

## LARGE SAMPLE THEORY FOR SEMIPARAMETRIC REGRESSION MODELS WITH TWO-PHASE, OUTCOME DEPENDENT SAMPLING

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Outcome-dependent, two-phase sampling designs can dramatically reduce the costs of observational studies by judicious selection of the most informative subjects for purposes of detailed covariate measurement. Here we derive asymptotic information bounds and the form of the efficient score and influence functions for the semiparametric regression models studied by Lawless, Kalbfleisch and Wild (1999) under two-phase sampling designs. We show that the maximum likelihood estimators for both the parametric and nonparametric parts of the model are asymptotically normal and efficient. The efficient influence function for the parametric part agrees with the more general information bound calculations of Robins, Hsieh and Newey (1995). By verifying the conditions of Murphy and van der Vaart (2000) for a least favorable parametric submodel, we provide asymptotic justification for statistical inference based on profile likelihood.

**1. Introduction.** Outcome-dependent, two-phase stratified sampling designs can dramatically reduce the costs of observational studies by selecting the most informative subjects for detailed covariate measurement. Although ad hoc, inefficient estimation methods often have been used with these designs, recent work has focused on maximum likelihood estimation for semiparametric regression models. Scott and Wild (1997), who considered simple random samples at the first phase of sampling, and Breslow and Holubkov (1997), who considered case-control sampling at phase one and worked exclusively with the logistic model, developed maximum likelihood estimators for binary response models. This work extended the classical theory of Prentice and Pyke (1979) to samples that were jointly stratified by outcomes and covariates. Lawless, Kalbfleisch and Wild (1999) (LKW) and Scott and Wild (2000) generalized the approach of Scott and Wild (1997) and demonstrated that computation of maximum likelihood estimators is feasible for a wide range of parametric regression models and two-phase designs provided that

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the phase one data are discrete. For an example of a two-phase design, see Breslow and Chatterjee (1999).

Robins, Hsieh and Newey (1995) (RHN) derived the semiparametric efficient scores for a more general problem in which a portion of the covariate vector is missing for some subjects, but the outcome variable and the other covariates are fully known for everyone. In the general case of continuous data, calculation of the optimal estimator involves numerical solution of an (infinite dimensional) integral equation. When the outcomes and covariates observed for everyone are discrete and used to define the sampling strata, in which case the problems considered by LKW and RHN are identical, RHN calculated an optimal estimator by solving finite dimensional linear equations to obtain the scores.

LKW remarked that the RHN methods “appear to be asymptotically equivalent” to theirs for the case of discrete phase one data, but offered no proof. They also remarked that they had “no theoretical justification” for their empirical observation that inferences based on the observed information for the profile likelihood “performed excellently” even when the covariates were continuous. Our goal is to provide asymptotic theory that resolves these outstanding issues. We first establish asymptotic lower bounds using the methods of Bickel, Klaassen, Ritov and Wellner (1993) to compute the efficient score functions, (efficient) information and efficient influence functions for the problem considered by LKW. For at least the i.i.d. special case of variable probability (Bernoulli) sampling, these results also follow from the more general information calculations of RHN. The models considered here yield sufficiently explicit formulas, however, that they deserve special consideration. Although we do not go beyond the i.i.d. Bernoulli sampling framework here, McNeney (1998) shows that the information bounds for the more realistic basic stratified sampling model (cf. LKW) agree with those for Bernoulli sampling under mild conditions. We intend to give a complete treatment of the stratified sampling model and other designs elsewhere.

In Section 3 we identify a least favorable parametric submodel and verify that it satisfies the key hypothesis of Theorem 1 of Murphy and van der Vaart (2000) (MvdV). In Section 4 we use the least favorable parametric submodel to justify the asymptotic expansion of the profile likelihood in terms of the efficient score and information, which allows it to be treated as an ordinary likelihood for purposes of statistical inference. A corollary of this development is asymptotic normality and efficiency of the maximum likelihood estimator  $\hat{\theta}_n$  of  $\theta$ . The final task, undertaken in Section 5, is to prove joint asymptotic normality and efficiency of the ML estimators. Results given for both the parametric and nonparametric components of the model are apparently new. Our approach, which requires only modest regularity assumptions, is via Theorem 1 of MvdV and a verification of their hypotheses for our particular class of models.

In Section 6 we discuss other designs and further problems. The more lengthy arguments, including derivation of the semiparametric likelihood under several sampling designs, direct computation of the information bounds using operator

theory, verification of regularity conditions for a least favorable parametric submodel, a statement of the infinite-dimensional  $Z$ -theorem, connections with the formulas of RHN and a derivation of the information formula for the important special case of logistic regression, are spelled out in complete detail in the companion technical report Breslow, McNeney and Wellner (2000) (BMW).

**2. Information bounds, Bernoulli sampling.** In this section we derive information bounds for estimation of the regression parameters assuming that the sampling design yields i.i.d. data. Suppose that  $(Y, X)$  has density  $f(y|x; \theta)g(x)$  with respect to a dominating measure  $\nu \times \mu$  on  $\mathcal{Y} \times \mathcal{X}$  for some  $\theta \in \Theta \subset R^m$  and some  $G \in \mathcal{G}$ , where

$$\mathcal{G} \equiv \{G : G \text{ is a distribution on } \mathcal{X} \text{ with density } g \text{ with respect to } \mu\},$$

and let  $Q_{\theta, G}$  denote the corresponding probability measure. Both  $X$  and  $Y$  may be multivariate. Let  $\mathcal{Y} \times \mathcal{X} = \bigcup_{j=1}^J \mathcal{S}_j$  for a partition  $\{\mathcal{S}_j\}$  into  $J$  mutually exclusive strata. Following LKW, we set

$$Q_j(\theta, G) = \Pr[(Y, X) \in \mathcal{S}_j] \quad \text{and} \quad Q_j^*(x, \theta) \equiv \Pr[(Y, x) \in \mathcal{S}_j | X = x] \mathbb{1}_{\mathcal{S}_j^*}(x),$$

for  $j = 1, \dots, J$  where  $\mathcal{S}_j^* = \{x \in \mathcal{X} : \text{for some } y, (y, x) \in \mathcal{S}_j\}$ . Thus  $Q_j(\theta, G) = \int Q_j^*(x, \theta) dG(x)$ . Note that the  $\mathcal{S}_j^*$ 's do *not* form a partition of  $\mathcal{X}$  and may in fact intersect in quite arbitrary ways.

Suppose that  $(Y_1, X_1), \dots, (Y_n, X_n)$  are i.i.d. as  $(Y, X)$  with density

$$(2.1) \quad p(y, x; \theta_0, g_0) = f(y|x; \theta_0)g_0(x).$$

We assume throughout that the true distribution governing the underlying data is given by (2.1) corresponding to  $(\theta_0, G_0) \in \Theta \times \mathcal{G}$ . We also assume that

$$(2.2) \quad Q_j(\theta_0, G_0) > 0, \quad j \in \{1, \dots, J\}.$$

At the first phase of sampling we do not observe the complete  $(Y_i, X_i)$  pairs, but only observe *stratum indicators*

$$\delta_{ij} = \mathbb{1}\{(Y_i, X_i) \in \mathcal{S}_j\}, \quad i = 1, \dots, n, \quad j = 1, \dots, J.$$

Thus

$$\underline{\delta}_i = (\delta_{i1}, \dots, \delta_{iJ}) \sim \text{Mult}_J(1, \underline{Q} = (Q_1, \dots, Q_J)^T)$$

where  $Q_j \equiv Q_j(\theta, G)$ ,  $j = 1, \dots, J$ . We will sometimes use the alternative and completely equivalent stratum variables  $S_i$ , defined by  $S_i = s$  if and only if  $\delta_{is} = 1$  for  $i = 1, \dots, n$ . Now suppose that selection of subjects for complete response and covariate ascertainment at the second phase of sampling is defined by the indicators

$$R_i = \begin{cases} 1, & \text{if } (Y_i, X_i) \text{ is fully observed,} \\ 0, & \text{if only } S_i \text{ is observed.} \end{cases}$$

We set  $D_j = \{i : \delta_{ij} = 1, R_i = 1\}$ ,  $N_j = \sum_{i=1}^n \delta_{ij} = \#\{i : (Y_i, X_i) \in \mathcal{S}_j\}$  and  $n_j = \#(D_j)$ , for  $j = 1, \dots, J$ , so that  $\underline{N} = (N_1, \dots, N_J)^T \sim \text{Mult}_J(n, \underline{Q})$ .

We confine our attention in this paper to *variable probability sampling* (VPS): units are inspected sequentially as they arise from the density (2.1). When  $(Y_i, X_i) \in \mathcal{S}_j$ , the  $i$ th unit is selected for full observation ( $R_i = 1$ ) with specified probability  $p_j$ ; thus

$$\Pr(R_i = 1 | Y_i, X_i) = \sum_{j=1}^J p_j \mathbb{1}\{(Y_i, X_i) \in \mathcal{S}_j\} = \sum_{j=1}^J p_j \delta_{ij} = p_{S_i}.$$

Two variants of this plan depend on how the sampling is terminated:

VPS1: Inspect a pre-specified number  $n$  of units (Bernoulli sampling).

VPS2: Inspect units until a total of  $k$  have been selected (Negative Binomial sampling).

As shown by Scott and Wild (1997) or Appendix 1A of BMW, VPS1 (Bernoulli) sampling results in the following density for the observed data  $(R, Z) \equiv (R, (Y, X)\mathbb{1}_{[R=1]} + \underline{\delta}\mathbb{1}_{[R=0]}) \equiv (R, (Y, X)\mathbb{1}_{[R=1]} + S\mathbb{1}_{[R=0]})$ : with  $q_j \equiv 1 - p_j$ ,  $j = 1, \dots, J$ ,

$$\begin{aligned} p(r, z; \theta, g) &\equiv \left\{ f(y|x; \theta)g(x) \left( \sum p_j \delta_j \right) \right\}^r \left\{ \prod_{j=1}^J Q_j^{\delta_j} \right\}^{1-r} \left\{ \sum q_j \delta_j \right\}^{1-r} \\ (2.3) \qquad &= \prod_{j=1}^J \left\{ [f(y|x; \theta)g(x)]^{\delta_j r} Q_j^{\delta_j(1-r)} \right\} \left\{ \sum p_j \delta_j \right\}^r \left\{ \sum q_j \delta_j \right\}^{1-r}. \end{aligned}$$

This is our starting point for information calculations in the i.i.d. version of the model. Let  $\mathcal{P}$  be the collection of all probability distributions  $P_{\theta, G}$  with densities given by (2.3) for  $\theta \in \Theta$ ,  $G \in \mathcal{G}$ .

PROPOSITION 2.1 (Scores for the i.i.d. model). *Suppose that  $(R, Z)$  has the density (2.3), that (2.2) holds and that for a fixed  $G_0 \in \mathcal{G}$*

$$\mathcal{Q}_{G_0} \equiv \left\{ Q_{\theta, G_0} : \frac{dQ_{\theta, G_0}}{d(v \times \mu)}(y, x) = f(y|x; \theta)g_0(x), \theta \in \Theta \right\}$$

*is a regular parametric model. Suppose  $\theta_0 \in \Theta^0$ , the interior of  $\Theta$ , and write  $P_0$  for  $P_{(\theta_0, G_0)}$  and  $E_0$  for expectation under  $P_0$ , respectively. Then the score for  $\theta$  and the score operator for  $g$  at  $P_0$  in the VPS1 model are given by*

$$\begin{aligned} (2.4) \qquad \dot{\mathbf{i}}_{\theta}(r, z) &= r \dot{\mathbf{i}}_{\theta}(y|x) + (1-r) \sum_{j=1}^J \delta_j \dot{\underline{Q}}_j(\theta_0, G_0) / Q_j(\theta_0, G_0) \\ &= r \dot{\mathbf{i}}_{\theta}(y|x) + (1-r) E_0 \{ \dot{\mathbf{i}}_{\theta}(Y|X) | S = s \} \end{aligned}$$

where

$$\dot{\mathbf{I}}_{\theta}(y|x; \theta_0) \equiv \dot{\mathbf{I}}_{\theta}(y|x) \equiv \frac{\partial}{\partial \theta} \log f(y|x; \theta) \Big|_{\theta=\theta_0} \equiv \nabla_{\theta} \log f(y|x; \theta_0),$$

$$\underline{\dot{Q}}_j(\theta_0, G_0) \equiv \nabla_{\theta} Q_j(\theta_0, G_0) \equiv \int \underline{\dot{Q}}_j^*(x, \theta_0) dG_0(x)$$

and, for  $h \in L_2^0(G_0) \equiv \{h \in L_2(G_0) : \int h dG_0 = 0\}$ ,

$$\begin{aligned} \dot{\mathbf{I}}_g h(r, z) &\equiv A_{\theta_0, G_0} h(r, z) \equiv A_{\theta_0, G_0} h(r, r(y, x) + (1-r)\underline{\delta}) \\ (2.5) \quad &= rh(x) + (1-r)E_0\{h(X) \mid S = s\} \\ &= rh(x) + (1-r)\underline{\delta}^T \text{diag}(1/\underline{Q}) \langle \underline{Q}^*, h \rangle \end{aligned}$$

where  $\langle h_1, h_2 \rangle = \int h_1 h_2 dG_0$  denotes the inner product in  $L_2(G_0)$ .

