias

Let \( \mathcal{X} \) be a population of \( N = |\mathcal{X}| \) individuals of which those in \( A \subset \mathcal{X} \) have a certain disease, whereas the other subjects in \( \mathcal{X}^c = \mathcal{X} \setminus A \) have not. Let \( P_0 \) refer to the uniform probability measure on \( \mathcal{X} \), which assigns a probability of \( 1/N \) to each individual. The objective is to estimate the population prevalence

\[
p_0 = P_0(A) = \frac{|A|}{N}
\]

of the disease from a subgroup of individuals that are tested. To this effect, first divide

\[
\mathcal{X} = \bigcup_{s=0}^{S-1} \bigcup_{i=0}^{1} \mathcal{X}_{si},
\]

into a number of subpopulations of unknown sizes \( |\mathcal{X}_{si}| = N \rho_{si} \), where \( \mathcal{X}_{si} \) consists of those individuals with symptoms \( s \in \{0, \ldots, S-1\} \) and infection status \( i \in \{0,1\} \). The first variable \( s \) is measured on an ordinal scale with increasingly stronger symptoms, so that \( s = 0 \) represents no symptoms whereas \( s = S - 1 \) codes for the strongest possible symptoms. Infection status, on the
other hand, is a binary variable such that $i = 0$ and $i = 1$ correspond to a non-infected and infected individual, respectively. For each $x \in \mathcal{X}$ we let

$$I(x) \in \{(0, 0), \ldots, (S - 1, 0), (0, 1), \ldots, (S - 1, 1)\}$$

(3)

signify the subpopulation $\mathcal{X}_{si}$ to which $x$ belongs.

Let also $T_x$ be a variable that equals 1 or 0 depending on whether $x$ is tested for the disease or not. The collection $\{T_x; x \in \mathcal{X}\}$ is assumed to be formed by independent Bernoulli variables, with $P(T_x = 1) = \pi_{I(x)}$. This corresponds to an assumption whereby individuals in different groups are tested with different sampling probabilities $\pi_{si}$. Consequently, the weighted probability measure

$$P(x) = \frac{\pi_{I(x)}}{\sum_{y \in \mathcal{X}} \pi_{I(y)}}, \quad x \in \mathcal{X}$$

(4)

represents a prediction of the tested population, before testing has occurred. In particular, the testing prevalence

$$p = P(A) = \sum_{x \in A} P(x)$$

(5)

is the expected prevalence in the tested subpopulation. The active information due to testing bias is defined as

$$I^+_T = \log \frac{p}{p_0} = \log \frac{P(A)}{P_0(A)}$$

(6)

To estimate $p$ and $I^+_T$, the subpopulation

$$\mathcal{X}_T = \{x \in \mathcal{X}; T_x = 1\}$$

(7)

of $N_T = |\mathcal{X}_T|$ tested individuals is introduced. Since $N_T$ is known, this gives rise to an estimator

$$\hat{p} = \hat{p}(A) = \frac{|A \cap \mathcal{X}_T|}{N_T}$$

(8)

of $p$. The expected fraction of sampled individuals is also introduced as

$$\pi = \sum_{i=0}^{S-1} \sum_{s=0}^{S-1} \rho_{si} \pi_{si},$$

(9)

which is estimated by

$$\hat{\pi} = \frac{N_T}{N}$$

(10)

3. Active information after bias correction

The relation between $p$ and $p_0$ depends crucially on the sampling probabilities $\pi_{si}$. This can be seen by noting that the population and testing prevalences are different functions

$$p_0 = \sum_{s=0}^{S-1} \rho_{s1}, \quad p = \sum_{s=0}^{S-1} \rho_{s1} \pi_{s1}/\sum_{s,i} \rho_{si} \pi_{si}$$

(11)
of $\rho_{01}, \ldots, \rho_{S-1,1}$. Regarding non-tested individuals as missing data, concepts from the missing data literature (Little and Rubin, 2002) are helpful to explain the way in which data is missing. Random sampling, or data missing completely at random (MCAR), occurs when

$$\pi_{si} = \pi.$$  \hfill (12)

From (11), $p = p_0$ and $I^+_T = 0$ whenever (12) holds. Condition (12) is usually very unrealistic, since people with stronger symptoms (larger $s$) are more likely to be tested (have larger $\pi_{s0}$ and $\pi_{s1}$) than those with weaker symptoms. A weaker assumption of data missing at random (MAR) occurs when the sampling probabilities only depend on variables that are known. In an example of a MAR sampling scheme $\rho_s = \rho_{s0} + \rho_{s1}$ is known and

$$\pi_{si} = \pi_s$$ \hfill (13)

for $s = 0, \ldots, S - 1$. The most challenging missingness mechanism (neither MCAR or MAR) is referred to as data missing not at random (MNAR).

