

Characterizing the Exposome: Critical Analysis of

Exposome-Wide Association Studies

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Public Health

INTRODUCTION/ABSTRACT

The 'exposome' is a conceptual framework of all exposures encountered by an individual during his or her lifetime. The framework posits that exposures can be mapped, i.e. like the genome, and all types of exposures must be considered. Types of exposures include internal (biological processes), specific external (physical and chemical factors), and general external (psycho-social factors) (Figure 1) (8).

Researchers have begun studying the exposome by developing exposome- and environment-wide association studies (EWAS). This study design utilizes a hypothesis-free, un-targeted approach to regression analysis in which all exposures are concurrently considered for association with the disease of interest (7).

The ProQuest Environmental Science Collection was queried for EWAS. Five studies met EWAS criteria. The studies were analyzed following epidemiological study critical analysis guidelines (1).

All studies conducted similar regression analyses of extensive exposure variables with a single health outcome as the dependent variable. All studies utilized validation procedures and examined results using a false discovery rate (FDR) (2, 4, 5, 6, 9).

All EWAS research papers currently available in the literature conducted extensive validation procedures to demonstrate statistical significance of regression analyses. Therefore, EWAS will likely be a valuable resource in future studies of the exposome (2, 3, 4, 5, 6, 9).

PURPOSE: RESEARCH QUESTIONS & AIMS

RESEARCH QUESTIONS

- How are exposome- and environment-wide association studies (EWAS) currently conducted and analyzed in the literature?
- In what ways could study of the "exposome" advance epidemiological knowledge of the relationship between exposures and health outcomes?

SPECIFIC AIMS

- Examine existing research articles that conduct EWAS to determine if these articles demonstrate how a hypothesis-free approach to associating exposures with disease returns significant results that could advance epidemiological knowledge.
- Use epidemiological critical analysis techniques to examine the research methods and statistical analyses used in these studies to determine similarities or differences in approach, as well as strengths and weaknesses.
- Determine whether the available EWAS studies in the literature describe methods that conform to theoretical proposals of the exposome; and furthermore, using results of the methods analysis, conclude how these studies can inform future study of the exposome

METHODS

LITERATURE REVIEW

Tools:

Proquest Environmental Science Collection

Search terms:

- "exposome wide association study;" "environment wide association study"

ANALYSIS OF LITERATURE REVIEW RESULTS

Guide:

- Epidemiological study critical analysis as described in Aschengrau and Seage (2014).

Key considerations:

- Studies were examined for exploration of the full spectrum of the exposome, which includes internal; specific external; and general external environments (Figure 1).
- Search for commonalities in data analysis and other methods.

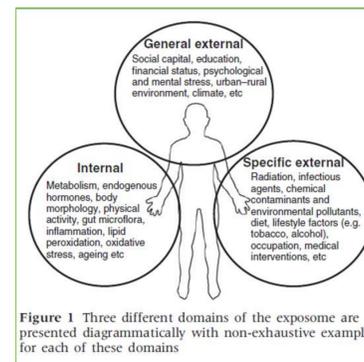


Figure 1. Composition of the Exposome. Wild (2012).

RESULTS

The literature review returned five results (Figure 2). These studies are listed below:

(1) Bessonneau et al. (2016)

Design: Case-control study of white-sucker fish.
Data Collection: Micro-extraction of metabolites.
Outcome of Interest: CYAP1 expression.
Exposome-type design: Exposome-wide association study.

(2) Patel, Bhattacharya, and Butte (2010)

Design: Case-control study.
Data Collection: NHANES exposure data.
Outcome of Interest: Type 2 diabetes mellitus
Exposome-type design: Environment-wide association study

(3) Patel et al. (2013)

Design: Case-control study.
Data Collection: NHANES exposure data.
Outcome of Interest: All-cause mortality.
Exposome-type design: Environment-wide association study

(4) McGinnis, Brownstein, and Patel (2016)

Design: Case-control study
Data Collection: NHANES exposure data
Outcome of Interest: Blood pressure
Exposome-type study: Environment-wide association study

(5) Zhong et al. (2016)

Design: Case-control study
Data Collection: Guangzhou Biobank Cohort Study
Outcome of Interest: Hematocrit level
Exposome-type design: Environment-wide association study

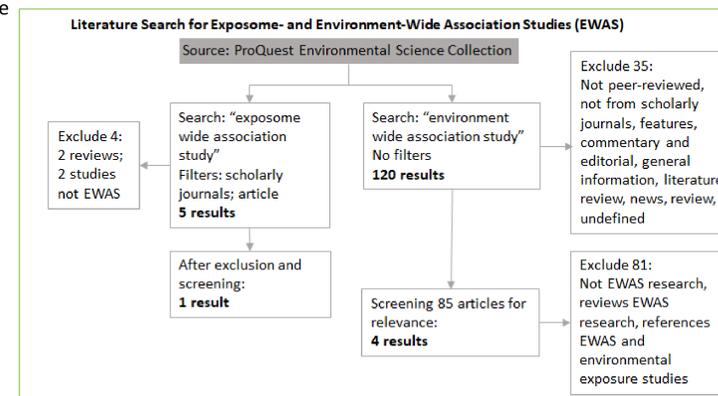


Figure 2. Results of literature search

	(1)	(2)	(3)	(4)	(5)
Novel associations with health outcome?	No	Yes	Yes	No	Yes
Validation Methods	N/A	Replicate significance in >1 cohort; include confounders based on chemical characteristics of exposures	Replicate significance	Replicate significance from meta-analysis of 1/2 cohort in one independent cohort; all cohort meta-analysis	'Internal cross-validation' (rotate 80% of all factors in regression analysis)
FDR used? (alpha level)	Yes 10%	Yes 1%	Yes 5%	Yes 10%	Yes 5%

Figure 3. Results of study analysis by study (1-5) and commonalities discovered.

CONCLUSIONS

Challenges:

- Challenges were evident in maintaining statistical power when conducting regression analyses with substantial variables in EWAS studies (3).
- EWAS was not clearly defined in the literature (2, 4, 5, 6, 9).

Successes:

- Studies minimized biases by utilizing existing datasets (i.e. NHANES) and validated questionnaires.
- Statistically significant findings were supported by extensive validation (2, 4, 5, 6, 9).

Key Findings:

- FDR and validation procedures were nearly universal among the five studies.
- Significant associations between exposures and disease lends to proof-of-concept of EWAS utility in advancing study of the exposome by validating exposure-health outcome associations (2, 4, 5, 6, 9).

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