Computation of the scores in Proposition 2.1 and inversion of the information operator  $A_{\theta_0, G_0}^T A_{\theta_0, G_0}$ , carried out explicitly in Section 2 of BMW, lead directly to the information bounds for  $\theta$  given in the following proposition. Since the derivation is rather lengthy, however, the proof here relies instead on results of RHN.

PROPOSITION 2.2 (Efficient scores and information bounds for the i.i.d. model). *Suppose that the assumptions of Proposition 2.1 hold at  $P_0$  and that  $0 < p_j < 1$  for each  $j \in \{1, \dots, J\}$ . Define*

$$\begin{aligned} \psi(y, x) &\equiv \dot{\mathbf{I}}_{\theta}(y|x) - \frac{\underline{\dot{Q}}^*}{\pi^*}(x)\underline{p} - (\underline{\dot{Q}} - \mathbf{C})\mathbf{M}^{-1} \frac{\underline{Q}^*}{\pi^*}(x) \\ (2.6) \quad &= \dot{\mathbf{I}}_{\theta}(y|x) - E_0\{\dot{\mathbf{I}}_{\theta}(Y|X) \mid R = 1, X = x\} \\ &\quad - E_0\{(\underline{\dot{Q}} - \mathbf{C})\mathbf{M}^{-1} \text{diag}(1/\underline{p})\underline{\delta} \mid R = 1, X = x\}, \end{aligned}$$

where

$$(2.7) \quad \pi^*(x) \equiv \sum_{j=1}^J p_j Q_j^*(x, \theta_0) = E_0(p_S \mid X = x),$$

$$(2.8) \quad \mathbf{M} \equiv \text{diag}(\underline{Q}/\underline{q}) + \left\langle \underline{Q}^*, \frac{1}{\pi^*} \underline{Q}^{*T} \right\rangle$$

is always nonsingular,  $\underline{\dot{Q}} \equiv (\underline{\dot{Q}}_1, \dots, \underline{\dot{Q}}_J)$  is an  $m \times J$  matrix,  $\underline{\dot{Q}}^* \equiv (\underline{\dot{Q}}_1^*, \dots, \underline{\dot{Q}}_J^*)$  is an  $m \times J$  matrix of functions and

$$(2.9) \quad \mathbf{C} \equiv \left\langle \underline{\dot{Q}}^* \underline{p}, \frac{\underline{Q}^{*T}}{\pi^*} \right\rangle \quad (\text{an } m \times J \text{ matrix}).$$

Then the efficient score function for  $\theta$  is given by

$$(2.10) \quad \mathbf{I}_g^*(r, z) = r\psi(y, x) + (1-r)E_0\{\psi(Y, X) \mid \underline{\delta}\},$$

the information for  $\theta$  at  $(\theta_0, G_0)$  is

$$\begin{aligned} I(\theta_0) &= E_0 \left\{ R \left[ \dot{\mathbf{l}}_\theta(Y|X) - \frac{\dot{\mathbf{Q}}^*}{\pi^*}(X) \underline{p} \right]^{\otimes 2} \right\} + (\dot{\mathbf{Q}} - \mathbf{C}) \mathbf{M}^{-1} (\dot{\mathbf{Q}} - \mathbf{C})^T \\ (2.11) \quad &= E_0 \left\{ R [\dot{\mathbf{l}}_\theta(Y|X) - E_0 \{ \dot{\mathbf{l}}_\theta(Y|X) \mid R = 1, X \}]^{\otimes 2} \right\} \\ &\quad + (\dot{\mathbf{Q}} - \mathbf{C}) \mathbf{M}^{-1} (\dot{\mathbf{Q}} - \mathbf{C})^T, \end{aligned}$$

and the efficient influence function is

$$(2.12) \quad \tilde{\mathbf{l}}_\theta(r, z) = I(\theta_0)^{-1} \mathbf{I}_\theta^*(r, z).$$

REMARK 2.1. The efficient score function for  $\theta$  given by (2.10) agrees with the calculations of RHN after making the following minor correction to their Proposition 1. According to their equations (11), (17) and (23) and the arguments on page 421, the expressions for the optimal  $U^{(2)}(\phi_{\text{op}})$  on pages 413 and 414 should read

$$U^{(2)}(\phi_{\text{op}}) = -\Delta E \left[ \frac{1 - \pi(W)}{\pi(W)} \phi_{\text{op}}(W) \mid \Delta = 1, X, V \right] + (1 - \Delta) \phi_{\text{op}}(W).$$

Then, with  $\underline{q} = \underline{1} - \underline{p}$ ,

$$(2.13) \quad \xi(\underline{\delta}) \equiv E_0 \{ \psi(Y, X) \mid \underline{\delta} \} = (\dot{\mathbf{Q}} - \mathbf{C}) \mathbf{M}^{-1} \text{diag}(1/\underline{q}) \underline{\delta}$$

plays the role of RHN's  $\phi_{\text{op}}(W)$  and satisfies the finite dimensional, integral (linear) equation

$$\begin{aligned} (2.14) \quad \xi(\underline{\delta}) &= E_0 \{ \dot{\mathbf{l}}_\theta - E_0 \{ \dot{\mathbf{l}}_\theta \mid R = 1, X \} \mid \underline{\delta} \} \\ &\quad - E_0 \{ E_0 [ \xi(\underline{\delta}) \underline{q}^T \text{diag}(1/\underline{p}) \underline{\delta} \mid R = 1, X ] \mid \underline{\delta} \} \end{aligned}$$

that corresponds to their equation (8); see Section 3 and Appendix 1C of BMW. For an independent recent derivation of the more general integral equation of RHN, see Nan, Emond and Wellner (2000).

REMARK 2.2. Calculations based on the score operator (2.5) also lead easily to an information bound for estimation of the distribution  $G$  as in Begun, Hall, Huang and Wellner [(1983), Theorem 4.1, page 441], or Bickel, Klaassen, Ritov and Wellner [(1993), Corollary 3, page 215]. See the statement of Theorem 4.1 and Section 4 of BMW.

REMARK 2.3. The hypothesis that  $0 < p_j < 1$  for all  $j = 1, \dots, J$  in Proposition 2.2 can be weakened to  $0 < p_j \leq 1$  for all  $j = 1, \dots, J$ . This is important in practice since often the  $p_j$ 's in strata with relatively small  $Q_j$ , and

hence small counts  $N_j$ , will be taken to be 1. Note that the second term in (2.11) can be rewritten as

$$(2.15) \quad [(\dot{Q} - C) \text{diag}(\sqrt{q})] \tilde{M}^{-1} [\text{diag}(\sqrt{q})(\dot{Q} - C)^T]$$

where

$$\tilde{M} \equiv \text{diag}(Q) + \text{diag}(\sqrt{q}) \left\langle \underline{Q}^*, \frac{1}{\pi^*} \underline{Q}^{*T} \right\rangle \text{diag}(\sqrt{q})$$

is always invertible (even if some  $p_j = 1, q_j = 0$ ) by virtue of (2.2). Also note that if all  $p_j = 1$  so that all  $q_j = 0$ , then the second term [as rewritten in (2.15)] vanishes,  $R = 1$  identically, and the first term becomes

$$(2.16) \quad E_0 \left\{ (\dot{\mathbf{i}}_\theta(Y|X) - E_0(\dot{\mathbf{i}}_\theta(Y|X) | X))^{\otimes 2} \right\} = E_0 \{ \dot{\mathbf{i}}_\theta(Y|X)^{\otimes 2} \},$$

the information for  $\theta$  with complete data from (2.1).

REMARK 2.4. Any (locally regular) estimator of  $\theta$  in the i.i.d. two-phase sampling model has an influence function of the form

$$(2.17) \quad \phi(r, z) = \frac{r}{\pi(y, x)} \dot{\chi}(y, x) - \frac{r - \pi(y, x)}{\pi(y, x)} c(s)$$

for some function  $c : \{1, \dots, J\} \rightarrow R^m$  where  $\dot{\chi}$  is an influence function for some estimator of  $\theta$  in the complete data model  $\mathcal{Q}$ , with true element  $Q_0$ , in which all the  $(Y_i, X_i)$ 's are observed; that is

$$\dot{\chi}(y, x) = I_{11}^{-1}(\theta_0) \dot{\mathbf{i}}_\theta(y|x) + h(y, x)$$

where  $I_{11}(\theta_0) = E_{Q_0} \dot{\mathbf{i}}_\theta^{\otimes 2}$ ,  $h = (h_1, \dots, h_m)$  and  $h_i \perp L_2^0(G)$  in  $L_2(Q_0)$  for  $i = 1, \dots, m$ . For a proof of (2.17), see van der Vaart [(1998), pages 379–383]. In particular, all of the inefficient estimators considered in LKW have influence functions of this form for some  $h$  and  $c$ .

EXAMPLE 2.1 (Logistic regression for stratified case-control studies). Suppose that

$$(2.18) \quad f(y|x) = f(y|x; \theta) = \left( \frac{e^{\theta^T x}}{1 + e^{\theta^T x}} \right)^y \left( \frac{1}{1 + e^{\theta^T x}} \right)^{1-y},$$

$$y \in \{0, 1\}, x \in R^m, \theta \in R^m.$$

Then, since the logit is the canonical link function for the Bernoulli distribution [see McCullagh and Nelder (1989), pages 28–31],  $\dot{\mathbf{i}}_\theta(y|x) = x[y - f(1|x)]$ . For stratified case-control sampling, as discussed by Scott and Wild (1997) or Breslow and Holubkov (1997), the partition of  $\mathcal{Y} \times \mathcal{X}$  is formed by intersecting a partition of  $\mathcal{X}$  into  $J$  sets  $\{\mathcal{X}_j\}$  with the sets  $\mathbb{1}\{y = 0\}$  and  $\mathbb{1}\{y = 1\}$ . This leads to  $2J$  strata  $\mathcal{Y}_{yj} = \mathbb{1}\{Y = y, X \in \mathcal{X}_j\}$  for  $y = 0, 1; j = 1, \dots, J$ . Continuing this double subscript system, let  $p_{yj}$  denote the corresponding sampling probabilities for selection at phase two.

COROLLARY 2.1 (Information for  $\theta$ , logistic regression special case). *Suppose that the model is given by (2.18). Then (2.11) yields*

$$(2.19) \quad I(\theta) = \sum_{j=1}^J \int_{\mathcal{X}_j} \underline{x} \underline{x}^T \frac{p_{0j} p_{1j} f(0|x) f(1|x)}{\pi_j^*(x)} dG(x) \\ + \sum_{j=1}^J \frac{p_{0j} p_{1j} \left( \int_{\mathcal{X}_j} \underline{x} \frac{f(0|x) f(1|x)}{\pi_j^*(x)} dG(x) \right)^{\otimes 2}}{\frac{Q_{0j} Q_{1j}}{p_{0j} Q_{0j} + p_{1j} Q_{1j} - p_{0j} p_{1j} G(\mathcal{X}_j)} - \int_{\mathcal{X}_j} \frac{f(0|x) f(1|x)}{\pi_j^*(x)} dG(x)}$$

where  $\pi_j^*(x) \equiv p_{0j} f(0|x) + p_{1j} f(1|x)$  for  $x \in \mathcal{X}_j$ .

