Standardized Cross-Sectional Study Protocol to Assess Respiratory and Other Health Impacts from Volcanic Eruptions

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1. Introduction

Volcanic eruptions emit substantial quantities of ash, including particulate matter (PM), and gases, such as SO_2. Once an eruption has occurred, local officials will want to know if there have been any detectable adverse health effects (morbidity) or deaths (mortality) in the surrounding population.

This document presents a standardized protocol to undertake a cross-sectional study to examine respiratory, and other, short-term health effects of individuals who have been exposed to volcanic emissions from a specific event, including those environmentally or occupationally exposed. The intent is for this protocol to be applicable in all volcanic contexts and settings, and to be tailored to suit resource availability. With this in mind, a cross-sectional study is better suited to identify effects from acute exposures, rather than from chronic exposures (for which it would be more appropriate to use a longitudinal design, to follow-up individuals over time).

As individual exposures will be matched to health outcomes in the same individuals, the cross-sectional study will provide more reliable information on any association between health effects and exposure to volcanic emissions, particularly if the basic study (presented in a separate document) of hospital visits has indicated an overall increase in adverse health outcomes. The main advantage of a standardized protocol is the ability to compare and pool results from studies involving different populations, settings, and exposure levels. This is helpful in generating dose-response data, which are currently absent from the existing evidence on health impacts from exposure to volcanic ash and gases.

This protocol can be of use to governmental/non-governmental health agencies or research institutes that wish to produce more detailed information than that provided by the basic study to assess the extent to which exposure to volcanic emissions causes adverse respiratory and other health effects. As discussed below, the cross-sectional study requires more resources and time than the basic study, but, as a result of these extra efforts, does generate more detailed data and create the possibility of future longitudinal research. Study findings can be used to encourage people to reduce their exposures to safe levels, whenever possible. To expedite study implementation, it is recommended that studies be planned in advance, where possible, ***including the initiation of a dialogue with the relevant ethics board***.

2. Cross-Sectional Study Protocol

Cross-sectional studies include a representative sample from a population at a point in time and investigate the relationship between different levels of exposure and one or more specific health outcomes[1]. They can also provide useful baseline data for continued follow-up in a longitudinal study of the same population.

Additional time and resources will be needed to undertake a cross-sectional study, compared to the basic study that is presented in a separate document, with study results not likely available for several months. Although the time required to complete this study will depend on the specific context and numbers of participants included, to assist with planning and costing, we estimate the allocation of 1 to 2 hours per individual to undertake data collection, including the administration of an interview form. In addition to data collection are numerous other required activities to consider when developing timelines and budgeting, including planning, submitting and receiving study clearances (e.g., ethical), recruitment, data analysis, and writing and disseminating results. Whereas the basic

[1] Rothman et al., 2008

protocol could potentially be completed within weeks following an eruption, the cross-sectional study would require months before results would be available.

With primary data collection, it is very important that study personnel receive sufficient training and that strict quality control is maintained throughout the study. Within the protocol, links are included to established guidelines, e.g., lung function tests, to help ensure standardization across different study teams. Where possible and practical, collection of medical data should be administered by trained and qualified individuals and should be replicated among study personnel. The appropriateness and effectiveness of pooling study results is strongly dependent on the standardization of methods.

1. Study Area

The first step in a cross-sectional study is to determine the area to be examined. Here, this includes the area(s) subject to ashfall and/or volcanic gases where communities live and work.

The study area should include all exposed populated areas, which would maximise **the statistical power** of the study (i.e., the ability to detect health impacts specifically related to the eruption), as well as generating dose-response data from a range of exposure levels, rather than a simple exposed or unexposed distinction. It is essential that the study population contains individuals with a **range of exposure levels to volcanic emissions**.

2. Study Recruitment

Study participants are identified and recruited from the defined area(s). They should be selected to be representative of the whole population, or of particular subgroups that may be more sensitive to volcanic emissions e.g., older individuals, individuals with asthma, or subject to higher exposures, e.g., clean-up workers. Attempts should be made to recruit groups with comparable age and sex distributions and proportion of smokers, though these variables can be adjusted for in the analysis. If residents of the selected area(s) are exposed to broadly similar amounts of volcanic emissions, residents from a comparable, unexposed or less exposed area should be selected as a reference group to allow a comparison of health between exposed and less or unexposed individuals.

Identification of individuals can be from a range of local record sources, depending on availability and, more practically, population size. For simplicity, **a random sample of street addresses to identify households** in the study area (including the reference area, if required) is suggested and that all residents of each household selected be included in the study. Researchers should aim to survey a sufficient number of households to achieve adequate study power, but accounting for non-participation. If possible, researchers should collect demographic information on non-participants to assess if there are any differences between those who did and did not participate. If the study is to focus on a specific sub-group, it may be advisable to include most or all individuals, e.g., clean-up workers or children.

