or even the correct correlation structure within the data – the mean model parameter estimators are unbiased if the mean model is correctly specified. However, a working correlation that is close to the structure of the true data-generating mechanism provides greater efficiency than a poorly specified working correlation.[1] Thus, it is tempting to employ some method of *choosing* the working correlation structure – potentially reducing standard errors and improving the power to detect an association between a covariate and the outcome.

To this end, several criteria for specifically selecting the working correlation structure (as opposed to selecting covariates in the mean model) have been proposed, including Pan's seminal quasi-likelihood information criterion[2] and variations thereof.[3,4] Many of these criteria have been implemented in commonly used software such as SAS and Stata, which facilitates their use by data analysts, some of whom may not be fully aware of the drawbacks of the criteria.

While such information criteria have sound theoretical bases, their use can have unintended consequences if their application leads the analyst to choose an inappropriate working correlation structure for the chosen mean model. For instance, GEEs yield biased estimators of cross-sectional model parameters when the true data-generating mechanism relies on covariate history[5] (such as when a "cross-sectional" model is being fit to data and the true underlying data-generating mechanism is not cross-sectional) unless an independence correlation structure is assumed. For example, one may wish to understand the predictive value of current covariate measurements on current health status to understand what can be learned from the information available in a given visit without relying on historical measurements. Current health is highly likely to be predicted by additional antecedent factors, e.g., previous health status. In this setting, data analysts must use an independence working correlation when regressing health status on covariates using GEEs.

We have previously demonstrated[6] that type I error is distorted because of postselection inference, i.e., the use of confidence intervals or significance tests following model selection. Moreover, in the eAppendix; http://links.lww.com/EDE/B384, we demonstrate via brief simulations that bias can arise due to using information criteria in settings where an independence working correlation is required. While these limitations of model selection in the GEE context are well-known to statisticians, this message appears to be insufficiently disseminated to other fields. For instance, more than 80% of the citations of Pan's quasi-likelihood information criterion are in nonstatistical journals,[6] suggesting that the criterion is being used in routine data analysis, in, for example, epidemiology and cancer biology. Even in our institution, the routine use of these criteria is encouraged, without mentioning the potential perils discussed above. Moreover, new criteria continue to be developed[7,8] despite these potential perils.

We urge data analysts to consider selection of the working correlation structure based on the data-generating mechanism and not solely on information criteria. The development or extensions of ever more methods for choosing among different correlation structures is of little use and may even be counterproductive if used in the same manner as the previously developed criteria already in use. Thus, while GEEs offer consistency without perfect knowledge of the correlation structure, reliance on this known and proven property may be the most prudent and fruitful analysis approach.

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REFERENCES

1. Diggle PJ, Heagerty P, Liang K-Y, Zeger SL. *Analysis of Longitudinal Data*. 2nd ed. Oxford University Press: Oxford, UK; 2002.
2. Pan W. Akaike's information criterion in generalized estimating equations. *Biometrics*. 2001;57:120–125.
3. Hardin JW, Hilbe JM. *Generalized Linear Models and Extensions*. Stata Press: College Station, TX,; 2007.
4. Hin LY, Wang YG. Working-correlation-structure identification in generalized estimating equations. *Stat Med*. 2008;28:642–658.
5. Pepe MS, Anderson GL. A cautionary note on inference for marginal regression models with longitudinal data and general correlated response data. *Commun Stat Simul Comput*. 1994;23:939–951.
6. Wang Y, Murphy O, Turgeon M, et al. The perils of quasi-likelihood information criteria. *Stat*. 2015;4:246–254.
7. Jaman A, Latif MA, Bari W, Wahed AS. A determinant-based criterion for working correlation structure selection in generalized estimating equations. *Stat Med*. 2016;35:1819–1833.
8. Wang P, Zhou J, Qu A. Correlation structure selection for longitudinal data with diverging cluster size. *Can J Stat*. 2016;44:343–360.

