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.

OPEN

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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TABLE 1. Qualitative Assessment of Extensions to STROBE Checklist

Section on STROBE Checklist	STROBE Checklist Item	Extensions Containing Additions	Total Items Added	Field-Specific Items, No. (%)
Title/abstract	1. Title/abstract	8	11	9 (82)
Introduction	2. Background/rationale	5	6	5 (83)
	3. Objectives	5	6	5 (83)
Methods	4. Study design	5	19	18 (95)
	5. Setting	8	21	18 (86)
	6. Participants	12	29	17 (59)
	7. Variables	11	28	19 (68)
	8. Data Sources	10	20	12 (60)
	9. Bias	5	5	1 (20)
	10. Study size	3	5	2 (40)
	11. Quantitative variables	4	6	5 (83)
	12. Statistical methods	10	44	24 (55)
Results	13. Participants	9	18	14 (78)
	14. Descriptive data	10	17	11 (65)
	15. Outcome data	4	11	7 (64)
	16. Main results	10	16	7 (44)
	17. Other analyses	6	8	3 (38)
Discussion	18. Key results	0	0	0 (0)
	19. Limitations	10	11	4 (36)
	20. Interpretation	3	3	2 (67)
	21. Generalizability	2	2	1 (50)
Other	22. Funding	0	0	0 (0)
	Other additions	8	12	2 (17)

Two independent reviewers assessed additions in each extension and categorized them as field specific or nonspecific (Intraclass correlation coefficient = 0.92).

efforts are valuable, but inconsistencies may arise because extension production is not coordinated, and there is no clear guidance on their creation.

We qualitatively assessed the published STROBE extensions to identity perceived gaps and deficiencies in the current STROBE checklist and to detect nonspecific or redundant guidance. As detailed in the protocol,[16] as of 1 March2017, we found 13 STROBE extensions.[3–15] Collectively, there were 298 additions to the STROBE checklist (Table 1). Most additions were directly related to the field on which the extension was focused but, based on independent coding by two reviewers, over one third were not specific to the extension's field. Rather, they were general epidemiologic or methodologic tenets applicable to most observational research (e.g., details about potential confounders, biases, etc.). The Methods section contained the most changed or added items, one third of which were nonspecific changes (Table 1).

Nonspecific additions were mainly in the following areas (Table 2):

- Participants, including sample size rationale, changes in exposure status, time points of assessment, and recruitment details;
- Potential confounders and biases;
- Subgroup and sensitivity analyses;
- Generalizability;
- Ethics disclosure/approval; and
- Access to supplemental information (e.g., open source data, code, or protocols).

These results, highlighting nonspecific recommendations, complement previous research demonstrating particular problems with the reporting of bias, study size calculations, and subgroup and sensitivity analyses.[17,18] Nonspecific additions were of particular concern when they were found to be nearly identical to original STROBE checklist items (Table 3).

While the focused nature of the extensions varies widely, nonspecific additions could represent perceived gaps in content or indicate that information in the explanation and elaboration should be included in the checklist. Checklists provide valuable structure to research articles and serve as a reminder of what should be considered while writing. One cannot expect that all relevant epidemiologic or statistical information will be included; however, the trend of extensions adding general epidemiologic tenets points to a different reality.

The majority of additions made across the extensions were valuable, field-specific recommendations that experts in their respective disciplines determined necessary to report. However, nonspecific and redundant suggestions should not be ignored. EQUATOR (the Enhancing the QUAlity and Transparency Of health Research) Network guidance for guideline developers is a useful starting point to the process of *how* to develop an extension,[19] but more direction is needed in terms of *what* to report about the process. For example, why it was deemed necessary to duplicate existing items in different words or to add nonspecific information.

Erik von Elm conceived of reporting guidelines as life jackets, not strait jackets.[20] STROBE is not meant to be a strict and rigid list, hence why many authors have used it as a base for their own more focused extensions. However, redundant or nonspecific content additions may create confusion rather than help. STROBE is an "evolving document that requires continual assessment, refinement, and if necessary change."[2] The adaptable nature of STROBE is indispensable to its successful implementation. Updating STROBE was discussed at a 2010 meeting,[21] but only minor revisions were identified, thus not justifying a new version of the guidelines; perhaps, this should now be reconsidered.