Also from (11), typically $p \neq p_0$ and $I^+_T \neq 0$ when data is MAR or MNAR. To construct a bias-corrected estimator $\hat{p}_0$ of $p_0$, the biased prevalence estimator can be rewritten as

$$\hat{p} = \frac{\sum_{s=0}^{S-1} \rho_{s1} \hat{\pi}_{s1}}{\sum_{s=0}^{S-1} \rho_{s1} \hat{\pi}_{s1}} = \sum_{s=0}^{S-1} \rho_{Ts1},$$ \hfill (14)

where the sampling fractions

$$\hat{\pi}_{si} = \frac{|X_T \cap X_{si}|}{|X_{si}|} = \frac{|X_{Ts1}|}{|X_{si}|} = \frac{N_{Ts1}}{N_{si}} = \frac{N_{Ts1}}{N_{\rho_{si}}}$$ \hfill (15)

for different subpopulations approximate $\pi_{si}$, whereas

$$\rho_{Ts1} = \frac{\rho_{s1} \hat{\pi}_{s1}}{\sum_{r,k} \rho_{rk} \hat{\pi}_{rk}} = \frac{N_{Ts1}}{N_T}$$ \hfill (16)

are the known fractions at which the subpopulations appear in the sample. A comparison between (11) and (16) suggests an estimate

$$\hat{p}_0 = \frac{\sum_{s=0}^{S-1} \rho_{Ts1} \hat{\pi}_{s1}^{-1}}{\sum_{s=0}^{S-1} \rho_{Ts1} \hat{\pi}_{s1}^{-1}} = \frac{\sum_{s=0}^{S-1} N_{Ts1} \hat{\pi}_{s1}^{-1}}{\sum_{s=0}^{S-1} N_{Ts1} \hat{\pi}_{s1}^{-1}}$$ \hfill (17)

of the population prevalence $p_0$, where $\hat{\pi}_{si}$ is an estimate of $\pi_{si}$ (and thereby also an estimate of $\pi_{si}$). Plugging (8) and (17) into (6), the estimator

$$\hat{I}_T^+ = \log \frac{\hat{p}}{\hat{p}_0}$$ \hfill (18)

of the active information $I^+_T$ due to testing bias is obtained. Furthermore,

$$I^+ = \log \frac{E(\hat{p}_0)}{p_0} = \log \frac{p}{p_0} + \log \frac{E(\hat{p}_0)}{p} = I^+_T + I^+_C$$ \hfill (19)
will be referred to as the active information of the bias-adjusted prevalence estimate (17), which is a sum of two terms: the active information (6) due to testing bias and the active information $I^C$ due to bias correction. If the bias correction is completely successful ($I^+ = 0$), then $I^C = -I^T$. This suggests an estimate

$$\hat{I}_C^- = -\hat{I}_T^- = -\log \frac{\hat{p}}{p_0}$$

of $I^C$.

**Example 1 (MCAR).** Whenever (12) holds, $I^+_T = I^+_C = 0$ follows from (6) and (11). In this context, to assume that the estimated sampling fractions $\hat{\pi}_{si}^{MCAR} = \hat{\pi}_{si}^{MCAR}$ are the same for all subpopulations $X_{si}$ is natural. Since $\hat{\pi}_{si}^{MCAR}$ cancels out in the prevalence estimator (17), it simplifies to

$$\hat{p}_0^{MCAR} = \frac{\sum_{s=0}^{S-1} \rho_{Ts1}}{\sum_{s,i} \rho_{Tsi}} = \sum_{s=0}^{S-1} \rho_{Ts1} = \frac{1}{N_T} \sum_{s=0}^{S-1} N_{Ts1} = \frac{N_{T1}}{N_T} = \hat{p},$$

and consequently $\hat{I}^+_T = \hat{I}^+_C = 0$ under MCAR sampling. From Fisher’s exact test, $N_{T1}$ has a hypergeometric distribution

$$N_{T1} \mid N_T \sim \text{Hyp}(N, N_T, p_0)$$

conditionally on $N_T$. Taking expectations in both sides of (21), by (16) and (14), $E(\hat{p}_0^{MCAR}) = p_0$ and $I^+ = 0$.

**Example 2 (MAR).** The MAR sampling scheme (13) can be viewed as an instance of stratified sampling (Groves et al., 2009), where the relative sizes $\rho_s$ of the strata (symptom classes) are known. Although the sampling fractions $\hat{\pi}_{si}^{MAR}$ in (15) are unknown when (13) holds, they may be estimated consistently by means of

$$\hat{\pi}_{si}^{MAR} = \hat{\pi}_{si}^{MAR} = \frac{N_{Ts0} + N_{Ts1}}{N \rho_{s0} + N \rho_{s1}} = \frac{N_{Ts}}{N \rho_s},$$

where in the last step $N_{Ts} = N_{Ts0} + N_{Ts1}$ was introduced. Plugging (23) into (17), the estimator

$$\hat{p}_0^{MAR} = \frac{\sum_{s=0}^{S-1} \rho_{Ts1} (N \rho_s / N_{Ts})}{\sum_{s,i} \rho_{Tsi} (N \rho_s / N_{Ts})} = \frac{\sum_{s=0}^{S-1} \rho_s (N_{Ts1} / N_{Ts})}{\sum_{s=0}^{S-1} \rho_s} = \sum_{s=0}^{S-1} \rho_s \hat{p}_0s$$

of $p_0$ is obtained. It is a weighted average of estimates

$$\hat{p}_0s = \frac{N_{Ts1}}{N_{Ts}}$$

of the prevalences

$$p_0s = \frac{\rho_{s1}}{\rho_s}$$
in symptom classes $\mathcal{X}_s = \mathcal{X}_{s0} \cup \mathcal{X}_{s1}$, using data from cohorts $\mathcal{X}_{Ts} = \mathcal{X}_{Ts0} \cup \mathcal{X}_{Ts1}$.