PROOF. See Appendix 1D of BMW. The same expression may be derived by using the linearization discussed in Section 4 of Breslow and Holubkov (1997), and additional Taylor series expansions, in a direct computation of the influence function for the maximum likelihood estimator.  $\square$

REMARK 2.5. Consider the special case where  $J = 1$ , so that sampling depends only on the binary outcome, and drop the  $j$  subscript in what follows. Suppose the linear predictor contains an intercept:  $f(0|x) = (1 + e^{\theta_1 + \theta_2^T x})^{-1}$ . Let  $f^\pi(y|x) = p_y e^{y(\theta_1 + \theta_2^T x)} / (p_0 + p_1 e^{\theta_1 + \theta_2^T x}) = \Pr(Y = y|X = x, R = 1)$  denote the logistic regression probabilities of the “biased sampling model”  $Q = Q_{\theta, G}$  induced by the condition  $R = 1$ . Then the information matrix may be written

$$I(\theta) = E_Q[\text{Var}_Q(Y|X)] \left\{ \begin{bmatrix} 1 & \mu^T \\ \mu & \mu_2 \end{bmatrix} + c \begin{bmatrix} 1 & \mu^T \\ \mu & \mu \mu^T \end{bmatrix} \right\}$$

where

$$c = \frac{\pi E_Q[\text{Var}_Q(Y|X)](p_0 Q_0 + p_1 Q_1 - p_0 p_1)}{p_0 p_1 Q_0 Q_1 - \pi E_Q[\text{Var}_Q(Y|X)](p_0 Q_0 + p_1 Q_1 - p_0 p_1)}, \\ \mu = \frac{E_Q[X \text{Var}_Q(Y|X)]}{E_Q[\text{Var}_Q(Y|X)]} = \frac{\int x f^\pi(0|x) f^\pi(1|x) \pi^*(x) dG(x)}{\int f^\pi(0|x) f^\pi(1|x) \pi^*(x) dG(x)}$$

and

$$\mu_2 = \frac{E_Q[XX^T \text{Var}_Q(Y|X)]}{E_Q[\text{Var}_Q(Y|X)]} = \frac{\int x x^T f^\pi(0|x) f^\pi(1|x) \pi^*(x) dG(x)}{\int f^\pi(0|x) f^\pi(1|x) \pi^*(x) dG(x)},$$

and where  $\pi = \pi(\theta, G) = \Pr(R = 1)$ . Now the information for  $\theta_2$  is

$$I(P|\theta_2, \mathcal{P}) = I_{22}(\theta) - I_{21}(\theta) I_{11}^{-1}(\theta) I_{12}(\theta) \\ = E_Q[\text{Var}_Q(Y|X)](\mu_2 - \mu \mu^T) \\ = E_Q \left\{ \left( X - \frac{E_Q[X \text{Var}_Q(Y|X)]}{E_Q[\text{Var}_Q(Y|X)]} \right)^{\otimes 2} \text{Var}_Q(Y|X) \right\}.$$

This expression, which agrees with formulas (4) and (9) of Breslow, Robins and Wellner (2000), is precisely the information about  $\theta_2$  obtained by fitting an ordinary logistic regression model to the second phase data alone. It confirms once again that, for simple case-control sampling, “prospective” logistic regression analysis of the “retrospectively” sampled data yields efficient estimates of the odds ratio parameters in logistic regression models [Prentice and Pyke (1979)].

PROOF OF PROPOSITION 2.2. This follows from Proposition 1 of RHN after the corrections noted in Remark 2.1. We rewrite (2.14) [or equation (4.2) of Nan, Emond and Wellner (2000)] as a matrix equation and express the solution in terms of the inverse of a certain matrix. First,

$$(2.20) \quad E_0\{\dot{\mathbf{l}}_\theta \mid \underline{\delta}\} = \dot{\mathbf{Q}} \text{diag}(1/\underline{Q})\underline{\delta}$$

and

$$(2.21) \quad E_0\{E_0(\dot{\mathbf{l}}_\theta \mid R = 1, X) \mid \underline{\delta}\} = \mathbf{C} \text{diag}(1/\underline{Q})\underline{\delta}$$

where  $\mathbf{C}$  is as defined in (2.9). Thus the first term on the right-hand side of (2.14) is

$$(2.22) \quad E_0\{\dot{\mathbf{l}}_\theta - E_0(\dot{\mathbf{l}}_\theta \mid R = 1, X) \mid \underline{\delta}\} = (\dot{\mathbf{Q}} - \mathbf{C}) \text{diag}(1/\underline{Q})\underline{\delta}.$$

Furthermore, writing  $\xi(\underline{\delta}) = \sum_{j=1}^J \xi_j \delta_j = \underline{\xi} \underline{\delta}$  for an  $m \times J$  matrix  $\underline{\xi} = (\xi_1, \dots, \xi_J)$ , we can rewrite the second term on the right-hand side of (2.14) as

$$(2.23) \quad E_0\{E_0[\xi(\underline{\delta})\underline{q}^T \text{diag}(1/\underline{p})\underline{\delta} \mid R = 1, X] \mid \underline{\delta}\} = \underline{\xi} \text{diag}(\underline{q})\mathbf{D} \text{diag}(1/\underline{Q})\underline{\delta}$$

where  $\mathbf{D} = \langle \underline{Q}^*, \frac{1}{\pi^*} \underline{Q}^{*T} \rangle$ . Substitution of (2.22) and (2.23) into (2.14) and rearranging yields

$$(2.24) \quad \underline{\xi}(\mathbf{I} + \text{diag}(\underline{q})\mathbf{D} \text{diag}(1/\underline{Q})) = (\dot{\mathbf{Q}} - \mathbf{C}) \text{diag}(1/\underline{Q}),$$

or, with  $\mathbf{M} \equiv \text{diag}(\underline{Q}/\underline{q}) + \mathbf{D}$  as in (2.8),

$$(2.25) \quad \underline{\xi} \text{diag}(\underline{q})\mathbf{M} = (\dot{\mathbf{Q}} - \mathbf{C}).$$

Note that

$$\underline{a}^T \mathbf{M} \underline{a} = \sum_{j=1}^J (Q_j/q_j) a_j^2 + \|\underline{a}^T \underline{Q}^* / \sqrt{\pi^*}\|^2 > 0$$

for all  $\underline{a} \neq \underline{0}$ . Therefore the matrix  $\mathbf{M}$  is nonsingular,  $\mathbf{M}^{-1}$  exists and

$$(2.26) \quad \underline{\xi} = (\dot{\mathbf{Q}} - \mathbf{C})\mathbf{M}^{-1} \text{diag}(1/\underline{q}).$$

Using (2.26) in the (corrected) formula for  $U^{(2)}(\phi_{op})$  in Remark 2.1, together with  $U^{(1)}$  in RHN’s Proposition 1, yields the claimed efficient score given in (2.10).  $\square$

**3. A least favorable parametric submodel.** An alternative approach to understanding of the efficient scores and influence function for  $\theta$  in the semiparametric model (2.3) is to determine a least favorable submodel for  $G$  as in MvdV. We initially determine a candidate least favorable submodel by partial maximization of the expected log-likelihood, assuming that  $G$  is discrete. Subsequent calculations show that our submodel satisfies MvdV's key conditions for a least favorable parametric submodel; we give regularity conditions under which the remaining hypotheses of their Theorem 1 hold. This provides theoretical confirmation for LKW's simulation studies, which showed that inferences based on the observed information matrix of the profile likelihood function had appropriate frequency properties.

Suppose then that  $X$  takes  $K$  values  $\{x_k\}$  with probabilities  $g_k$ ,  $\sum_k g_k = 1$ . Define

$$(3.1) \quad \pi_j(Q) \equiv 1 - \frac{Q_j(1-p_j)}{Q} \quad \text{for } Q \in (0, 1],$$

where  $Q_j = Q_j(\theta, G)$  is defined in Section 2, and note that  $\pi_j(Q_j) = p_j$ . With  $E \equiv E_{\theta, G}$  denoting expectation with respect to  $(\theta, G)$ , we also define

$$g_k^* \equiv g_k^*(\theta, G) \equiv E(R \mathbb{1}_{\{X=x_k\}}) = \sum_{j=1}^J p_j Q_j^*(x_k; \theta) g_k.$$

For  $t$  in a neighborhood of  $\theta$  and  $H$  ranging over the discrete distributions for  $X$ , our goal is to find the distribution

$$G_t \equiv G_t(\theta, G) \equiv \arg \max_H E[\log p(R, Z; t, H)]$$

that maximizes the expected log-likelihood  $\ell(t, H) \equiv \ell(t, H; \theta, G)$  given by

$$(3.2) \quad \begin{aligned} \ell(t, H) \equiv & E[R \log f(Y|X; t)] + E[R \log h(X)] \\ & + E[(1-R) \log Q_S(t, H)]. \end{aligned}$$

Towards this end we fix  $t$  and maximize (3.2) as a function of  $H = \{h_k\}$  subject to  $\sum_k h_k = 1$ . Following the arguments in Scott and Wild (1997) and LKW, introduce the Lagrange multiplier  $\lambda$  for the side condition  $(\sum_k h_k - 1) = 0$  and jointly solve the  $K + 1$  equations

$$(3.3) \quad \frac{\partial[\ell(t, H) + \lambda(\sum h - 1)]}{\partial h_k} = \frac{g_k^*}{h_k} + \sum_j (1-p_j) Q_j \frac{Q_j^*(x_k, t)}{\sum_\ell Q_j^*(x_\ell, t) h_\ell} + \lambda = 0$$

for  $k = 1, \dots, K$ , and

$$\sum_k h_k - 1 = 0.$$

Multiplying (3.3) by  $h_k$  and summing over  $k$  gives  $ER + (1 - ER) + \lambda = 0$  or  $\lambda = -1$ . This allows (3.3) to be reexpressed as

$$(3.4) \quad h_k = \frac{g_k^*}{\sum_j \pi_j [Q_j(t, H)] Q_j^*(x_k, t)}.$$

Substituting for  $h_k$  in (3.2) using (3.4) yields the profile expected log-likelihood

$$(3.5) \quad \begin{aligned} E \log p(R, Z; t, G_t) &= E[R \log f(Y|X; t)] \\ &\quad - \sum_k g_k \log \sum_j \pi_j [Q_j(t, G_t)] Q_j^*(x_k, t) \\ &\quad + \sum_j (1 - p_j) Q_j \log Q_j(t, G_t) + \text{constant}. \end{aligned}$$

This depends on  $G_t = \{g_t(x_k)\}$  only through the values of

$$(3.6) \quad Q_j^\dagger(t) \equiv Q_j(t, G_t) = \sum_k Q_j^*(x_k, t) g_t(x_k).$$

By substitution of  $g_t(x_k) = h_k$  from (3.4) into (3.6), the  $Q_j^\dagger(t)$  are determined for each  $t$  from the equations

$$(3.7) \quad Q_j^\dagger(t) = \sum_k \frac{Q_j^*(x_k; t) g_k^*}{\sum_\ell \pi_\ell [Q_\ell^\dagger(t)] Q_\ell^*(x_k; t)}, \quad j = 1, \dots, J.$$

It follows that  $G_t$  has point masses  $g_t(x_k)$  that arise by substitution of  $Q_j^\dagger(t)$  for the  $Q_j(t, G_t)$  in (3.4). Thus for  $x = x_k, k = 1, \dots, K$ ,

$$(3.8) \quad g_t(x) = \frac{\sum_{j=1}^J p_j Q_j^*(x, \theta)}{\sum_{j=1}^J \pi_j [Q_j^\dagger(t)] Q_j^*(x, t)} g(x).$$

Generalizing (3.7) and (3.8), suppose now that  $G_t \equiv G_t(\theta, G)$  has density  $g_t$  with respect to  $G$  given by

$$(3.9) \quad g_t(x) \equiv \frac{dG_t}{dG}(x) = \frac{\sum_{j=1}^J p_j Q_j^*(x, \theta)}{\sum_{j=1}^J \pi_j [Q_j^\dagger(t)] Q_j^*(x, t)}$$

where the  $Q_j^\dagger(t) \equiv Q_j(t, G_t)$  satisfy

$$(3.10) \quad Q_j^\dagger(t) = \int \frac{\sum_{\ell=1}^J p_\ell Q_\ell^*(x, \theta)}{\sum_{\ell=1}^J \pi_\ell [Q_\ell^\dagger(t)] Q_\ell^*(x, t)} Q_j^*(x, t) dG(x), \quad j = 1, \dots, J.$$

[In the next section we will also use the notation  $Q_j^\dagger(t, \theta, G) = Q_j(t, G_t(\theta, G))$ .] The log-likelihood for one observation for our proposed least favorable submodel

is given by

$$\begin{aligned}
 l(t, \theta, G)(r, z) &\equiv l(t, G_t(\theta, G))(r, z) \\
 &= r \left( \log f(y|x; t) + \log \frac{dG_t}{dG}(x, \theta, G) \right) \\
 (3.11) \quad &+ (1-r) \sum_{j=1}^J \delta_j \log Q_j^\dagger(t).
 \end{aligned}$$