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TABLE 2. Examples of Nonspecific Additions Added in STROBE Extensions

"Indicate the time points for assessment of serial follow-up"
"Provide reasons (epidemiological and clinical) for choosing matching criteria"
"Explain the length of time planned to follow participants for determination of outcomes"
"Report results of any adjustments for multiple comparisons"
"Describe the intervention/exposure with sufficient detail to permit replication"
"Describe any unique restrictions placed on the study sample size"
"Report any sensitivity analysis (e.g., exclusion of misreporters or outliers) and data imputation, if applicable"
"Describe informed consent and approval from ethical committee(s). Specify whether samples were anonymous, anonymized or identifiable"
"Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code"
"Describe the main limitations of the data sources and assessment methods used and implications for the interpretation of the findings"

REFERENCES

1. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Epidemiology*. 2007;18:800–804.
2. Vandenbroucke JP, von Elm E, Altman DG, et al; STROBE Initiative. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Epidemiology*. 2007;18:805–835.
3. Gallo V, Egger M, McCormack V, et al. STrengthening the Reporting of OBservational studies in Epidemiology—Molecular Epidemiology (STROBE-ME): an extension of the STROBE statement. *Eur J Clin Invest*. 2012; 42:1–16.
4. Field N, Cohen T, Struelens MJ, et al. Strengthening the Reporting of Molecular Epidemiology for Infectious Diseases (STROME-ID): an extension of the STROBE statement. *Lancet Infect Dis*. 2014;14:341–352.
5. Dixon WG, Carmona L, Finckh A, et al. EULAR points to consider when establishing, analysing and reporting safety data of biologics registers in rheumatology. *Ann Rheum Dis*. 2010;69:1596.
6. Benchimol EI, Manuel DG, To T, Griffiths AM, Rabeneck L, Guttmann A. Development and use of reporting guidelines for assessing the quality of validation studies of health administrative data. *J Clin Epidemiol*. 2011;64: 821–829.
7. Little J, Higgins JP, Ioannidis JP, et al; STrengthening the REporting of Genetic Association Studies. STrengthening the REporting of Genetic Association Studies (STREGA): an extension of the STROBE statement. *PLoS Med*. 2009;6:e22.

TABLE 3. Examples of Redundant Suggestions

Proposed Addition in Extension	Extension	Corresponding Original STROBE Item
1a) Indicate that the study was an observational study and, if applicable, use a common study design term	STROBE-VET (Veterinary research)[15]	1 Indicate the study's design with a commonly used term in the title or the abstract
6a Provide a clear definition of the exposed and nonexposed cohorts. Justify the choice of comparator	STROBE-EULAR (Rheumatology)[5]	6a) Give the eligibility criteria and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed
7(a) If applicable, clearly define all outcomes, correlates, predictors, potential confounders, effect modifiers, and diagnostic criteria	STROBE-RDS (Response-Driven Sampling)[14]	7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria if applicable
7.6 Include description of potential confounders (other than epidemiological variables)	STROBE-AMS (Antimicrobial Stewardship)[4]	7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria if applicable
8 Provide evidence to support the validity and reliability of assessment tools in this context (if available)	STROBE-SBR (Simulation-Based Research)[10]	8 For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Explanation and Elaboration: …report the findings of any studies of the validity or reliability of assessments or measurements, including details of the reference standard that was used