Since $\pi_{s0} = \pi_{s1} = \pi_s$, from Fisher’s exact test,

$$N_{Ts1} \mid N_{Ts} \sim \text{Hyp}(N_s, N_{Ts}, p_{0s})$$  \hspace{1cm} (27)

for $s = 0, \ldots, S - 1$. In view of (11), this implies

$$E(\hat{p}_{0s}^{\text{MAR}}) = \sum_{s=0}^{S-1} \rho_s E(\hat{p}_{0s}) = \sum_{s=0}^{S-1} \rho_s p_{0s} = p_0.$$  \hspace{1cm} (28)

Consequently, $I^+ = 0$ under MAR sampling, although in general $I^+_C = -I^+_C$ differs from zero.

**Example 3** (A model for COVID-19 testing). In the context of COVID-19 testing, Díaz-Pachón and Rao (2021) and Zhou et al. (2021) considered a model of convenience sampling with $S = 2$ symptom classes such that

$$\pi_{00} = \pi_{01} = \pi_0, \quad \pi_{10} = \pi_{11} = \pi_1, \quad \pi_1 > \pi_0.$$  \hspace{1cm} (29)

Since $p_0$ and $\rho_1$ are unknown, this is not a MAR model in the sense of the condition (13). In fact, the third assumption of (29) says that in convenience sampling symptomatic individuals are more likely to get tested than asymptomatic ones, which implies that with high probability $\rho_1 < N_{T1}/N$. On the other hand, the presence of $N_{T1}$ symptomatic individuals in the sample implies that $N_{T1}/N \leq \rho_1$.

From a Bayesian approach and the maximum entropy principle (Jaynes, 1968; Díaz-Pachón and Marks II, 2020), $\rho_1$ is then assumed to be uniformly distributed inside the interval $(N_{T1}/N, N_{T1}/N)$. Therefore, $\hat{\rho}_1 = E(\rho_1)$ is taken as the estimator of the proportion of symptomatic individuals in the population, and $\hat{\rho}_0 = 1 - \hat{\rho}_1 = E(\rho_0)$ estimates the proportion of the asymptomatic group. From this viewpoint, a modification of (23) produces

$$\hat{\pi}_{si}^{\text{MaxEnt}} = \frac{\hat{\pi}_s^{\text{MaxEnt}}}{NE(\rho_s)} = \frac{N_{Ts}}{NE(\rho_s)},$$  \hspace{1cm} (30)

and plugging (30) into (17), the estimator of prevalence is

$$\hat{p}_0 = \frac{N_{T01}(\hat{\pi}_0^{\text{MaxEnt}})^{-1} + N_{T11}(\hat{\pi}_1^{\text{MaxEnt}})^{-1}}{N_{T0}(\hat{\pi}_0^{\text{MaxEnt}})^{-1} + N_{T1}(\hat{\pi}_1^{\text{MaxEnt}})^{-1}} = \frac{N_{T01}}{N_{T0}}(1 - \hat{\rho}_1) + \frac{N_{T11}}{N_{T1}} \hat{\rho}_1,$$  \hspace{1cm} (31)

where (31) is obtained using the first two assumptions of (29), which imply that inside each group of symptoms the sampling of infected and non-infected is random.
4. Asymptotics

This section is focused on the asymptotic properties of the estimates $\hat{p}$ and $\hat{p}_0$ of the test-biased and population-based prevalences $p$ and $p_0$, as the population size gets large ($N \to \infty$). The second part of the MAR condition is assumed:

$$\pi_{s|t} = \pi_s, \quad s = 0, \ldots, S - 1,$$

(32)

In conjunction with (11) and (26), this makes possible to rewrite the expected prevalence among the tested individuals as

$$p = \sum_{s=0}^{S-1} \hat{\rho}_s p_0 s,$$

(33)

where

$$\hat{\rho}_s = \frac{\rho_s \pi_s}{\sum_{r=0}^{S-1} \rho_r \pi_r}.$$

(34)

is the expected proportion of tested individuals with symptoms $s$. The estimator of $p$ can equivalently be expressed as

$$\hat{p} = \sum_{s=0}^{S-1} \rho_{Ts} \hat{\rho}_0 s,$$

(35)

where

$$\rho_{Ts} = \frac{N_{Ts}}{N_T} = \rho_{Ts0} + \rho_{Ts1}$$

(36)

is an estimate of $\hat{\rho}_s$.