Since the  $Q_j$  themselves satisfy (3.10) when  $t = \theta$ , it follows that  $G_\theta = G$  and thus that the submodel passes through  $(\theta, G)$  as required by MvdV's equation (8). To calculate  $\dot{l}(\theta, \theta, G)$ , the  $t$  derivative of (3.11), let  $\Delta_{.j} \equiv \partial Q_j^\dagger(t)/\partial t$  evaluated at  $t = \theta$ . The corresponding  $m \times J$  matrix  $\mathbf{\Delta}$  has elements  $\Delta_{kj}$ , rows  $\Delta_k$  and columns  $\Delta_{.j}$ . Differentiating both sides of (3.10) with respect to  $t$  shows that, for each  $k$ , the  $1 \times J$  gradient vector  $\Delta_k$  solves a system of linear equations. In fact, with  $\mathbf{M}$  and  $\mathbf{C}$  as defined in equations (2.8) and (2.9), it is given by

$$(3.12) \quad \Delta_k = (\dot{\mathbf{Q}} - \mathbf{C})_k \mathbf{M}^{-1} \text{diag}(\underline{Q}/\underline{q})$$

where  $\dot{\mathbf{Q}} - \mathbf{C}$  has components

$$\begin{aligned}
 (\dot{\mathbf{Q}} - \mathbf{C})_{kj} &= Q_j (E[\dot{\mathbf{i}}_{\theta_k}(Y|X) | S = j] \\
 (3.13) \quad &- E\{E[\dot{\mathbf{i}}_{\theta_k}(Y|X) | R = 1, X] | S = j\}).
 \end{aligned}$$

One interpretation of equations (3.12) and (3.13) is that the finite dimensional random variable  $\xi(S) = \Delta_{.S}/Q_S$  satisfies the linear equation [cf. equation (2.14)]

$$(3.14) \quad \xi(S) = E[\dot{\mathbf{i}}_\theta - E[\dot{\mathbf{i}}_\theta | R = 1, X] | S] - E\{E[q_S p_S^{-1} \xi(S) | R = 1, X] | S\}.$$

From (3.9) we have

$$\begin{aligned}
 \nabla_t \log g_t(x)|_{t=\theta} &= - \frac{\sum_j \dot{\pi}_j \Delta_{.j} Q_j^*(x, \theta) + \sum_j p_j \dot{Q}_{.j}^*(x, \theta)}{\pi^*(x)} \\
 (3.15) \quad &= -E \left[ \frac{q_S \Delta_{.S}}{p_S Q_S} \mid R = 1, X = x \right] - E[\dot{\mathbf{i}}_\theta | R = 1, X = x],
 \end{aligned}$$

where  $\dot{\pi}_j \equiv \partial \pi_j / \partial Q |_{Q=Q_j} = (1 - p_j)/Q_j$ . Similarly,

$$\begin{aligned}
 \nabla_t \log Q_j(\theta, G_t)|_{t=\theta} &= - \frac{1}{Q_j} \sum_\ell \dot{\pi}_\ell \Delta_{.\ell} \left\langle \frac{Q_\ell^*}{\pi^*}, Q_j^* \right\rangle - \frac{1}{Q_j} \sum_\ell p_\ell \left\langle \frac{\dot{Q}_{.\ell}^*}{\pi^*}, Q_j^* \right\rangle \\
 (3.16) \quad &= -E \left\{ E \left[ \frac{q_S \Delta_{.S}}{p_S Q_S} + \dot{\mathbf{i}}_\theta(Y|X) \mid R = 1, X \right] \mid S = j \right\}.
 \end{aligned}$$

Combining equations (3.11)–(3.16), we find

$$(3.17) \quad \dot{l}(\theta, \theta, G)(r, z) = r \psi(y, x) + (1-r) E[\psi(Y, X) | S = s]$$

where

$$(3.18) \quad \psi(y, x) = \dot{\mathbf{l}}_{\theta}(y|x) - E[\dot{\mathbf{l}}_{\theta} \mid R = 1, X = x] - E\left[\frac{q_S \Delta \cdot S}{p_S Q_S} \mid R = 1, X = x\right].$$

In view of (3.14),

$$E(\psi|S) = \xi(S) = \frac{\Delta \cdot S}{Q_S} = \mathbf{\Delta} \operatorname{diag}(1/\underline{Q})\underline{\delta} = (\dot{\mathbf{Q}} - \mathbf{C})\mathbf{M}^{-1} \operatorname{diag}(1/\underline{q})\underline{\delta}.$$

Consequently, we see that

$$(3.19) \quad \dot{\ell}(\theta, \theta, G)(r, z) = \mathbf{l}_{\theta}^*(r, z) = r\psi(y, x) + (1 - r)\xi(s)$$

is the efficient score given by (2.10). Equation (3.19), corresponding to MvdV’s equation (9), is the key condition for a least favorable submodel.

**4. Asymptotic theory via the least favorable submodel.** The main goal here is to give hypotheses which imply the conditions, and hence also the conclusions, of Theorem 1 of MvdV. Then we will prove a theorem giving joint asymptotic normality and efficiency of the estimators  $(\hat{\theta}_n, \hat{G}_n)$ .

The first issue is consistency. Although the models we are considering are quite closely related to those treated by van der Vaart and Wellner (1992) (they are exactly the same if  $\theta$  is known), the sufficient conditions for consistency given there fail in the present situation. In particular, (3.3) on page 138 of van der Vaart and Wellner (1992) fails in our current setting. However, a slightly different approach yields consistency in our case. van der Vaart and Wellner (2001) have established consistency of  $(\hat{\theta}_n, \hat{G}_n)$ . For completeness we give a brief statement of their results.

- A1.  $p_j > 0$  for  $j = 1, \dots, J$ .
- A2. The pair of parameters  $(\theta, G)$  is identifiable in the model

$$\mathcal{Q} = \{Q_{\theta, G} : dQ_{\theta, G}/d(v \times \mu) = q(\cdot; \theta, G), \theta \in \Theta, G \in \mathcal{G}\},$$

where  $q(y, x; \theta, G) = f(y|x; \theta)g(x)$  as in (2.1).

- A3.  $Q_j(\theta_0, G_0) \in (0, 1)$  for  $j = 1, \dots, J$ ; this holds without loss of generality.
- C1.  $\mathcal{X}$  is a semimetric space that has a completion that is compact and contains  $\mathcal{X}$  as a Borel set.
- C2. The maps  $(\theta, x) \mapsto Q_j^*(x, \theta)$  are uniformly continuous and  $\theta \mapsto f(y|x; \theta)$  are upper semicontinuous for all  $(y, x) \in \mathcal{Y} \times \mathcal{X}$ .
- C3.  $\Theta$  is a compact metric space.
- C4.  $P_0(\sup_{\theta \in \Theta} \log(f(Y|X; \theta)/f(Y|X; \theta_0))) < \infty$ .

**PROPOSITION 4.1** [Consistency of  $(\hat{\theta}_n, \hat{G}_n)$ ]. *Suppose that A1–A3 and C1–C4 hold. Then  $\hat{\theta}_n \rightarrow_{a.s.} \theta_0$  and  $\sup_{h \in \mathcal{H}} |(\hat{G}_n - G_0)h| \rightarrow_{a.s.} 0$  for every  $G$   $C$ -class  $\mathcal{H}$  that is bounded in  $L_1(G_0)$ .*

The proof of Proposition 4.1 is given in van der Vaart and Wellner (2001).

With consistency established, we now turn to a study of the asymptotic distributions of the profile likelihood and the maximum likelihood estimators for the special case of VPS1 (Bernoulli) sampling. We will rely on the results of MvdV [see also Murphy and van der Vaart (1997), (1999)]. We have already verified the key condition (9) of Theorem 1 of MvdV in (3.19) of the previous section.

Now let the log-profile likelihood  $\ell_n^P(\theta)$  be defined by

$$\ell_n^P(\theta) = \log L_n(\theta, \widehat{G}_n(\cdot, \theta))$$

where  $\widehat{G}_n(\cdot, \theta)$  is the maximizer of  $\log L_n(\theta, G)$  over distributions  $G$  concentrated at the observed  $X_i$ 's as in LKW. Thus for a Borel subset  $A$  of  $\mathcal{X}$

$$(4.1) \quad \widehat{G}_n(A, \theta) = \mathbb{P}_n \left( \mathbb{1}_A(X) \frac{R}{\widehat{s}_n(X, \underline{Q}_n(\theta), \theta)} \right)$$

where, with  $N_j = n\mathbb{P}_n \mathbb{1}_{[S=j]}$  and  $n_j = n\mathbb{P}_n(R\mathbb{1}_{[S=j]})$  as defined in Section 2,

$$(4.2) \quad \widehat{s}_n(x, \underline{Q}, \theta) = \sum_{j=1}^J \left( 1 - \frac{N_j - n_j}{nQ_j} \right) Q_j^*(x, \theta),$$

and  $\underline{\widehat{Q}}_n = \underline{Q}_n(\theta)$  satisfies

$$(4.3) \quad \underline{\widehat{Q}}_n(\theta) = \mathbb{P}_n \left( \frac{R}{\widehat{s}_n(\cdot, \underline{\widehat{Q}}_n(\theta), \theta)} \underline{Q}^*(\cdot, \theta) \right).$$

Then  $\widehat{\theta}_n = \arg \max_{\theta} \ell_n^P(\theta)$ , and  $\widehat{G}_n = \widehat{G}_n(\cdot, \widehat{\theta}_n)$ .

In order to establish the remaining conditions of MvdV's Theorem 1 we assume the following:

L0. Assumptions A1–A3 and C1–C4 hold.

L1. The maps  $\theta \mapsto \{\dot{l}_{\theta}(y|x) : y \in \mathcal{Y}, x \in \mathcal{X}\}$ ,  $\theta \mapsto Q^*(\cdot, \theta)$  and  $\theta \mapsto \dot{Q}^*(\cdot, \theta)$  are all Lipschitz in the sense that, for all  $t, s$  in a neighborhood of  $\theta_0$  and all  $(y, x) \in \mathcal{Y} \times \mathcal{X}$ :

$$|\dot{l}_t(y|x) - \dot{l}_s(y|x)| \leq M(y, x)|t - s|$$

where

$$P_0 M^2 = \int M^2(y, x) f(y|x, \theta_0) dv(y) dG_0(x) < \infty;$$

$$|Q^*(x, t) - Q^*(x, s)| \leq M(x)|t - s|$$

where

$$G_0 |M|^2 = \int M^2(x) dG_0(x) < \infty;$$

and

$$|\dot{Q}^*(x, t) - \dot{Q}^*(x, s)| \leq \dot{M}(x)|t - s|$$

where

$$G_0|\dot{M}|^2 = \int \dot{M}^2(x) dG_0(x) < \infty.$$

L2. For some  $\delta_0 > 0$  the collections of functions

$$\{r\ddot{l}_{l,k,l}(y|x) : |t - \theta_0| \leq \delta_0, k, l = 1, \dots, m\}$$

and

$$\{r\ddot{Q}_{j,k,l}^*(x, t) : |t - \theta_0| \leq \delta_0, j = 1, \dots, J, k, l = 1, \dots, m\}$$

are  $P_0$ -Glivenko–Cantelli classes of functions.

L3. There is no  $m$ -vector  $a$  such that  $a^T \dot{\mathbf{I}}_\theta(Y|X)$  is constant in  $Y$  for  $G$ -a.e.  $X$ . [Equivalently, the information matrix for  $\theta$  with no missing data given in (2.16) is nonsingular.]

**THEOREM 4.1.** *Suppose that L0–L3 hold. Then for any random sequence  $\tilde{\theta}_n \rightarrow_p \theta_0$  it follows that*

$$(4.4) \quad \begin{aligned} \ell_n^P(\tilde{\theta}_n) &= \ell_n^P(\theta_0) + (\tilde{\theta}_n - \theta_0)^T \sum_{i=1}^n \mathbf{I}_\theta^*(R_i, Z_i) - \frac{1}{2}n(\tilde{\theta}_n - \theta_0)^T I(\theta_0)(\tilde{\theta}_n - \theta_0) \\ &\quad + o_p(\sqrt{n}\|\tilde{\theta}_n - \theta_0\| + 1)^2 \end{aligned}$$

where  $\mathbf{I}_\theta^*$  is given by (2.10) and  $I(\theta_0)$  is given by (2.11).

