Characterizing the Exposome: Critical Analysis of Exposome-Wide Association Studies

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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 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

Guides:
• 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.

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: CYMP1 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

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

CONCLUSIONS

Challenges:
• Challenges were evident in maintaining statistical power when conducting regression analyses with substantial variables in EWAS studies (3).

Successes:
• Studies minimized biases by utilizing existing datasets (i.e. NHANES) and validated questionnaire.
• 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 advanced study of the exposome by validating exposure-health outcome associations (2, 4, 5, 6, 9).

REFERENCES


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