In view of (32), the requirement is made that $\hat{\pi}_{s|t} = \hat{\pi}_s$, and

$$\hat{\rho}_s = \frac{N_{Ts} \hat{\pi}_s^{-1}}{\sum_{r=0}^{S-1} N_{Tr} \hat{\pi}_r^{-1}},$$

(37)

is introduced, so that the bias-corrected prevalence estimator in (17) simplifies to

$$\hat{p}_0 = \sum_{s=0}^{S-1} \hat{\rho}_s \hat{p}_0 s.$$

(38)

The quality of $\hat{p}_0$ as an estimator of $p_0$ in (28), depends on how well $\hat{\rho}_s$ estimates $\rho_s$. Therefore,

$$\bar{p}_{0N} = E \left( \hat{p}_0 | \{ \hat{\rho}_s \}_{s=0}^{S-1} \right) = \sum_{s=0}^{S-1} \hat{\rho}_s p_0 s$$

(39)

is introduced.

The following theorem provides the asymptotic properties of $\hat{p}_0$, $\hat{p}$, and $\hat{I_T}$:
**Theorem 1.** Suppose \( N \to \infty \) in such a way that \( \rho_s = N_s/N \) are kept fixed, that (32) holds for fixed \( \pi_1, \ldots, \pi_s \) and

\[
\hat{p}_s \to_p \bar{p}_s \quad (40)
\]
as \( N \to \infty \), for \( s = 0, \ldots, S-1 \), where \( \to_p \) refers to convergence in probability. Then \( \hat{p}, \bar{p}_0, \hat{L}_T^* \) are asymptotically normally distributed as \( N \to \infty \), in the sense that

\[
N^{1/2} (\hat{p} - p) \toL N(0, V_1 + V_2), \quad (41)
\]

and

\[
N^{1/2} (\bar{p}_0 - \bar{p}_0N) \toL N(0, V_3), \quad (42)
\]

where \( \toL \) refers to weak convergence as \( N \to \infty \),

\[
\bar{p}_0 = \sum_{s=0}^{S-1} \hat{p}_s p_{0s} \quad (44)
\]
is the asymptotic limit of \( \bar{p}_{0N} \) as \( N \to \infty \) (i.e. \( \bar{p}_{0N} \to_p \bar{p}_0 \)), whereas \( V_1, V_2, V_3, \) and \( V_4 \) are defined in the proof of Theorem 1.

**Remark 1 (Standard errors in confidence intervals).** The asymptotic variances \( \sigma_p^2 = (V_1 + V_2)/N, \sigma_{\bar{p}_0}^2 = V_3/N, \) and \( \sigma_{\hat{L}_T^*}^2 \) in formulas (41)-(43) are functions of \( p_0, \bar{p}_0, p, \rho_s, \hat{p}_s, \) and \( \pi_s \). If estimates \( \hat{p}_{0s}, \hat{p}, \bar{p}_s, \hat{p}_s, \) and \( \hat{\pi}_s \) of these quantities are plugged into the asymptotic variances in (41)-(43), it is possible to obtain standard errors \( \hat{\sigma}_p, \hat{\sigma}_{p_0}, \) and \( \hat{\sigma}_{\hat{L}_T^*} \) of \( \hat{p}, \hat{p}_0, \) and \( \hat{L}_T^* \), respectively. The corresponding confidence interval of \( \hat{L}_T^* \), with asymptotic coverage probability \( 1 - \alpha \), is

\[
\text{CI}_{\hat{L}_T^*} = \left( \hat{L}_T^* - \lambda_{\alpha/2} \hat{\sigma}_{\hat{L}_T^*}, \hat{L}_T^* + \lambda_{\alpha/2} \hat{\sigma}_{\hat{L}_T^*} \right),
\]

where \( \lambda_{\alpha/2} \) is the \((1 - \alpha/2)\)-quantile of a standard normal distribution. The delta method is first used to determine confidence intervals for logit transformed versions \( \logit(p) = \log[p/(1 - p)] \) and \( \logit(p_0) \) of the prevalence parameters (Agresti, 2013; Lehmann and Casella, 1998). A logistic back-transformation \( \logit^{-1}(z) = \exp(z)/(1 + \exp(z)) \) yields confidence intervals

\[
\text{CI}_p = \left( \logit^{-1} \left( \logit(\hat{p}) - \frac{\lambda_{\alpha/2} \hat{\sigma}_p}{\hat{p}(1 - \hat{p})} \right), \logit^{-1} \left( \logit(\hat{p}) + \frac{\lambda_{\alpha/2} \hat{\sigma}_p}{\hat{p}(1 - \hat{p})} \right) \right)
\]

and

\[
\text{CI}_{\hat{p}_0} = \left( \logit^{-1} \left( \logit(\hat{p}_0) - \frac{\lambda_{\alpha/2} \hat{\sigma}_{\hat{p}_0}}{\hat{p}_0(1 - \hat{p}_0)} \right), \logit^{-1} \left( \logit(\hat{p}_0) + \frac{\lambda_{\alpha/2} \hat{\sigma}_{\hat{p}_0}}{\hat{p}_0(1 - \hat{p}_0)} \right) \right)
\]
of \( p \) and \( p_0 \) respectively, with approximate coverage probability \( 1 - \alpha \).
Remark 2 (MAR). Since $\rho_s$ is known, $\hat{\rho}_s = \bar{\rho}_s = \rho_s$ and $\bar{p}_{0\mathcal{N}} = \bar{p}_0 = p_0$ for the MAR sampling scheme. Then $\hat{I}_T^+$ is an asymptotically unbiased estimator of $I_T^+$, and (43) simplifies to

$$N^{1/2}(\hat{I}_T^+ - I_T^+) \longrightarrow_{\mathcal{L}} N \left(0, \frac{V_1}{p^2} + \frac{V_3}{p_0^2} - \frac{2V_4}{p^0p_0} \right)$$

as $N \to \infty$.

