

Environmental Temperature and Human Epigenetic Modifications

Key Points

- This study is a systematic review on the epidemiological studies that have evaluated the association between environmental temperature and human epigenetic modifications.
- Six cohort (a group of people who share a defining characteristic) studies and one cross-sectional (prevalence) study ranging from 2009 to 2019 with a focus on samples from elderly and infants/placenta samples.
- Evidence of short-term ambient temperatures could affect global human DNA methylation was observed, with 15 candidate genes identified.
- Data still remains scarce, and limited to only short-term linear effects of cold temperature on DNA methylation on sampled populations.
- More studies investigating epigenetic changes in response to environmental climate change is needed.

Introduction

- A previous multi-country study estimates 7.3% and 0.4% of mortality attributed by exposure to low and high temperatures, respectively.
 - Other countries, such as Brazil and China, had even higher mortality rates from both cold and hot temperature exposure.
- It is thought that environmental temperature may affect various epigenetic alterations in the DNA sequence, which may be contributing factor (for or against) to the mortality rates, but is still unclear to what degree.
 - Epigenetic changes in various plants and animals have been shown to help the organisms adapt changing environmental temperatures; the range of its effects on human beings' adaptability is still remain unclear, but there is increasing relevance due to climate change.
- The review summarizes the existing epidemiological evidence relating to humans in an attempt to provide better understanding the underlying mechanism in temperature-health associations and adaptability for the emerging field.

Methods

- **Independent literature screening based on exclusions:**
 - studies for non-human species;
 - *in vitro* studies;
 - non-original investigations;
 - studies without epigenetic biomarkers.
 - non-environmental temperature related induced changes;

◦ **Independent eligibility criteria based on inclusions:**

- be on humans;
- use first-hand collected data;
- be reported **in vivo**;
- examine epigenetic biomarkers;
- examine exposure to environmental temperatures.