Re. Trends in Control of Unobserved Confounding

We appreciate thoughtful commentary by Shahn[1] on the use of methods such as the newly developed trend-in-trend design[2] to control for unmeasured confounding. We would like to clarify two of the assumptions that Shahn enumerated as underlying this research design.

Code for replication: The computer code is available as an R package "TrendInTrend" on CRAN.

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Assumption (b) enumerated by Shahn is that "the individual level outcome model at each person–time is a linear logistic regression in exposure, calendar time, and the set of measured and unmeasured intrinsic covariates that influence the exposure and/or outcome."[1] While the trend-in-trend design does require the outcome to be logistic with respect to some specified function of covariates, that function does not need to be linear, even though that was the functional form used in the original paper.[2] Any specified function will suffice to derive the population-average model that is obtained by integrating out the set of measured and unmeasured covariates in the individual-level outcome model.

Assumption (g) enumerated by Shahn is that "there are no calendar time trends in confounders within strata."[1] This is stated slightly more strictly than is actually needed. In truth, the design is unbiased as long as any trends in the prevalence of measured or unmeasured causes of the outcome are equal across strata defined by the cumulative probability of exposure, and unmeasured confounders over time can be modeled as depending on time-invariant latent variables and independent, identically distributed time-varying variables. In the eAppendix; http://links.lww.com/EDE/B380, we rigorously justify this relaxation and prove the unbiasedness of the trend-in-trend design under this less restrictive assumption. Moreover, Ji et al[2] presented simulated scenarios (Table 3) in which covariates were serially correlated, and the results remained unbiased.

We would therefore propose a friendly amendment to the list of assumptions underlying the trend-in-trend design, as follows: (a) there is a constant instantaneous subject-specific treatment effect, which is the estimand; (b) the individual-level outcome model at each person-time is a logistic regression with respect to some specified function exposure, calendar time, and the set of measured and unmeasured factors that influence the exposure and/or outcome; (c) the outcome model given exposure, calendar time, and stratum is a logistic regression that is linear in exposure, calendar time, and an exposure-stratum interaction; (d) there is a strong population-level calendar time trend in treatment prevalence; (e) intrinsic covariates at baseline and calendar time have a multiplicative effect on probability of exposure; (f) the outcome is rare; and (g) any time trends in the prevalence of confounders are equal across strata of the cumulative probability of exposure. As noted by Shahn, assumptions (c), (d), and (f) can be assessed empirically for any given application of the method.

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REFERENCES

1. Shahn Z. Trends in control of unobserved confounding. *Epidemiology*. 2017;28:537–539.
2. Ji X, Small DS, Leonard CE, Hennessy S. The trend-in-trend research design for causal inference. *Epidemiology*. 2017;28:529–536.

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The STROBE Extensions

Considerations for Development

To the Editor:

A decade after the publication of the STROBE (STrengthening the Reporting of Observational studies in Epidemiology) Statement, we use this anniversary as a time to reflect on STROBE's impact and future avenues for addressing the incomplete reporting of observational studies.[1,2] As an aid to authors, the STROBE Statement and an explanation and elaboration article were published in 2007 with generic guidance for reporting cohort, case–control, or cross-sectional studies. Subsequently, several extensions to STROBE were published, some including authors involved in the original Statement, to provide more nuanced and tailored guidance.[3–15] In principal, these

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D.G.A. is a co-founder of the EQUATOR Network and the Director of the UK EQUATOR Centre. He has been involved in the creation of several reporting guidelines, such as Consolidated Standards of Reporting Trials (CONSORT), Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), STrengthening the Reporting of OBservational studies in Epidemiology (STROBE), and REporting recommendations for tumour MARKer prognostic studies (REMARK). The EQUATOR Network is also a member of the Methods in Research on Research Network, which D.G.A., D.H., and M.K.S. are members of. M.K.S. has a placement with the EQUATOR Network as part of her doctoral studies.

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