Remark 3 (A conditional version of active information). Suppose that the interest is in active information due to sampling bias conditionally on the number $N_{T_0}, \ldots, N_{T,S-1}$ of individuals with different symptoms that are tested. The corresponding prevalence and active information are

$$\bar{p} = E (\hat{p}(N_{Ts})_{s=0}^{S-1}) = \sum_{s=0}^{S-1} \rho_{Ts} p_{0s}.$$ (45)

and

$$\bar{I}_T^+ = \log \frac{\bar{p}}{p_0}.$$ (46)

respectively. Using the same type of argument as in the proof of Theorem 1, then

$$N^{1/2}(\hat{p} - \bar{p}) \longrightarrow_{\mathcal{L}} N(0, V_1)$$ (47)

and

$$N^{1/2} \left( \hat{I}_T^+ - \left( \hat{I}_T^+ - \log \frac{\bar{p}_{0\mathcal{N}}}{p_0} \right) \right) \longrightarrow_{\mathcal{L}} N \left(0, \frac{V_1}{p^2} + \frac{V_3}{p_0^2} - \frac{2V_4}{p^0p_0} \right)$$ (48)

as $N \to \infty$. The $V_2$ term is missing in (47) and (48), compared to (41) and (43). This term corresponds to the fact that the actual proportions $\rho_{Ts}$ of tested individuals with different symptoms deviate slightly from the corresponding expected proportions $\hat{\rho}_s$. Because of the missing variance terms of (47) and (48), the standard errors of $\hat{p}$ and $\hat{I}_T^+$ are smaller when a conditional rather than an unconditional approach is used, and the confidence intervals of $\bar{p}$ and $\bar{I}_T^+$ are shorter compared to those of $p$ and $I_T^+$.

Example 4 (Maximum entropy approach). Consider a MNAR sampling scheme where the sizes $\rho_s$ of symptom classes are unknown, although lower and upper bounds $0 \leq a_s N \leq \rho_s \leq b_s N \leq 1$ are known. The maximum entropy approach of Example 3 is generalized assuming that the vector $\rho = (\rho_0, \ldots, \rho_{S-1})$ is a random variable supported on the set

$$\mathcal{R} = \{ \rho = (\rho_0, \ldots, \rho_{S-1}); \ a_s N \leq \rho_s \leq b_s N; \ \sum_{s=0}^{S-1} \rho_s = 1 \},$$ (49)

a subset of the $S$-dimensional simplex of dimension $0 \leq d \leq S$. By the maximum entropy principle, $\rho$ has a uniform density $f_\rho$ on $\mathcal{R}$, which degenerates to a point mass at $\mathcal{R}$ when $d = 0$. This gives rise to estimates

$$\hat{\pi}_s = \frac{N_{Ts}}{N E(\rho_s)}.$$ (50)
of the sampling probabilities \( \pi_s \). Inserting (50) into (37),

\[
\hat{\rho}_s = \frac{E(\rho_s)}{\sum_{r=0}^{S-1} E(\rho_s)} = \int_r f_{\rho_s}(r) dr,
\]

with \( r = (r_0, \ldots, r_{S-1}) \). In particular, the MAR sampling scheme of Example 2 corresponds to the special case \( a_s \pi_s = b_s \pi_s = E(\rho_s) = \rho_s = \hat{\rho}_s \) and \( d = 0 \).

For the COVID-19 model of Example 3, using (30) to rewrite (37),

\[
\hat{\rho}_0 = 1 - \frac{N_{T1}}{N}, \quad \hat{\rho}_1 = \frac{N_{T1} N}{N}. \tag{52}
\]

With an apriori assumption \( \hat{\pi}_0 \leq \hat{\pi}_1 \), equation (52) implies that \( R \) has dimension \( d = S = 2 \), since the conditions

\[
\begin{align*}
a_{0N} &= 1 - \frac{N_{T1}}{N}, & b_{0N} &= 1 - \frac{N_{T1}}{N},
\end{align*}
\]

\[
\begin{align*}
a_{1N} &= \frac{N_{T1}}{N}, & b_{1N} &= \frac{N_{T1}}{N}
\end{align*}
\]

imply

\[
\hat{\rho}_0 = 1 - \frac{N_{T1}}{2N} \left( \frac{N}{N^2} + 1 \right), \quad \hat{\rho}_1 = \frac{N_{T1}}{2N} \left( \frac{N}{N^2} + 1 \right). \tag{53}
\]

Insertion of (25) and (53) into (38) finally leads to (31).