As shown by MvdV in their Corollaries 1 and 2, the expansion (4.4) together with invertibility of  $I(\theta_0)$  implies  $\tilde{\theta}_n$  is asymptotically linear with efficient influence function  $\tilde{\mathbf{I}}_\theta = I(\theta_0)^{-1}\mathbf{I}_\theta^*$  given by (2.12),

$$(4.5) \quad \sqrt{n}(\tilde{\theta}_n - \theta_0) = \frac{1}{\sqrt{n}} \sum_{i=1}^n I(\theta_0)^{-1}\mathbf{I}_\theta^*(R_i, Z_i) + o_p(1).$$

Moreover, the expansion

$$(4.6) \quad \begin{aligned} \ell_n^P(\tilde{\theta}_n) &= \ell_n^P(\hat{\theta}_n) + (\tilde{\theta}_n - \hat{\theta}_n)^T \sum_{i=1}^n \mathbf{I}_\theta^*(R_i, Z_i) - \frac{1}{2}n(\tilde{\theta}_n - \hat{\theta}_n)^T I(\theta_0)(\tilde{\theta}_n - \hat{\theta}_n) \\ &\quad + o_p(\sqrt{n}\|\tilde{\theta}_n - \theta_0\| + 1)^2, \end{aligned}$$

also holds and the likelihood ratio statistic based on the profile likelihood is asymptotically  $\chi_m^2$ :

$$(4.7) \quad 2\{\ell_n^P(\hat{\theta}_n) - \ell_n^P(\theta_0)\} \rightarrow_d \chi_m^2.$$

PROOF OF THEOREM 4.1. We begin by verifying conditions (8)–(10) of MvdV. Condition (8) of MvdV is indeed satisfied by the submodel  $(t, G_t(\theta, G))$  given by (3.9);  $(t, G_t(\theta, G))$  passes through  $(\theta, G)$  at  $t = \theta$ . We have already seen in (3.19) that condition (9) of MvdV holds. Condition (10) of MvdV requires that  $\widehat{G}_n(\theta)$ , the maximizer of the log-likelihood over  $G$  for fixed  $\theta$ , satisfies

$$(4.8) \quad \widehat{G}_n(\tilde{\theta}_n) \rightarrow_p G_0$$

for every random sequence  $\tilde{\theta}_n$  with  $\tilde{\theta}_n \rightarrow_p \theta_0$ . This holds by virtue of the arguments in van der Vaart and Wellner [(2001), pages 281 and 282].

We will postpone verification of condition (11) of MvdV; in fact, verification of this condition will occupy most of our proof.

To verify the Donsker and Glivenko–Cantelli hypotheses of Theorem 1 of MvdV, we need first to compute the functions  $\dot{l}_t(t, \theta, G)$  and  $\ddot{l}_t(t, \theta, G)$ . The log-likelihood for one observation for the least favorable submodel is given by  $l(t, \theta, G)$  in (3.11) where  $Q_j^\dagger(t) \equiv Q_j(t, G_t(\theta, G))$ ,  $j = 1, \dots, J$ . We need to calculate the first and second derivatives of this function with respect to  $t$ . To do this, we first calculate the first and second derivatives of  $\log(dG_t/dG)$

$$(4.9) \quad \begin{aligned} &\nabla_t \log\left(\frac{dG_t}{dG}(x; \theta, G)\right) \\ &= \frac{-\sum_{j=1}^J \nabla_t \{(1 - (Q_j(1 - p_j)/Q_j^\dagger(t)))Q_j^*(x, t)\}}{\sum_{j=1}^J (1 - (Q_j(1 - p_j)/Q_j^\dagger(t)))Q_j^*(x, t)} \\ &= -\frac{\sum_{j=1}^J (1 - (Q_j(1 - p_j)/Q_j^\dagger(t)))\dot{Q}_j^*(x, t)}{\sum_{j=1}^J (1 - (Q_j(1 - p_j)/Q_j^\dagger(t)))Q_j^*(x, t)} \\ &\quad + \frac{\sum_{j=1}^J Q_j^*(x, t)(Q_j(1 - p_j)/[Q_j^\dagger(t)]^2)\nabla_t Q_j^\dagger(t)}{\sum_{j=1}^J (1 - (Q_j(1 - p_j)/Q_j^\dagger(t)))Q_j^*(x, t)}. \end{aligned}$$

Here the derivative vector  $\nabla_t Q_j^\dagger(t)$  satisfies a linear equation which can be derived by differentiating across (3.10); see (3.12) and (A.3). Note that this is basically a ratio of a (family of) linear combination(s) of the functions  $Q_j^*(\cdot, t)$ ,  $\dot{Q}_j^*(\cdot, t)$  and the family of functions  $s_t$  given by

$$(4.10) \quad s_t(x) \equiv \sum_{j=1}^J \left(1 - \frac{Q_j(1 - p_j)}{Q_j^\dagger(t)}\right) Q_j^*(x, t).$$

We also define

$$(4.11) \quad s_0(x, \underline{Q}, \theta) = \sum_{j=1}^J \left(1 - \frac{Q_j^0(1 - p_j)}{Q_j}\right) Q_j^*(x, \theta)$$

where  $Q_j^0 = Q_j(\theta_0, G_0)$ . Note that  $s_{\theta_0}(x; \theta_0, G_0) = \pi^*(x) = s_0(x, \underline{Q}^0, \theta_0)$  for all  $x \in \mathcal{X}$  with  $\pi^*$  as defined in (2.7). Thus we also write (in a slight abuse of notation)

$s_0$  instead of  $\pi^*$ . Calculation of the second derivatives yields

$$\begin{aligned}
 & \nabla_t \left( \nabla_t \log \left( \frac{dG_t}{dG}(x; \theta, G) \right) \right) \\
 &= \left\{ \nabla_t \log \left( \frac{dG_t}{dG}(x; \theta, G) \right) \right\}^{\otimes 2} \\
 & \quad - \sum_{j=1}^J \left\{ \left( 1 - \frac{Q_j(1-p_j)}{Q_j^\dagger(t)} \right) \ddot{Q}_j^*(x, t) \right. \\
 (4.12) \quad & \quad \quad + \frac{Q_j(1-p_j)}{[Q_j^\dagger(t)]^2} (\dot{Q}_j^*(x, t))^{\otimes 2} \\
 & \quad \quad + \dot{Q}_j^*(x, t) \frac{Q_j(1-p_j)}{[Q_j^\dagger(t)]^2} \nabla_t Q_j^\dagger(t) \\
 & \quad \quad - 2Q_j^*(x, t) \frac{Q_j(1-p_j)}{[Q_j^\dagger(t)]^3} (\nabla_t Q_j^\dagger(t))^{\otimes 2} \\
 & \quad \quad \left. + Q_j^*(x, t) \frac{Q_j(1-p_j)}{[Q_j^\dagger(t)]^2} \ddot{Q}_j^\dagger(t) \right\} / s_t(x)
 \end{aligned}$$

where  $s_t$  is defined in (4.10). Thus we find that

$$\begin{aligned}
 \dot{l}(t, \theta, G)(r, z) &\equiv \nabla_t l(t, \theta, G)(r, z) \\
 (4.13) \quad &= r \left( \dot{l}_t(y|x) + \nabla_t \log \left( \frac{dG_t}{dG}(x; \theta, G) \right) \right) \\
 & \quad + (1-r) \sum_{j=1}^J \delta_j \frac{\nabla_t Q_j(t, G_t)}{Q_j(t, G_t)}
 \end{aligned}$$

and

$$\begin{aligned}
 (4.14) \quad \ddot{l}(t, \theta, G)(r, z) &\equiv \nabla_t \dot{l}(t, \theta, G)(r, z) \\
 &= r \left( \ddot{l}_t(y|x) + \nabla_t \left( \nabla_t \log \left( \frac{dG_t}{dG}(x; \theta, G) \right) \right) \right) \\
 (4.15) \quad & \quad + (1-r) \sum_{j=1}^J \delta_j \left\{ \frac{\ddot{Q}_j^\dagger(t)}{Q_j^\dagger(t)} - \frac{[\dot{Q}_j^\dagger(t)]^2}{[Q_j^\dagger(t)]^2} \right\}.
 \end{aligned}$$

We now show that there is a neighborhood  $V$  of  $(\theta_0, \theta_0, G_0)$  such that the classes of functions

$$\{ \dot{l}_k(t, \theta, G) : (t, \theta, G) \in V, k = 1, \dots, m \}$$

with  $\dot{l}(t, \theta, G)$  as given by (4.13) and (4.9) are  $P_0$ -Donsker with square integrable envelope function. First note that by L1 the collections

$$\begin{aligned}
 & \{ r \dot{l}_{k,t} : (t, \theta, G) \in V, k = 1, \dots, m \}, \\
 & \{ r Q_j^*(\cdot, t) : (t, \theta, G) \in V, j = 1, \dots, J \}
 \end{aligned}$$

and

$$\{r\dot{Q}_{jk}^*(\cdot, t) : (t, \theta, G) \in V, j = 1, \dots, J, k = 1, \dots, m\}$$

are  $P_0$ -Donsker by virtue of the Jain–Marcus CLT [see Example 2.11.13, page 213, van der Vaart and Wellner (1996)]. Then, since products of these functions with bounded families of constants are also  $P_0$ -Donsker by an application of Corollary 2.10.13, page 193, van der Vaart and Wellner (1996), the individual terms appearing in the numerator of (4.9) are also  $P_0$ -Donsker, and hence also their sum by application of Example 2.10.7, page 192, van der Vaart and Wellner (1996). Then, since  $s_0(x)$  is bounded uniformly away from zero by A1 and  $\sum_j Q_j^*(x, \theta_0) = 1$ ,  $s_t(x)$  is also bounded away from zero uniformly in  $x$  and  $t$  in a sufficiently small neighborhood of  $\theta_0$ . Hence the ratio appearing in (4.9) is also  $P_0$ -Donsker by virtue of Example 2.10.9, page 192, van der Vaart and Wellner (1996). Furthermore, the neighborhood  $V$  of  $(\theta_0, \theta_0, G_0)$  can be chosen so that the class of functions

$$\{\ddot{l}(t, \theta, G) : (t, \theta, G) \in V\}$$

with  $\ddot{l}(t, \theta, G)$  given by (4.15) and (4.12) is  $P_0$ -Glivenko–Cantelli with integrable envelope function. This follows from L2 [to handle the terms involving  $\ddot{l}_t(y|x)$  and  $\ddot{Q}_{j,k,l}^*(x, t)$ ], Lemma 2.10.14, page 194, van der Vaart and Wellner (1996), and the Glivenko–Cantelli preservation theorem of van der Vaart and Wellner (2000) to handle the remaining terms.

We now turn our attention to verification of the remaining condition (11) of MvdV. The discussion leading to MvdV’s (16) applies so that, in place of their condition (11), it suffices to verify that for convergent sequences  $\tilde{\theta}_n$

$$(4.16) \quad P_0 \dot{\ell}(\theta_0, \theta_0, \widehat{G}_n(\tilde{\theta}_n)) = o_p(\|\tilde{\theta}_n - \theta_0\| + n^{-1/2}).$$

As argued by MvdV, page 458, (4.16) can be shown to hold if their display (18) holds; in our context their display (18) becomes

$$(4.17) \quad \|\widehat{G}_n(\tilde{\theta}_n) - G_0\|_{\mathcal{H}} = O_p(\|\tilde{\theta}_n - \theta_0\|) + O_p(n^{-1/2})$$

where  $\mathcal{H}$  is a universal-Donsker class of real-valued (measurable) functions on  $\mathcal{X}$ . Once again the key observation comes from LKW: to find  $\widehat{G}_n$  one does not need to estimate all of  $G$ , but just the quantities  $Q_j(\theta, G)$  which, for fixed  $\theta$ , are determined by equations (3.10). We view this system of equations as processes in  $\theta$  in a neighborhood of  $\theta_0$  and show that the convergence of the corresponding  $\widehat{Q}_j(\theta)$  processes is uniform in  $\theta$ . Towards this end, consider

$$\Psi_n(\underline{Q})(\theta) \equiv \underline{Q} - \mathbb{P}_n \left( \frac{R}{\widehat{s}_n(\cdot, \underline{Q}, \theta)} \underline{Q}^*(\cdot, \theta) \right)$$

and

$$\Psi(\underline{Q})(\theta) \equiv \underline{Q} - P_0 \left( \frac{R}{s_0(\cdot, \underline{Q}, \theta)} \underline{Q}^*(\cdot, \theta) \right);$$

here  $\widehat{s}_n$  is given by (4.2) and  $s_0(\cdot, \underline{Q}, \theta)$  is given by (4.11). Note that  $\Psi_n(\widehat{Q}_n(\theta))(\theta) = \underline{0}$  defines  $\widehat{Q}_n(\theta)$ , while  $\Psi(\underline{Q}_0(\theta))(\theta) = \underline{0}$  defines  $\underline{Q}_0(\theta)$ . Also note that  $\underline{Q}_0(\theta_0) = \underline{Q}^0 = \underline{Q}(\theta_0, G_0)$ .

