

## Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our [Editorial Policies](#) and the [Editorial Policy Checklist](#).

### Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

- | n/a                                 | Confirmed  |
|-------------------------------------|--|
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> The exact sample size ( $n$ ) for each experimental group/condition, given as a discrete number and unit of measurement  |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly  |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> The statistical test(s) used AND whether they are one- or two-sided<br><i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>   |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A description of all covariates tested   |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons  |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals) |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> For null hypothesis testing, the test statistic (e.g. $F$ , $t$ , $r$ ) with confidence intervals, effect sizes, degrees of freedom and $P$ value noted<br><i>Give <math>P</math> values as exact values whenever suitable.</i>                            |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings  |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes  |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> Estimates of effect sizes (e.g. Cohen's $d$ , Pearson's $r$ ), indicating how they were calculated   |

*Our web collection on [statistics for biologists](#) contains articles on many of the points above.*

### Software and code

Policy information about [availability of computer code](#)

Data collection

Data analysis

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio [guidelines for submitting code & software](#) for further information.

### Data

Policy information about [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

Anonymised data and supporting documents are available upon request from the General Responder Data Center of the WTCHP via [christopher.dasaro@mssm.edu](mailto:christopher.dasaro@mssm.edu). A Data Transfer and Use Agreement and IRB approval is required before data release.

## Human research participants

Policy information about [studies involving human research participants and Sex and Gender in Research](#).

|                             |   |
|-----------------------------|---|
| Reporting on sex and gender | This is secondary data analyses. Gender was collected and used as a co-variate.   |
| Population characteristics  | Covariates that are known predictors of health or strong potential confounders included a priori in the models, based on biological plausibility, were gender, age at the time of 9/11, and race (self-reported by participants at enrollment). |
| Recruitment                 | This is a secondary data analyses, participants were recruited through the World Trade Center Health Program (WTCHP) General Responder Cohort (GRC).  |
| Ethics oversight            | Institutional Review Board of the Icahn School of Medicine at Mount Sinai (STUDY-19-01072).   |

Note that full information on the approval of the study protocol must also be provided in the manuscript.

## Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

Life sciences  Behavioural & social sciences  Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see [nature.com/documents/nr-reporting-summary-flat.pdf](https://nature.com/documents/nr-reporting-summary-flat.pdf)

## Ecological, evolutionary & environmental sciences study design

All studies must disclose on these points even when the disclosure is negative.

|                          |  |
|--------------------------|--|
| Study description        | This study comprehensively examines associations between self-reported experience of World Trade Center (WTC) Responders on 9/11 and during rescue and recovery efforts, and the development of WTC-related adverse health outcomes. This study uses an exposomic approach, encompassing the mixture of responders' WTC-related experiences, mental and physical health status, current/prior occupation, traumatic and environmental exposures, socioeconomic status, and social support during rescue and recovery efforts (defined as the WTC exposome). The association between the WTC exposure and health outcomes is analyzed using generalized weighted quantile sum (gWQS) regression, an advanced statistical approach for analyzing health outcomes associated with complex mixtures. This approach allows us to look at the mixture of baseline factors that may increase risk for and promote resilience against developing adverse health outcomes.  |
| Research sample          | This study is secondary data analyses that uses an existing dataset that includes members of the World Trade Center General Responder Cohort (WTC GRC) who were seen for monitoring at any of the NIOSH/CDC-funded Clinical Centers of Excellence (CCE) and who consented for research. It leverages the Division of Biostatistics and World Trade Center Health Program Data Center (DC), both housed within the Department of Environmental Medicine and Public Health at Mount Sinai. The GRC comprises workers and volunteers who were part of rescue and recovery efforts that followed the 9/11 attack on the WTC towers. This self-selecting cohort began to form within a month of 9/11, when rescue and recovery workers began presenting a variety of respiratory complaints at Mount Sinai's Irving J. Selikoff Center for Occupational and Environmental Medicine. Upon enrollment into the WTC GRC, all responders complete comprehensive baseline visit including a battery of self and interviewer-administered questionnaires and scales related to their WTC-related experience, physical and mental health status at the time of the tragedy, and sociodemographic characteristics, exposure assessment questionnaires and physical examination. |
| Sampling strategy        | The sample size was chosen based on the number of responders who consented to having their data aggregated for research purposes, had an exposure assessment questionnaire record, and had a mental health diagnostic interview. This sample size was sufficient as it allowed inclusion of the greatest number of responders in the WTC GRC and comprehensively examine the totality of their experience.   |
| Data collection          | This is secondary data analyses. Data was collected through the General Responder Cohort (GRC) of the World Trade Center Health Program (WTCHP) through a battery of self and interview-administered questionnaires and scales related to their WTC-related experience, physical and mental health status at the time of the tragedy, and sociodemographic characteristics, exposure assessment questionnaires and physical examination.   |
| Timing and spatial scale | This is secondary data analyses coming from an existing dataset. This dataset contains data from a self-selected cohort that began to form within a month of 9/11 (2001), when rescue and recovery workers began presenting a variety of respiratory complaints at Mount Sinai's Irving J. Selikoff Center for Occupational and Environmental Medicine. In 2002, the the National Institute for Occupational Safety and Health (NIOSH) provided funding for a one-time medical evaluation followed by continued funding in 2004 and 2006 for additional medical evaluations and treatments of physical and mental health conditions. With the passing of the James Zadroga 9/11 Health and Compensation Act, and continued reauthorization of this act extending coverage to 2090, responders are still continuously enrolled into the cohort. With continuous enrollment, all available data, at the time data was shared from the General Responder Data Center of the WTCHP, was used in this observational study for secondary data analyses.  |
| Data exclusions          | Data was excluded from responders that did not consent to have their data aggregated for research purposes. Data was also excluded from responders that did not have an exposure assessment questionnaire record and/or did not have a mental health   |

diagnostic interview. These exclusions were applied as the study aims to look at the totality of the responders' WTC experience, including mental and physical health, occupational history, traumatic and environmental exposures.

Reproducibility

As this is an observational study, there were no experiments performed and thus no experimental findings.

Randomization

Randomization was not relevant to this study as this study is secondary data analyses and thus an observational study.

Blinding

Blinding was not relevant to this study. This is secondary data analyses (an observational study) and anonymised data was shared by from the General Responder Data Center of the WTCHP.

Did the study involve field work?  Yes  No

## Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

### Materials & experimental systems

| n/a                                 | Involvement in the study                               |
|-------------------------------------|--|
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Antibodies                    |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Eukaryotic cell lines         |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Palaeontology and archaeology |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Animals and other organisms   |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Clinical data                 |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Dual use research of concern  |

### Methods

| n/a                                 | Involvement in the study                        |
|-------------------------------------|---|
| <input checked="" type="checkbox"/> | <input type="checkbox"/> ChIP-seq               |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Flow cytometry         |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> MRI-based neuroimaging |