5. Numerical Illustrations

This section illustrates with simulations the methodology under the framework of Examples 1 and 2. In these simulations, \( N \) denotes known population size which is increased from 1000 to 1000000. The true population prevalence is set at \( p_0 = 0.20 \). Only two levels of symptoms will be considered, \( s \in \{0, 1\} \). The proportion of people with symptoms \( \rho_1 \) in the population is 0.20 and without symptoms, \( \rho_0 \) is 0.80. The proportion of positive cases with symptoms \( \rho_{11} = 0.15, \) and the proportion of positive cases without symptoms \( \rho_{01} = 0.05. \) Notice that \( \rho_{11} + \rho_{01} = p_0. \) The testing group within each symptom class is also assumed to be independent of the disease condition, in accordance with (13).

Let \( \pi_1 \) be the probability of testing the symptomatic group, and \( \pi_0 \) be the probability of testing the asymptomatic group. In the case of MCAR, \( \pi_1 = \pi_0 = \pi \) is set to 0.6. Thus, the overall prevalence rate can be estimated by the positive rate (21) in the testing sample.

For the MAR scenario, the probability of testing in symptomatic group \( \pi_1 \) is set to 0.10, while the probability of testing in the asymptomatic group is \( \pi_0 = 0.90. \) Thus, the estimated population prevalence is a weighted average of the positive test rate by proportion of testing.

Finally an MNAR situation is also considered. Unlike MAR, the simulations were repeated without assuming \( \pi_{si} = \pi_s. \) Here, \( \pi_{00} = 0.20, \pi_{01} = 0.30, \pi_{10} = 0.70, \pi_{11} = 0.80. \) Thus, using the weighted positive test rate as MAR, biased
results, for which the bias will not vanish asymptotically, are expected. Each experiment is repeated 500 times.

Table 1 shows the active information of MCAR. Here the probabilities were averaged over the 500 realizations before calculating the active information values. The estimated active information of the correction, $\hat{I}^+_C$, is 0 because $\hat{p}_0 = \hat{p}$ in MCAR. Thus, the active information of the bias-adjusted prevalence estimate for MCAR, $\hat{I}^+$, is obtained from $\hat{I}^+_T$.

Table 1: Empirical active information under MCAR

| Population | 1000   | 10000  | 100000 | 1000000 |
|------------|--------|--------|--------|---------|
| $\hat{I}^+_T$ | 0.0022 | 0.00002 | 0.0003 | 0.00003 |
| $\hat{I}^+_C$ | 0      | 0      | 0      | 0       |
| $\hat{I}^+$  | 0.0022 | 0.00002 | 0.0003 | 0.00003 |

Next, active information values under the MAR simulation were obtained, as shown in Table 2. The active information of the bias-adjusted prevalence estimate in MAR is seen to increase as population increases, removing asymptotically the effect of a small overcorrection.

Table 2: Empirical active information under MAR

| Population | 1000   | 10000  | 100000 | 1000000 |
|------------|--------|--------|--------|---------|
| $\hat{I}^+_T$ | 0.9873 | 0.9901 | 0.9903 | 0.9905  |
| $\hat{I}^+_C$ | -0.9917 | -0.9914 | -0.9892 | -0.9907 |
| $\hat{I}^+$  | -0.0044 | -0.0013 | 0.0011 | -0.0002 |

For MNAR, $\hat{I}^+_T = \log \frac{E(\hat{p})}{\hat{p}_0}$, and $\hat{I}^+_C = \log \frac{E(\hat{p}_0)}{E(\hat{p})}$. Then $\hat{I}^+ = \frac{E(\hat{p}_0)}{\hat{p}_0}$. The active information of the bias-adjusted prevalence estimate for this simulation is shown in Table 3, showing that the strategy partially corrects the sampling bias.

Table 3: Empirical active information under MNAR

| Population | 1000   | 10000  | 100000 | 1000000 |
|------------|--------|--------|--------|---------|
| $\hat{I}^+_T$ | 0.994  | 0.990  | 0.990  | 0.990   |
| $\hat{I}^+_C$ | -0.398 | -0.396 | -0.396 | -0.396  |
| $\hat{I}^+$  | 0.596  | 0.594  | 0.594  | 0.594   |

Empirical root mean squared errors (RMSE) for the bias-corrected population prevalence estimates under each scenario are reported in Table 4, together with their standard deviations in parentheses. Clearly empirical RMSEs drop to zero with increasing $N$ under MAR and MCAR but not under MNAR where even
for very large population sizes, the estimation of population prevalence cannot be improved.

Table 4: Empirical RMSE for three sampling model simulations

| N         | MCAR       | MAR        | MNAR       |
|-----------|------------|------------|------------|
| 1000      | 0.0058 (0.0042) | 0.0218 (0.0129) | 0.164 (0.006) |
| 10000     | 0.0020 (0.0015) | 0.0072 (0.0045) | 0.162 (0.002) |
| 100000    | 0.0006 (0.0005) | 0.0023 (0.0014) | 0.162 (0.001) |
| 1000000   | 0.0002 (0.0001) | 0.0007 (0.0004) | 0.162 (0.001) |

5.1. Asymptotics

Section 4 develops the asymptotic limiting distribution of the bias-corrected population prevalence estimator $\hat{p}_0$ in (38). Two scenarios are explored here: i) small $p_0$, where the proportion of symptomatic individuals in the population $\rho_1$ is set to 0.1, and the population prevalence $p_0$ is set to 0.05; and ii) large $p_0$, where $\rho_1 = 0.2$ and $p_0 = 0.15$.