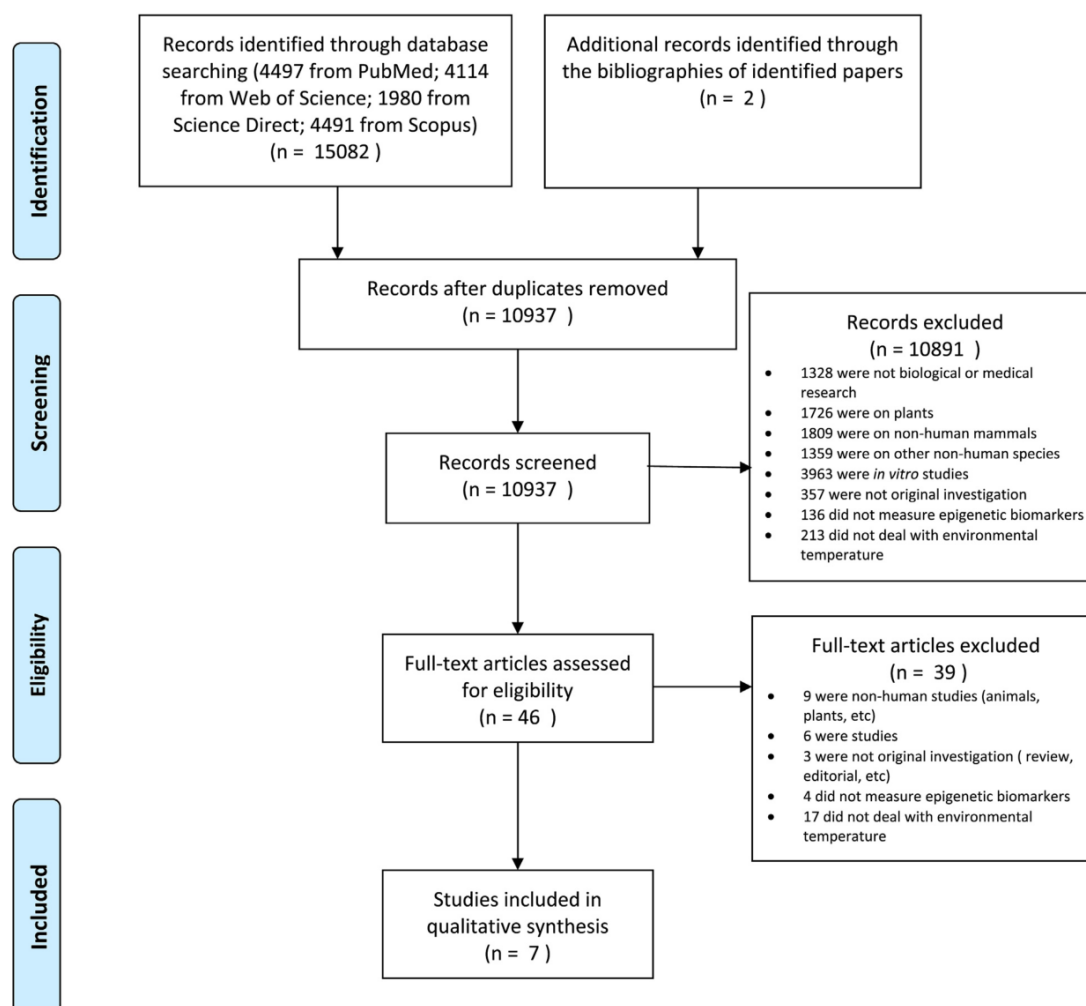


Fig. 1. Flow diagram for identifying relevant original articles on the association between environmental temperature and human epigenetic changes, following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Results

- Short-term ambient temperature could affect global DNA methylation;
- A total of 15 candidate genes (ICAM-1, CRAT, F3, TLR-2, iNOS, ZKSCAN4, ZNF227, ZNF595, ZNF597, ZNF668, CACNA1H, AIRE, MYEOV2, NKX1-2 and CCDC15) with methylation status associated with short-term ambient temperature have been identified;
- DNA methylation on ZKSCAN4, ICAM-1 partly mediated the effect of short-term cold temperature on high blood pressure and ICAM-1 protein (related to cardiovascular events), respectively;

- Short-term ambient temperature might affect the human's proportions of leukocyte subtypes estimated by Illumina 450 k data in blood sample.

Discussion

- Many questions remained unanswered and limited data of this study provided little conclusive findings, so the authors of this paper created a mind map with various hierarchical subject areas of interest that should be investigated to better understand the link between epigenetic modifications and environmental temperature exposure.

- **Epigenetic modifications:**

- Multi-omics integration; other epigenetic regulation factors could be at play.
- Further study of DNA methylation; cost, number of studies, and limited data provide little data to connect the multidimensional aspect of many of the modifications.
- Tissue specific epigenetic profiles; most studies rely on easily accessible tissue, but DNA methylation can work differently cross-tissue, especially early in development.

- **Environmental temperature:**

- Exposure assessment; many studies did not focus on temperature, it was merely a covariant, so many were not measured on an individual level.
- Time windows; many studies focused on short term effects, long term effects of sub-optimal temperature exposure needs to be measured.
- Exposure level; many studies only related to low temperatures, there little data examining range of temperatures (and warmer).
- Other environmental factors; temperature could play a small role, air pollution, humidity, green space, socioeconomic status, and more may affect epigenetic responses to temperature.

- **Methodological issues:**

- Study design; all studies were observational, both twin studies, randomized controlled trials could be helpful, but are costly.
- Study population; studies focused on young and elderly, which may be more vulnerable to temperature exposure, research is needed on general population samples.
- Statistical methods; many Bayesian and machine learning models could be applied to the data rather than just linear regressions.

References

Xu, R., Li, S., Guo, S., Zhao, Q., Abramson, M. J., Li, S., & Guo, Y. (2020). Environmental temperature and human epigenetic modifications: a systematic review. *Environmental Pollution*, 259, 113840.