PROPOSITION 4.2. *Suppose that L0–L3 hold. Then for some (sufficiently small) closed ball  $B(\theta_0)$  in  $R^m$  centered at  $\theta_0$ ,*

$$(4.18) \quad \sqrt{n}(\widehat{Q}_n(\theta) - \underline{Q}_0(\theta)) \Rightarrow \mathbb{Q}(\theta) \quad \text{in } C[B(\theta_0)]^J$$

where  $\mathbb{Q}(\theta)$  is a zero-mean Gaussian process.

Once we have proved (4.18), the next step is to show that (4.17) holds for any random sequence  $\tilde{\theta}_n \rightarrow_p \theta_0$ . In other words, we want to show that

$$(4.19) \quad \|\sqrt{n}(\widehat{G}_n(h; \tilde{\theta}_n) - G_0(h))\|_{\mathcal{H}} = O_p(1) + \sqrt{n}(\tilde{\theta}_n - \theta_0).$$

To this end, we first abbreviate notation slightly:  $\widehat{s}_n(x, \widehat{Q}_n(\tilde{\theta}_n), \tilde{\theta}_n) \equiv \widehat{s}_n(x, \tilde{\theta}_n)$ . Then we have

$$(4.20) \quad \begin{aligned} \sqrt{n}(\widehat{G}_n(h; \tilde{\theta}_n) - G_0(h)) &= \sqrt{n}\left(\mathbb{P}_n\left(\frac{R}{\widehat{s}_n(\cdot, \tilde{\theta}_n)}h\right) - P_0\left(\frac{R}{s_0}h\right)\right) \\ &= \sqrt{n}\left(\mathbb{P}_n\left(\frac{R}{s_0}h\right) - P_0\left(\frac{R}{s_0}h\right)\right) \\ &\quad + \sqrt{n}\mathbb{P}_n\left(Rh\left(\frac{1}{\widehat{s}_n(\cdot, \tilde{\theta}_n)} - \frac{1}{s_0}\right)\right) \\ &= \mathbb{G}_n\left(\frac{R}{s_0}h\right) - \mathbb{P}_n\left(\frac{Rh\sqrt{n}(\widehat{s}_n(\cdot, \tilde{\theta}_n) - s_0)}{\widehat{s}_n(\cdot, \tilde{\theta}_n)s_0}\right) \\ &\equiv I_n(h) - II_n(h). \end{aligned}$$

Here  $\mathbb{G}_n \equiv \sqrt{n}(\mathbb{P}_n - P_0)$  is the empirical process and hence  $\|I_n\|_{\mathcal{H}} = O_p(1)$  easily via standard theory. To understand the term  $II_n(h)$ , we write

$$(4.21) \quad \begin{aligned} II_n(h) &= -\mathbb{P}_n\left(\frac{Rh}{s_0\widehat{s}_n(\cdot, \tilde{\theta}_n)}\sqrt{n}\right. \\ &\quad \times \left.\sum_{j=1}^J\left(\frac{N_j - n_j}{n}\frac{1}{\widehat{Q}_j(\tilde{\theta}_n)}Q_j^*(\cdot, \tilde{\theta}_n) - \frac{Q_j^0(1 - p_j)}{Q_j^0}Q_j^*(\cdot, \theta_0)\right)\right) \\ &\quad + \mathbb{P}_n\left(\frac{Rh}{s_0\widehat{s}_n(\cdot, \tilde{\theta}_n)}\sum_{j=1}^J\sqrt{n}(Q_j^*(\cdot, \tilde{\theta}_n) - Q_j^*(\cdot, \theta_0))\right) \\ &= -\sum_{j=1}^J\sqrt{n}\left(\frac{N_j - n_j}{n} - Q_j^0(1 - p_j)\right)\frac{1}{\widehat{Q}_j(\tilde{\theta}_n)}\mathbb{P}_n\left(\frac{Rh}{s_0\widehat{s}_n(\cdot, \tilde{\theta}_n)}Q_j^*(\cdot, \tilde{\theta}_n)\right) \end{aligned}$$

$$\begin{aligned}
 &+ \sum_{j=1}^J \sqrt{n} \left\{ \frac{\widehat{Q}_j(\tilde{\theta}_n) - Q_j(\tilde{\theta}_n)}{\widehat{Q}_j(\tilde{\theta}_n) Q_j^0} \right\} Q_j^0 (1 - p_j) \mathbb{P}_n \left( \frac{Rh}{s_0 \widehat{s}_n(\cdot, \tilde{\theta}_n)} Q_j^*(\cdot, \tilde{\theta}_n) \right) \\
 &+ \sum_{j=1}^J \sqrt{n} \left\{ \frac{Q_j(\tilde{\theta}_n) - Q_j^0}{\widehat{Q}_j(\tilde{\theta}_n) Q_j^0} \right\} Q_j^0 (1 - p_j) \mathbb{P}_n \left( \frac{Rh}{s_0 \widehat{s}_n(\cdot, \tilde{\theta}_n)} Q_j^*(\cdot, \tilde{\theta}_n) \right) \\
 &+ \mathbb{P}_n \left( \frac{Rh}{s_0 \widehat{s}_n(\cdot, \tilde{\theta}_n)} \right) \sum_{j=1}^J p_j \dot{Q}_j^*(\cdot, \theta_n^\sharp) \sqrt{n} (\tilde{\theta}_n - \theta_0) \\
 &\equiv A_n(h) + B_n(h) + C_n(h) + D_n(h).
 \end{aligned}$$

Here  $Q_j(\tilde{\theta}_n) \equiv Q_{j0}(\tilde{\theta}_n)$  satisfies  $\Psi(\underline{Q}_0(\tilde{\theta}_n))(\tilde{\theta}_n) = 0$ . Now  $\|A_n\|_{\mathcal{H}} = O_p(1)$  by  $\sqrt{n}((N_j - n_j)/n - Q_j^0(1 - p_j)) = O_p(1)$ , consistency of  $\widehat{G}_n$ , and uniform (in  $\theta$ ) convergence of  $\widehat{Q}_n(\theta)$  in a neighborhood of  $\theta_0$ ;  $\|B_n\|_{\mathcal{H}} = O_p(1)$  by Proposition 4.2 and consistency of  $\widehat{G}_n$ ;  $\|C_n\|_{\mathcal{H}} = O_p(\sqrt{n}(\tilde{\theta}_n - \theta_0))$  by differentiability of the maps  $\theta \mapsto Q_{0j}(\theta)$  and consistency of  $\widehat{G}_n$ ; and  $\|D_n\|_{\mathcal{H}} = O_p(\sqrt{n}(\tilde{\theta}_n - \theta_0))$  easily by consistency of  $\widehat{G}_n$ .

But in view of the differentiability of  $\underline{Q}^\dagger(\theta_0, \theta, G_0) \equiv \underline{Q}_0(\theta)$  with respect to  $\theta$  proved in (A.2) [using the definition of  $\underline{Q}_j^\dagger(t, \theta, G)$  following (3.10)], we have, by the mean-value theorem,

$$\sqrt{n}(\underline{Q}_0(\tilde{\theta}_n) - \underline{Q}_0(\theta_0)) = \nabla_\theta \underline{Q}_0(\theta)|_{\theta=\theta_n^\sharp} \cdot \sqrt{n}(\tilde{\theta}_n - \theta_0),$$

and thus we see, by combining  $I_n$  and  $II_n$  together with a bit more Glivenko–Cantelli, that (4.19) holds.  $\square$

PROOF OF NONSINGULARITY OF  $I(\theta_0)$  AND (4.5)–(4.7). We now prove that  $I(\theta_0)$  is nonsingular and hence, via Corollaries 1 and 2 of MvdV, that (4.5)–(4.7) hold. Recall the formula for  $I(\theta_0)$  given in (2.11),

$$(4.22) \quad I(\theta_0) = E_0 \left\{ R \left( \mathbf{i}_\theta(Y|X) - \frac{\dot{Q}^*}{\pi^*}(X) \underline{p} \right)^{\otimes 2} \right\} + (\dot{Q} - \mathbf{C}) \mathbf{M}^{-1} (\dot{Q} - \mathbf{C})^T.$$

It is clear from the form of the two terms in (4.22) that each is nonnegative definite. Thus, to be invertible, at least one term must be positive definite.

In the first term in (4.22) we have

$$\dot{Q}^*(X) \underline{p} = \sum_{j=1}^J p_j \dot{Q}_j^*(X) = E_0(\mathbf{R} \mathbf{i}_\theta(Y|X) | X)$$

since

$$\dot{Q}_j^*(X) = E_0(\delta_j \mathbf{i}_\theta(Y|X) | X)$$

and we recall that

$$\frac{\dot{Q}^*}{\pi^*}(X) \underline{p} = E_0(\mathbf{i}_\theta | X, R = 1).$$

Consider quadratic forms of this matrix with an arbitrary  $m$ -vector  $a$ . We have

$$\begin{aligned} & a^T E_0 \left\{ R \left( \mathbf{i}_\theta(Y|X) - \frac{E_0(R\mathbf{i}_\theta(Y|X) | X)}{\pi^*(X)} \right)^{\otimes 2} \right\} a \\ &= E_0 \left\{ \sum_{j=1}^J p_j \delta_j E_0 \left( \left( a^T \mathbf{i}_\theta(Y|X) - \frac{E_0(Ra^T \mathbf{i}_\theta(Y|X) | X)}{\pi^*(X)} \right)^2 \middle| \frac{\delta}{j} \right) \right\} \\ &\geq \min_j p_j E_0 \left\{ \left( a^T \mathbf{i}_\theta(Y|X) - \frac{E_0(Ra^T \mathbf{i}_\theta(Y|X) | X)}{\pi^*(X)} \right)^2 \right\} \end{aligned}$$

which is 0 if and only if

$$a^T \mathbf{i}_\theta(Y|X) = \frac{E_0(Ra^T \mathbf{i}_\theta(Y|X) | X)}{\pi^*(X)}, \quad P_0\text{-a.s.}$$

This would require  $a^T \mathbf{i}_\theta(Y|X)$  to be constant in  $Y$  in which case the equality follows from the fact that  $E_0(R | X) = \pi^*(X)$ . Thus L3 implies that the first term in (4.22) is positive definite, and hence  $I(\theta_0)$  is invertible.  $\square$

PROOF OF PROPOSITION 4.2. We will apply van der Vaart’s Z-theorem; see van der Vaart (1995) and van der Vaart and Wellner [(1996), Theorem 3.3.1, page 310]. To this end, note that

$$\begin{aligned} \mathbb{Z}_n(\underline{Q})(\theta) &\equiv \sqrt{n}(\Psi_n(\underline{Q})(\theta) - \Psi(\underline{Q})(\theta)) \\ &= -\mathbb{G}_n \left( \frac{R}{s_0(\cdot, \underline{Q}, \theta)} \underline{Q}^*(\cdot, \theta) \right) \\ &\quad - \mathbb{P}_n \left( R \frac{\sum_{j=1}^J \sqrt{n}[(N_j - n_j)/n - Q_j^0(1 - p_j)] Q_j^*(\cdot, \theta) / Q_j}{\widehat{s}_n(\cdot, \underline{Q}, \theta) s_0(\cdot, \underline{Q}, \theta)} \underline{Q}^*(\cdot, \theta) \right) \\ &= -\mathbb{G}_n \left( \frac{R}{s_0(\cdot, \underline{Q}, \theta)} \underline{Q}^*(\cdot, \theta) \right) \\ &\quad - \sum_{j=1}^J \sqrt{n} \left( \frac{N_j - n_j}{n} - Q_j^0(1 - p_j) \right) \\ &\quad \times \mathbb{P}_n \left( \frac{R Q_j^*(\cdot, \theta) / Q_j}{\widehat{s}_n(\cdot, \underline{Q}, \theta) s_0(\cdot, \underline{Q}, \theta)} \underline{Q}^*(\cdot, \theta) \right). \end{aligned}$$

Now it follows easily from L1 and the Jain–Marcus CLT that

$$\mathbb{Z}_n(\underline{Q}_0(\theta))(\theta) \Rightarrow \mathbb{Z}_0(\theta)$$

as a (vector of) process(es) indexed by  $\theta \in B(\theta_0)$ , and that

$$\sup_{\underline{Q} \in \text{Lip}[B(\theta_0)]^J : \|\underline{Q}(\theta) - \underline{Q}_0(\theta)\| \leq \delta_n} \|\mathbb{Z}_n(\underline{Q}) - \mathbb{Z}_n(\underline{Q}_0)\|_{B(\theta_0)} = o_p(1)$$

for every sequence  $\delta_n \rightarrow 0$ . Furthermore,

$$\begin{aligned}\nabla_Q \Psi(Q) &= I + P_0 \left( \frac{R}{s_0(\cdot, Q, \theta)^2} \underline{Q}^*(\cdot, \theta) \nabla_Q s_0(\cdot, Q, \theta) \right) \\ &= I + P_0 \left( \frac{R}{s_0(\cdot, Q, \theta)^2} \underline{Q}^*(\cdot, \theta) \text{diag}(Q_j^0(1-p_j)/Q_j^2) \underline{Q}^*(\cdot, \theta)^T \right)\end{aligned}$$

is always nonsingular, and hence via the chain rule we see that the derivative map  $\dot{\Psi} : \text{Lip}(B(\theta_0))^J \mapsto \text{Lip}(B(\theta_0))^J$  exists and has a bounded inverse at  $\underline{Q}_0 = \{\underline{Q}_0(\theta) : \theta \in B(\theta_0)\}$ .  $\square$

**5. Joint asymptotic normality and efficiency of  $(\hat{\theta}_n, \hat{G}_n)$ , Bernoulli sampling.** We now turn to a study of the joint asymptotic distributions of the maximum likelihood estimators (MLE)  $(\hat{\theta}_n, \hat{G}_n)$  for the special case of VPS1 (Bernoulli) sampling. The density for the data under VPS1 given in (2.3) is our starting point. We will use the infinite-dimensional Z-theorem given in van der Vaart (1995), van der Vaart and Wellner [(1996), pages 314–319], and van der Vaart [(1998), Section 25.12], primarily as a way to organize the statement of the theorem. In fact the proof will use the development of Section 4.