Remark 1 is used to estimate $\sigma^2_{p_0} = V_3/N$. Figures 1 and 2 show 95% CIs for $p_0$ over 500 realizations of the simulations for increasing $N$ for each scenario with the red dashed lines indicating the true value of $p_0$. Table 5 gives the empirical coverage probabilities for these scenarios.

Table 5: Fraction of confidence intervals CI $p_0$ for the two MAR scenarios of Figures 1 and 2 that capture the true prevalence $p_0$ out of 500 runs of the simulation. The nominal coverage is $1 – \alpha = 0.95$

| Population size $N$ | $\rho_1=0.1$, $p_0=0.05$ | $\rho_1=0.2$, $p_0=0.15$ |
|---------------------|--------------------------|--------------------------|
| 1000                | 0.85                     | 0.916                    |
| 10000               | 0.898                    | 0.928                    |
| 100000              | 0.912                    | 0.95                     |
| 1000000             | 0.916                    | 0.942                    |

6. Discussion

The results of this paper can be extended in various ways. A first extension is to consider prevalence estimation in different laboratories $l = 1, \ldots, L$, so that the population is divided into subpopulations $X_{ls}$ with different combinations of laboratories $l$, symptoms $s$ and infection status $i$. In this context, the prevalence can be made to not only depend on symptoms but also on labs. That is,

$$p_{0ls} = \frac{|X_{ls0}|}{|X_{ls0}| + |X_{ls1}|},$$
Figure 1: Confidence interval plots for 500 simulations and increasing population sizes under the MAR scenario 1, with $\rho_1 = 0.1$ and $p_0 = 0.05$. 
Figure 2: Confidence interval plots for 500 simulations and increasing population sizes under the MA1 scenario 2, with $\rho_1 = 0.2$ and $p_0 = 0.15$. 
within each lab-symptom stratum \((l, s)\), reflects that different labs have different testing procedures.

A second extension is to add errors in testing as in (Zhou et al., 2021). In this scenario the number of observed individuals in each group \(X_{si}\) are different than \(N_{Tsi}\), those actually sampled from that group.

A third extension, arising naturally from this article, is to consider MNAR settings more systematically. As mentioned in Section 3, this is the most challenging situation.

**Appendix: Proof of Theorem 1**

To prove (41), write

\[
\hat{p} - p = \sum_{s=0}^{S-1} \hat{\rho}_s (\hat{p}_{0s} - p_{0s}) + \sum_{s=0}^{S-1} (\rho_{Ts} - \hat{\rho}_s) p_{0s} + \sum_{s=0}^{S-1} (\rho_{Ts} - \hat{\rho}_s) (\hat{p}_{0s} - p_{0s}).
\]  

(54)

Each term in the right-hand side of (54) is now analyzed. From (25)-(27) and properties of the hypergeometric distribution (see, for instance, Gut, 1995),

\[
N_1^{1/2} \left( \hat{\rho}_{0s} - p_{0s} \right) \longrightarrow L N \left( 0, \rho_s^{-1} \frac{1 - \pi_s}{\pi_s} p_{0s} (1 - p_{0s}) \right)
\]

(55)

as \(N \rightarrow \infty\), for \(s = 0, \ldots, S - 1\). And from (25), the members of \(\{\hat{\rho}_{0s}\}_{s=0}^{S-1}\) are asymptotically independent. Together with (55), this implies

\[
N_1^{1/2} \sum_{s=0}^{S-1} \hat{\rho}_s (\hat{p}_{0s} - p_{0s}) \longrightarrow L N (0, V_1),
\]

(56)

where

\[
V_1 = \sum_{s=0}^{S-1} \hat{\rho}_s^2 \rho_s^{-1} \frac{1 - \pi_s}{\pi_s} p_{0s} (1 - p_{0s}) = \frac{\sum_{s=0}^{S-1} \rho_s \pi_s (1 - \pi_s) p_{0s} (1 - p_{0s})}{\left( \sum_{s=0}^{S-1} \rho_s \pi_s \right)^2},
\]

and in the second step (34) was used.

As for the second term of (54), the number of tested individuals with symptoms \(s\) is binomially distributed,

\[
N_{Ts} \sim \text{Bin}(N \rho_s, \pi_s),
\]

for \(s = 0, \ldots, S - 1\). Writing \(N_{Ts}/N = \rho_s \pi_s + \varepsilon_s\), (36) yields that

\[
\rho_{Ts} = \frac{\rho_s \pi_s + \varepsilon_s}{\sum_{r=0}^{S-1} (\rho_r \pi_r + \varepsilon_r)} = \hat{\rho}_s + \frac{\varepsilon_s}{\sum_{r=0}^{S-1} \rho_r \pi_r} - \frac{\rho_s \pi_s \sum_{r=0}^{S-1} \varepsilon_r}{\left( \sum_{r=0}^{S-1} \rho_r \pi_r \right)^2} + \frac{\sum_{r=0}^{S-1} \varepsilon_r}{\sum_{r=0}^{S-1} \rho_r \pi_r} \left[ \hat{\rho}_s - \frac{\rho_s \pi_s + \varepsilon_s}{\sum_{r=0}^{S-1} (\rho_r \pi_r + \varepsilon_r)} \right],
\]