8. Lachat C, Hawwash D, Ocké MC, et al. Strengthening the Reporting of Observational Studies in Epidemiology-Nutritional Epidemiology (STROBE-nut): an extension of the STROBE statement. *PLoS Med*. 2016;13:e1002036.
9. Horby PW, Laurie KL, Cowling BJ, et al; CONSISE Steering Committee. CONSISE statement on the reporting of Seroepidemiologic Studies for influenza (ROSES-I statement): an extension of the STROBE statement. *Influenza Other Respir Viruses*. 2017;11:2–14.
10. Cheng A, Kessler D, Mackinnon R, et al; International Network for Simulation-based Pediatric Innovation, Research, and Education (INSPIRE) Reporting Guidelines Investigators. Reporting guidelines for health care simulation research: extensions to the CONSORT and STROBE statements. *Adv Simul (Lond)*. 2016;1:25.
11. Fitchett EJA, Seale AC, Vergnano S, et al; SPRING (Strengthening Publications Reporting Infection in Newborns Globally) Group. Strengthening the Reporting of Observational Studies in Epidemiology for Newborn Infection (STROBE-NI): an extension of the STROBE statement for neonatal infection research. *Lancet Infect Dis*. 2016;16:e202–e213.
12. Tacconelli E, Cataldo MA, Paul M, et al. STROBE-AMS: recommendations to optimise reporting of epidemiological studies on antimicrobial resistance and informing improvement in antimicrobial stewardship. *BMJ Open*. 2016;6:e010134.
13. Creinin MD, Chen MJ. Medical abortion reporting of efficacy: the MARE guidelines. *Contraception*. 2016;94:97–103.
14. White RG, Hakim AJ, Salganik MJ, et al. Strengthening the Reporting of Observational Studies in Epidemiology for respondent-driven sampling studies: "STROBE-RDS" statement. *J Clin Epidemiol*. 2015;68:1463–1471.
15. O'Connor AM, Sargeant JM, Dohoo IR, et al. Explanation and elaboration document for the STROBE-Vet statement: strengthening the reporting of observational studies in epidemiology—veterinary extension. *Zoonoses Public Health*. 2016;63:662–698.
16. Sharp MK, Utrobičić A, Gómez G, Cobo E, Wager E, Hren D. The STROBE extensions: protocol for a qualitative assessment of content and a survey of endorsement. *BMJ Open*. 2017;7:e019043.
17. Langan S, Schmitt J, Coenraads PJ, Svensson A, von Elm E, Williams H; European Dermato-Epidemiology Network (EDEN). The reporting of observational research studies in dermatology journals: a literature-based study. *Arch Dermatol*. 2010;146:534–541.
18. Agha RA, Lee SY, Jeong KJ, Fowler AJ, Orgill DP. Reporting quality of observational studies in plastic surgery needs improvement: a systematic review. *Ann Plast Surg*. 2016;76:585–589.
19. Moher D, Schulz KF, Simera I, Altman DG. Guidance for developers of health research reporting guidelines. *PLoS Med*. 2010;7:e1000217.
20. The Epidemiology Monitor. Exclusive interview with developers of STROBE guidelines for reporting of epidemiologic studies. *Epi Monitor* (November 2007).
21. Cevallos M, Egger M. Chapter 17, STrengthening the Reporting of Observational studies in Epidemiology. In: Moher D, Altman DG, Schulz K, Simera I, Wager E, eds. *Guidelines for Reporting Health Research: A User's Manual, First Edition*. 1st ed. John Wiley & Sons, Ltd: Hoboken, New Jersey; 2014.

Re: Associations Between Childhood Thyroid Cancer and External Radiation Dose After the Fukushima Daiichi Nuclear Power Plant Accident

To the Editor:

Ohira et al[1] examined the association between childhood thyroid cancer and external radiation dose in Fukushima Prefecture. They concluded that "follow-up surveys should be recommend for several years before any conclusions can be drawn." In this letter, we make three points that must be addressed if recommendations for action are to be based on reliable evidence.

First, Ohira et al.[1] estimated individual external doses for defining exposure levels. However, the effect of radiation on thyroid cancer incidence is far more potent from internal radiation by radioactive iodine than from external exposures.[2] Furthermore, it has been demonstrated that the dispersion of radioactive iodine is different from that of cesium, the main source of external radiation.[3] The dispersion of radioactive iodine was toward the south, while cesium was dispersed toward the northwest. Therefore, external radiation exposure estimation tends to have a problem of nondifferential exposure misclassification, which introduces bias toward the null.[4] Ohira et al.[1] corroborate this pattern of dispersion. Yet, in their letter, they suggest that the thyroid cancer excess is attributable to internal radiation rather than to external sources.

Second, Ohira et al.[1] did their analysis using only an internal comparison within Fukushima Prefecture. In March 2011, radioactive iodine was detected not only in most of Fukushima Prefecture but also around the Tokyo metropolitan area. When exposures are so widely dispersed, to estimate the exposure effect validly, researchers should also compare disease rates in the target population with as uncontaminated a control group as possible. As indicated in our article[5] and in the related follow-up correspondence,[6] more valid external comparisons were indeed possible.

Third, Ohira et al.[1] used only the first round of screening. It is well known that some researchers[7,8] refuted the "screening effect" hypothesis of excess thyroid cancer after the Chernobyl accident to end the controversy about the relationship between that accident and excess thyroid cancer.[9] In Fukushima, the large excesses that were detected in the second and third rounds of screening also refute the hypothesis.[10]

To address these points, we have reported our latest findings at successive annual conferences of the International Society for Environmental Epidemiology (ISEE) since 2013. Finally, the ISEE Executive wrote a letter expressing some of the concerns noted here to the prefecture in 2016.[11] To date, no response has been received.

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