Our first job is to calculate the score functions  $\Psi_n$  [using the notation of van der Vaart (1998)]. It follows from (2.3) that

$$\begin{aligned}\log L_n(\theta, G) &= \sum_{j=1}^J \left\{ \sum_{i \in D_j} [\log f(Y_i | X_i; \theta) + \log g(X_i)] + (N_j - n_j) \log Q_j(\theta, G) \right\} \\ (5.1) \quad &= \sum_{i=1}^n \left\{ R_i (\log f(Y_i | X_i; \theta) + \log g(X_i)) \right. \\ &\quad \left. + (1 - R_i) \sum_{j=1}^J \delta_{ij} \log Q_j(\theta, G) \right\}.\end{aligned}$$

With the notation as in Proposition 2.1, this yields

$$\begin{aligned}\Psi_{n1}(\theta, G) &\equiv \frac{1}{n} \dot{\mathbf{l}}_{n\theta}(\theta, G) \equiv \frac{1}{n} \nabla_{\theta} \log L_n(\theta, G) \\ &= \frac{1}{n} \sum_{i=1}^n \left\{ R_i \dot{\mathbf{l}}_{\theta}(Y_i | X_i) + (1 - R_i) \sum_{j=1}^J \delta_{ij} \frac{\dot{Q}_j(\theta, G)}{Q_j(\theta, G)} \right\} \\ &= \mathbb{P}_n \left( R \dot{\mathbf{l}}_{\theta}(Y | X) + (1 - R) \frac{\dot{Q}_S(\theta, G)}{Q_S(\theta, G)} \right),\end{aligned}$$

so that the MLE  $(\hat{\theta}, \hat{G})$  of  $(\theta, G)$  satisfies  $\Psi_{n1}(\hat{\theta}, \hat{G}) = 0$ . Now let  $\hat{G}$  be the MLE of  $G$  and, for any bounded real-valued function  $h$  on  $\mathcal{X}$ , let

$$d\hat{G}_t \equiv \left( 1 + t(h - \int h d\hat{G}) \right) d\hat{G}.$$

Then, with

$$(5.2) \quad \Psi_{n2}(\theta, G)(h) = \mathbb{P}_n A_{\theta, G} h - P_{\theta, G} A_{\theta, G} h,$$

where  $A_{\theta, G}$  is given by (2.5), we find that the MLE  $(\hat{\theta}, \hat{G})$  of  $(\theta, G)$  also satisfies

$$(5.3) \quad \begin{aligned} 0 &= \frac{1}{n} \dot{l}_t(\hat{\theta}, \hat{G}) \\ &= \frac{1}{n} \sum_{i=1}^n \left\{ R_i \left( h(X_i) - \int h d\hat{G} \right) \right. \\ &\quad \left. + (1 - R_i) \sum_{j=1}^J \delta_{ij} \frac{\int Q_j^*(x, \hat{\theta})(h(x) - \int h d\hat{G}) d\hat{G}}{Q_j(\hat{\theta}, \hat{G})} \right\} \\ &= \mathbb{P}_n A_{\hat{\theta}, \hat{G}} h - P_{\hat{\theta}, \hat{G}} A_{\hat{\theta}, \hat{G}} h = \Psi_{n2}(\hat{\theta}, \hat{G})(h). \end{aligned}$$

The population version of the score for  $\theta$  is

$$(5.4) \quad \begin{aligned} \Psi_1(\theta, G) &= P_0(\dot{\mathbf{l}}_\theta(\theta, G)) = P_0 \left( R \dot{\mathbf{l}}_\theta(Y|X) + (1 - R) \sum_{j=1}^J \delta_j \frac{\dot{Q}_j(\theta, G)}{Q_j(\theta, G)} \right) \\ &= P_0(R \dot{\mathbf{l}}_\theta(Y|X) + \dot{\mathbf{Q}}(\theta, G) \text{diag}(Q^{-1}) \underline{\delta}(1 - R)). \end{aligned}$$

Similarly, the population version of the score for  $G$  is given by

$$(5.5) \quad \Psi_2(\theta, G)(h) = P_0 A_{\theta, G} h - P_{\theta, G} A_{\theta, G} h.$$

Under the hypotheses of the following theorem,  $\Psi = (\Psi_1, \Psi_2)$  is differentiable in a suitably strong sense with derivative  $\dot{\Psi} : (R^m \times \ell^\infty(\mathcal{H})) \rightarrow (R^m \times \ell^\infty(\mathcal{H}))$  at  $(\theta_0, G_0) \in \Theta \times \mathcal{G}$  given by

$$\dot{\Psi} \begin{pmatrix} \theta - \theta_0 \\ G - G_0 \end{pmatrix} = \begin{pmatrix} \dot{\Psi}_{11} & \dot{\Psi}_{12} \\ \dot{\Psi}_{21} & \dot{\Psi}_{22} \end{pmatrix} \begin{pmatrix} \theta - \theta_0 \\ G - G_0 \end{pmatrix},$$

where

$$(5.6) \quad \begin{aligned} \dot{\Psi}_{11} : R^m &\rightarrow R^m && \text{is given by } \dot{\Psi}_{11}(\theta - \theta_0) = -I_{11}(\theta_0)(\theta - \theta_0), \\ \dot{\Psi}_{12} : \ell^\infty(\mathcal{H}) &\rightarrow R^m && \text{is given by } \dot{\Psi}_{12}(G - G_0) = - \int A_0^T \dot{\mathbf{l}}_\theta d(G - G_0), \\ \dot{\Psi}_{21} : R^m &\rightarrow \ell^\infty(\mathcal{H}) && \text{is given by } \dot{\Psi}_{21}(\theta - \theta_0)h = -(\theta - \theta_0)^T \int A_0 h \dot{\mathbf{l}}_\theta dP_0, \\ \dot{\Psi}_{22} : \ell^\infty(\mathcal{H}) &\rightarrow \ell^\infty(\mathcal{H}) && \text{is given by } \dot{\Psi}_{22}(G - G_0)h = - \int A_0^T A_0 h d(G - G_0). \end{aligned}$$

Here

$$(5.7) \quad \begin{aligned} I_{11}(\theta_0) &= P_0(\dot{\mathbf{i}}_\theta^{\otimes 2}(R, Z; \theta_0, G_0)) \\ &= E_0\{\pi(Y, X)\dot{\mathbf{i}}_\theta^{\otimes 2}(Y|X)\} + \dot{\mathbf{Q}} \text{diag}(q/Q_0)\dot{\mathbf{Q}}^T, \end{aligned}$$

with  $\dot{\mathbf{i}}_\theta(R, Z; \theta_0, G_0)$  given by (2.4), is the information for  $\theta$  when  $G$  is known.

It is shown in Section 2 of BMW that the information operator  $A_0^T A_0 = \dot{\mathbf{i}}_g^T \dot{\mathbf{i}}_g$  given by

$$(5.8) \quad A_0^T A_0 h(x) = \pi^*(x)h(x) + \underline{Q}^{*T}(x) \text{diag}(q/Q) \langle \underline{Q}^*, h \rangle$$

is invertible with

$$(A_0^T A_0)^{-1} h(x) = \frac{1}{\pi^*(x)} h(x) - \left\langle h, \frac{\underline{Q}^{*T}}{\pi^*} \right\rangle M^{-1} \frac{\underline{Q}^*(x)}{\pi^*(x)}.$$

From this it follows, using standard formulas for inverses of operators defined in blocks as above (the same as for block-matrices), that the inverse  $\dot{\Psi}_0^{-1}: (R^m \times \ell^\infty(\mathcal{H})) \rightarrow (R^m \times \ell^\infty(\mathcal{H}))$  exists, is continuous, and is given by

$$(5.9) \quad \dot{\Psi}^{-1} = \begin{pmatrix} \dot{V}^{-1} & -\dot{V}^{-1} \dot{\Psi}_{12} \dot{\Psi}_{22}^{-1} \\ -\dot{\Psi}_{22}^{-1} \dot{\Psi}_{21} \dot{V}^{-1} & \dot{\Psi}_{22}^{-1} (\dot{\Psi}_{22} + \dot{\Psi}_{21} \dot{V}^{-1} \dot{\Psi}_{12}) \dot{\Psi}_{22}^{-1} \end{pmatrix}$$

where  $\dot{V} = \dot{\Psi}_{11} - \dot{\Psi}_{12} \dot{\Psi}_{22}^{-1} \dot{\Psi}_{21}$  and

$$\begin{aligned} \dot{\Psi}_{12} \dot{\Psi}_{22}^{-1} \dot{\Psi}_{21} (\theta - \theta_0) &= - \int A_0 (A_0^T A_0)^{-1} A_0^T \dot{\mathbf{i}}_\theta^T (\theta - \theta_0) dP_0 \\ &= - \int (A_0^T A_0)^{-1} A_0^T \dot{\mathbf{i}}_\theta A_0^T \dot{\mathbf{i}}_\theta^T (\theta - \theta_0) dG_0 \\ &= - \int (A_0^T A_0)^{-1} A_0^T \dot{\mathbf{i}}_\theta (A_0^T A_0) (A_0^T A_0)^{-1} A_0^T \dot{\mathbf{i}}_\theta^T (\theta - \theta_0) dG_0 \\ &= - \int A_0 (A_0^T A_0)^{-1} A_0^T \dot{\mathbf{i}}_\theta A_0 (A_0^T A_0)^{-1} A_0^T \dot{\mathbf{i}}_\theta^T (\theta - \theta_0) dP_0 \\ &= - E_0(A_0 (A_0^T A_0)^{-1} A_0^T \dot{\mathbf{i}}_\theta^{\otimes 2}) (\theta - \theta_0). \end{aligned}$$

Note that (5.9) is *not* the same as the block inverse form in van der Vaart [(1998), page 422]. Thus

$$\dot{V} = -I(\theta_0) = -I_{11} + E_0(A_0 (A_0^T A_0)^{-1} A_0^T \dot{\mathbf{i}}_\theta^{\otimes 2}) = -E_0(\dot{\mathbf{i}}_{\theta_0}^{*\otimes 2}),$$

which equals minus one times the efficient information matrix given in (2.11).

Here are the additional assumptions we will impose to establish joint asymptotic normality of  $(\hat{\theta}, \hat{G})$ .

L4.  $\mathcal{X}$  is a bounded convex subset of  $R^d$  with nonempty interior and  $\mathcal{H}$  is a universal Donsker class of real-valued measurable functions defined on  $(\mathcal{X}, \mathcal{B})$ .