15
and the last term on the right-hand side is \( o_p \left( N^{-1/2} \right) \). So the second sum of (54) reads

\[
\sum_{s=0}^{S-1} (p_T s - \hat{p}_s)p_{0s} = \frac{\sum_{s=0}^{S-1} \rho_{s}s_{0s} \varepsilon_s}{\sum_{s=0}^{S-1} \rho_{s}s_{0s} \pi_s} - \frac{\sum_{s=0}^{S-1} \rho_{s}s_{0s} \pi_s p_{0s}}{\left( \sum_{s=0}^{S-1} \rho_{s}s_{0s} \pi_s \right)^2} + o_p \left( N^{-1/2} \right).
\]

This gives

\[
N^{1/2} \sum_{s=0}^{S-1} (p_T s - \hat{p}_s)p_{0s} \longrightarrow L N(0, V_2),
\]

(57)

where

\[
V_2 = \sum_{s=0}^{S-1} \rho_{s}s_{0s}(1 - \pi_s) \left[ \frac{p_{0s}}{\sum_{r=0}^{S-1} \rho_{r}s_{0r} \pi_r} - \frac{\sum_{r=0}^{S-1} \rho_{r}s_{0r} \pi_r}{\left( \sum_{r=0}^{S-1} \rho_{r}s_{0r} \pi_r \right)^2} \right]^2,
\]

and

\[
\tilde{p}_0 = \frac{\sum_{s=0}^{S-1} \rho_{s}s_{0s} p_{0s}}{\sum_{s=0}^{S-1} \rho_{s}s_{0s}}
\]

is a weighted average of \( p_{00}, \ldots, p_{0S-1} \).

From the definitions, the first two terms in the right-hand side of (54) are asymptotically independent. Moreover, the last term of (54) is \( o_p \left( N^{-1/2} \right) \), since \( \hat{p}_0 \mathbf{s} - \bar{p}_s = O_p \left( N^{-1/2} \right) \) according to (55), and \( p_T s - \hat{p}_s = O_p \left( N^{-1/2} \right) \) according to the second displayed equation above (57). Equation (41) therefore follows from (54), (56), and (57), by summing the asymptotic variances of the latter two formulas.

To prove (42), (38) and (39) are first used, so that the estimation error of \( \hat{p}_0 \) is expressed as

\[
R_3 = \hat{p}_0 - \bar{p}_0 N = \sum_{s=0}^{S-1} \hat{p}_s(p_{0s} - \bar{p}_s).
\]

(58)

By (44) and a similar argument to the one that led to (56),

\[
N^{1/2} R_3 \longrightarrow L N(0, V_3),
\]

(59)

with

\[
V_3 = \sum_{s=0}^{S-1} \rho_{s}s_{0s}^{-1} \frac{1 - \pi_s}{\pi_s} p_{0s}(1 - p_{0s}).
\]

Only (43) remains to be proven. To this end,

\[
\hat{I}_T = I_T - \log \frac{\bar{p}_0 N}{\bar{p}_0} + \log \frac{\bar{p}_0}{\bar{p}_0 N}.
\]

(60)
Consequently, by a Taylor expansion of the logarithmic function around 1,

\[
\hat{I}_T^+ - \left( I_T^+ - \log \bar{p}_{0N} / \bar{p}_0 \right) = \frac{R_1 + R_2}{p} - \frac{R_3}{\bar{p}_{0N}} + o_p \left( N^{-1/2} \right),
\]

(61)

where \( R_1 = \sum_{s=0}^{S-1} \hat{\rho}_s (\hat{p}_0^s - \bar{p}_0^s) \) and \( R_2 = \sum_{s=0}^{S-1} (\rho^s T_s - \hat{\rho}_s) \bar{p}_0^s \) are the first two terms on the right hand side of (54).

In analogy with (56), (57) and (59), \( N^{1/2} (R_1, R_2, R_3) \) can be shown to converge weakly:

\[
N^{1/2} (R_1, R_2, R_3) \overset{\mathcal{L}}{\longrightarrow} N \left( (0, 0, 0), \left( \begin{array}{ccc} V_1 & 0 & V_4 \\ 0 & V_2 & 0 \\ V_4 & 0 & V_3 \end{array} \right) \right),
\]

(62)

where

\[
V_4 = \sum_{s=0}^{S-1} \hat{\rho}_s \rho_s^{-1} \frac{1 - \pi_s}{\pi_s} \bar{p}_0^s (1 - p_0^s) = \frac{\sum_{s=0}^{S-1} \hat{\rho}_s (1 - \pi_s) p_0^s (1 - p_0^s)}{\sum_{s=0}^{S-1} \rho_s \pi_s}.
\]

The proof of (43) is finalized using (61) and (62) and the fact that \( \bar{p}_{0N} \overset{p}{\longrightarrow} \bar{p}_0 \) as \( N \to \infty \), which follows from (40).

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