Let  $\underline{h}^* \in (L_2^0(G_0))^m$  given by

$$(5.10) \quad \underline{h}^*(x) \equiv (A_0^T A_0)^{-1} (A_0^T (\dot{\mathbf{I}}_\theta))(x) = \frac{\dot{Q}^*(x)}{\pi^*(x)} \underline{p} + (\dot{Q} - \mathbf{C})\mathbf{M}^{-1} \frac{Q^*}{\pi^*}(x)$$

denote the least favorable direction. Then we have:

**THEOREM 5.1** (Joint asymptotic normality and efficiency of the MLE, i.i.d. sampling). *Suppose that conditions L0–L4 hold. Then it follows that*

$$\sqrt{n} \begin{pmatrix} \hat{\theta}_n - \theta_0 \\ \hat{G}_n - G_0 \end{pmatrix} \Rightarrow -\dot{\Psi}_0^{-1}(\mathbb{Z}) \equiv \mathbb{W} \equiv \begin{pmatrix} \mathbb{W}_1 \\ \mathbb{W}_2 \end{pmatrix} \quad \text{in } R^d \times l^\infty(\mathcal{H})$$

where  $\mathbb{W}_1 \sim N_d(0, I(\theta_0)^{-1})$  and  $\mathbb{W}_2$  is a mean-zero Gaussian process indexed by  $\mathcal{H}$  with

$$\begin{aligned} \text{Cov}(\mathbb{W}_2(h_1), \mathbb{W}_2(h_2)) &= \langle h_1 - G(h_1), (A_0^T A_0)^{-1} (h_2 - G(h_2)) \rangle \\ &\quad + \langle h_1, \underline{h}^* \rangle^T I(\theta_0)^{-1} \langle h_2, \underline{h}^* \rangle, \quad h_1, h_2 \in \mathcal{H}, \end{aligned}$$

where the inner products are in  $L_2(G_0)$ . Moreover,

$$\text{Cov}(\mathbb{W}_1, \mathbb{W}_2(h)) = -I(\theta_0)^{-1} \langle \underline{h}^*, h \rangle, \quad h \in \mathcal{H}.$$

Further,  $(\hat{\theta}_n, \hat{G}_n)$  is asymptotically efficient; in particular  $\hat{\theta}_n$  has influence function  $\tilde{\mathbf{I}}_\theta$  given by (2.12).

**PROOF.** Replacing  $\tilde{\theta}_n$  by  $\hat{\theta}_n$  in (4.20) and (4.21) yields

$$\begin{aligned} \sqrt{n}(\hat{G}_n(h) - G_0(h)) &= \sqrt{n} \left( \mathbb{P}_n \left( \frac{R}{\hat{s}_n(\cdot, \hat{\theta}_n)} h \right) - P_0 \left( \frac{R}{s_0} h \right) \right) \\ (5.11) \quad &= \mathbb{G}_n \left( \frac{R}{s_0} h \right) - \mathbb{P}_n \left( Rh \frac{\sqrt{n}(\hat{s}_n(\cdot, \hat{\theta}_n) - s_0)}{\hat{s}_n(\cdot, \hat{\theta}_n) s_0} \right) \\ &\equiv I_n(h) - II_n(h), \end{aligned}$$

where the term  $II_n(h)$  can be written as

$$\begin{aligned} II_n(h) &= - \sum_{j=1}^J \sqrt{n} \left( \frac{N_j - n_j}{n} - Q_j^0(1 - p_j) \right) \frac{1}{\hat{Q}_j(\hat{\theta}_n)} \mathbb{P}_n \left( \frac{Rh}{s_0 \hat{s}_n(\cdot, \hat{\theta}_n)} Q_j^*(\cdot, \hat{\theta}_n) \right) \\ &\quad + \sum_{j=1}^J \sqrt{n} \left\{ \frac{\hat{Q}_j(\hat{\theta}_n) - Q_j(\hat{\theta}_n)}{\hat{Q}_j(\hat{\theta}_n) Q_j^0} \right\} Q_j^0(1 - p_j) \mathbb{P}_n \left( \frac{Rh}{s_0 \hat{s}_n(\cdot, \hat{\theta}_n)} Q_j^*(\cdot, \hat{\theta}_n) \right) \\ (5.12) \quad &\quad + \sum_{j=1}^J \sqrt{n} \left\{ \frac{Q_j(\hat{\theta}_n) - Q_j^0}{\hat{Q}_j(\hat{\theta}_n) Q_j^0} \right\} Q_j^0(1 - p_j) \mathbb{P}_n \left( \frac{Rh}{s_0 \hat{s}_n(\cdot, \hat{\theta}_n)} Q_j^*(\cdot, \hat{\theta}_n) \right) \\ &\quad + \mathbb{P}_n \left( \frac{Rh}{s_0 \hat{s}_n(\cdot, \hat{\theta}_n)} \right) \sum_{j=1}^J p_j \dot{Q}_j^*(\cdot, \theta_n^\dagger) \sqrt{n}(\hat{\theta}_n - \theta_0). \end{aligned}$$

Upon use of the differentiability arguments in the Appendix, careful grouping of terms and using Proposition 4.1, equations (4.5), (5.11) and (4.21), we find that

$$(5.13) \quad \sqrt{n}(\widehat{G}_n(h) - G_0(h)) = \mathbb{G}_n(A_0(A_0^T A_0)^{-1}h) - \mathbb{G}_n(\widetilde{\mathbf{I}}_\theta^T)(\underline{h}^*, h) + R_n(h)$$

where  $\widetilde{\mathbf{I}}_\theta = I(\theta_0)^{-1}\mathbf{I}_\theta^*$  is given by (2.12) and  $\|R_n\|_{\mathcal{H}} = o_p(1)$ . Theorem 5.1 follows immediately from (4.5), (5.13) and standard arguments.  $\square$

**6. Discussion: other designs and further problems.** The proof of Theorem 5.1 given in Section 5 differs from our first attempts which are given in BMW. Our present hypotheses L0–L4 are apparently weaker (and easier to verify) than the hypotheses imposed there in D0–D5 and especially D5. Another advantage is that the present Theorem 5.1 allows for many more classes of functions  $\mathcal{H}$ . We do not yet know how to use the Z-theorem approach of BMW to prove Theorem 5.1 under L0–L4.

*A. Other designs.* In this paper we have treated the variable probability sampling (VPS1) or Bernoulli (i.i.d.) version of the two-phase designs. We expect similar results to hold when the sampling is carried out without replacement within strata. Indeed, McNeney (1998) shows that the information bounds calculated here carry over to this. Proofs of asymptotic efficiency remain to be established for these versions of the designs.

*B. Choice of  $p_j$ 's to maximize information.* It would be of interest to study the optimal choice of  $p_j$ 's to minimize the asymptotic variance of some particular function of  $\theta$ . It is intuitively clear that an efficient choice of the  $p_j$ 's will often entail choosing  $p_j = 1$  for the strata with small (rare events)  $Q_j(\theta, G)$ .

*C. Other models.* If the basic model  $f(y|x; \theta)$  is not just parametric, but semiparametric as in the case-cohort sampling designs studied by Self and Prentice (1988), then the methods of the present paper do not apply. Although some work on information bounds has been carried out by Robins, Rotnitzky and Zhao (1994) and RHN, we do not know of any easily implementable efficient estimators in these models.

Although the LKW approach accommodates continuous outcomes, its key feature is that the phase one data, those available for all subjects, are reduced to counts of subjects in a finite number of strata. This implies a loss of information if in fact continuous outcome data are available. Chatterjee, Chen and Breslow (2003) developed a semiparametric “pseudo-score” estimator that only requires discretization of the phase one covariates. They demonstrated in simulations that its efficiency was sometimes substantially superior to that of the LKW profile likelihood estimator, even when 6 categories were used for discretization of the continuous outcomes. The information loss for the pseudo-score estimator in comparison with the semiparametric information bound for the general RHN problem has not yet been investigated.

D. *Asymptotic distribution of the estimators of the model.* It would be of interest to apply the Z-theorem when the parametric model does not hold to better understand what parameters are being estimated and how we should estimate variances robustly.

E. *Validity of the bootstrap.* If asymptotic normality of the estimators could be proved via the Z-theorem, then it would be straightforward to verify that the nonparametric bootstrap (and many other weighted bootstraps) is asymptotically valid via the results of Wellner and Zhan (1997).

APPENDIX

**Differentiability arguments.** At several points we need to understand how  $Q_j^\dagger(t, \theta, G)$  changes with  $t$  and  $\theta$ . Recall that  $Q_j^\dagger(t, \theta, G) = Q_j(t, G_t(\cdot; \theta, G))$ ,  $j = 1, \dots, J$ , satisfy the following system of equations:

$$(A.1) \quad Q_j^\dagger(t, \theta, G) = \int \frac{s(x, \theta)}{\sum_{l=1}^J (1 - (Q_l(\theta, G)(1 - p_l)) / Q_l^\dagger(t, \theta, G)) Q_l^*(x, t)} \times Q_j^*(x, t) dG(x), \quad j = 1, \dots, J.$$

Differentiation across (A.1) with respect to  $\theta$  yields

$$\begin{aligned} &\nabla_\theta Q_j^\dagger(t, \theta, G) \\ &= \int \frac{\sum_{l=1}^J p_l \dot{Q}_l^*(x, \theta)}{s_t(x; \theta, G)} Q_j^*(x, t) dG(x) \\ &\quad + \sum_{l=1}^J \frac{\nabla_\theta Q_l(\theta, G)(1 - p_l)}{Q_l^\dagger(t, \theta, G)} \int \frac{s(x, \theta)}{[s_t(x; \theta, G)]^2} Q_l^*(x, t) Q_j^*(x, t) dG(x) \\ &\quad - \sum_{l=1}^J \frac{Q_l(\theta, G)(1 - p_l)}{[Q_l^\dagger(t, \theta, G)]^2} \\ &\quad \quad \times \int \frac{s(x, \theta)}{[s_t(x; \theta, G)]^2} Q_l^*(x, t) Q_j^*(x, t) dG(x) \cdot \nabla_\theta Q_l^\dagger(t, \theta, G). \end{aligned}$$

Putting this in matrix form, we see that

$$(A.2) \quad \begin{aligned} &\left( I + \text{diag} \left( \frac{Q_l(1 - p_l)}{Q_l^\dagger(t, \theta, G)} \right) \int \frac{s(x, \theta)}{[s_t(x, \theta, G)]^2} \underline{Q}^*(x, t) \underline{Q}^*(x, t)^T dG(x) \right) \\ &\quad \times \nabla_\theta \underline{Q}^\dagger(t, \theta, G) \\ &= \int \frac{\sum_{l=1}^J p_l \dot{Q}_l^*(x, \theta)}{s_t(x, \theta, G)} \underline{Q}^*(x, t) dG(x) \\ &\quad + \dot{\mathbf{Q}} \text{diag} \left( \frac{(1 - p_l)}{Q_l^\dagger(t, \theta, G)} \right) \int \frac{s(x, \theta)}{[s_t(x, \theta, G)]^2} \underline{Q}^*(x, t) \underline{Q}^*(x, t)^T dG(x). \end{aligned}$$

Similarly, differentiating across (A.1) with respect to  $t$  yields

$$\begin{aligned} & \nabla_t Q_j^\dagger(t, \theta, G) \\ &= \int \frac{s(x, \theta)}{s_t(x; \theta, G)} \dot{Q}_j^*(x, t) dG(x) \\ & \quad - \int \frac{s(x, \theta)}{[s_t(x; \theta, G)]^2} \sum_{l=1}^J \left( 1 - \frac{Q_l(\theta, G)(1 - p_l)}{Q_l^\dagger(t, \theta, G)} \right) \dot{Q}_l^*(x, t) Q_j^*(x, t) dG(x) \\ & \quad - \int \frac{s(x, \theta)}{[s_t(x; \theta, G)]^2} \\ & \quad \quad \times \sum_{l=1}^J \frac{Q_l(\theta, G)(1 - p_l)}{[Q_l^\dagger(t, \theta, G)]^2} Q_l^*(x, t) \nabla Q_l(t, \theta, G) Q_j^*(x, t) dG(x), \end{aligned}$$

or, in matrix form

$$\begin{aligned} & \left( I + \int \frac{s(x, \theta)}{[s_t(x; \theta, G)]^2} \underline{Q}^*(x, t) \text{diag} \left( \frac{Q_l(\theta, G)(1 - p_l)}{[Q_l^\dagger(t, \theta, G)]^2} \right) \underline{Q}^{*T}(x, t) dG(x) \right) \\ & \quad \times \nabla_t \underline{Q}^\dagger(t, \theta, G) \\ (A.3) \quad &= \int \frac{s(x, \theta)}{s_t(x; \theta, G)} \dot{\mathbf{Q}}^*(x, t) dG(x) \\ & \quad - \int \frac{s(x, \theta)}{[s_t(x; \theta, G)]^2} \\ & \quad \quad \times \sum_{l=1}^J \left( 1 - \frac{Q_l(\theta, G)(1 - p_l)}{Q_l^\dagger(t, \theta, G)} \right) \dot{Q}_l^*(x, t) Q_j^*(x, t) dG(x). \end{aligned}$$

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