Attempts should be made to include individuals who were in the study area at the time of the eruption, but who may have moved since; this minimizes study bias caused if those who moved away were more vulnerable (e.g., asthmatics) than those who remained. Validity of the study findings will depend on both the number of study participants and the participation rate of the study. To achieve sufficient statistical power, at an absolute minimum, there should be at least 50 individuals[2] recruited from each exposure group (i.e., a study of at least 100 individuals, including (1) a higher and (2) lower exposed, or unexposed, group), though greater numbers of participants will ensure better detection of any

[2] As an example, based on 35% of exposed reporting cough in Carlsen et al., 2012 compared to 9% estimated in the general population (Jakeaways et al., 2003).

effects from exposure to the eruption, as well as an indication of dose-response effects. To improve the representativeness of the study, a high participation rate (e.g., 50% or greater) should be targeted and, if possible, reasons for not participating should be documented as there may well be recruitment bias e.g., the most vulnerable or 'worried well' may be more likely to participate (or not participate).

Once ethical applications and study clearances have been obtained, recruitment can be undertaken via letter, telephone, email or face-to-face visit. ***The use of local researchers, who are trusted in the community, can be beneficial in achieving a high participation rate***[3]. Participants should be asked for informed consent[4] to participate, based on a clear description of what the study will entail and be given information on their right to withdraw from the study at any time.

3. Exposure Assessment

Estimated exposure levels will be allocated to all individuals included in the study, based on each individual's location during the period of exposure, e.g., residence and/or work and their activities, such as ash clearing (domestic or occupational), combined where available with any objective measures of ash concentrations. It is possible to assess this exposure either by:

- Quantitative assessment (preferred) through measurements of:
  (i) **ambient air quality**, e.g., concentrations (µg/m^3 or ppm) of particulate matter (PM) or SO_2, or
  (ii) **sampling ash on the ground** (g/m^2); categories might be defined as follows: none, <1 mm, ≥1 mm[5]. Guidance for collection of ash samples is available on the IVHHN website[6].

  or, if neither is possible:

- Qualitative observations to indicate relative exposure, e.g., **the presence of any ash.** One approach would be to designate areas as having high/medium/low ash concentrations, though this categorisation would necessarily be subjective.

Estimates based on ambient PM concentrations, rather than ash on the ground, would (1) provide a clearer description of inhalable material and (2) better facilitate dose-response comparisons with other environmental exposures, e.g., urban air pollution. Exposure estimates could be refined if there are multiple air monitors (though unlikely) or clearly differing ash levels in different areas or for different activities, or for reported use of respiratory protection. If only one monitor is available, estimates can be adjusted upward or downward for different areas based on the estimated relative ash quantities.

Exposure duration should also be estimated in relation to: i) duration of eruptive emissions; ii) the implementation of interventions such as on-the-ground **clean-up activities** (to prevent the resuspension of ash) and protective measures; iii) timeframe of return to background ambient air quality concentrations.

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[3] Galea & Tracy, 2007
[4] The World Health Organisation (WHO) offers informed consent templates here: http://www.who.int/rpc/research_ethics/informed_consent/en/
[5] Hawaii Public Schools provided guidance with similar categories and action levels after the 2018 Kīlauea Eruption: http://www.hawaiipublicschools.org/DOE%20Forms/Safety/SchoolActionPlan-Ashfall.pdf
[6] https://www.ivhhn.org/guidelines

4. Health Outcomes

Studies of populations exposed to volcanic ash and gases have indicated the sensitivity of the respiratory system[7]; therefore, examining **respiratory health impacts** would, at a minimum, be most suitable for cross-sectional study. Depending on the amount of clinical testing equipment needed for data collection, health surveys could be completed either at the participant's residence or a local clinic.

The following outcomes have been used in many studies of respiratory health and would provide a comprehensive assessment of respiratory health status. All studies should have a minimum aim to collect data on the following endpoints:

1. **Lung function** – using spirometry measurements from an American Thoracic Society (ATS) compliant electronic spirometer[8], both Forced Expiratory Volume in one second (FEV_1) and Forced Vital Capacity (FVC) to calculate % of predicted values (equations to calculate these are provided by the Global Lung Initiative). Ideally, spirometry before and after a bronchodilator is preferred. The cost of a spirometer can range from US$400 to US$4,000 in the UK, but will vary according to where the eruption takes place.
2. **Presence & severity of respiratory and other symptoms** – self-reported, i.e., pre-existing conditions, and ongoing symptoms such as shortness of breath, wheezing, irritation or cough, nausea, headache, eye irritation; collected using a validated respiratory symptoms questionnaire, e.g., St George's Airways Questionnaire 20 (AQ20)[9]. One caveat for self-reporting is that more exposed individuals may be more likely to report symptoms, so it is important to also collect objective health data, such as lung function.
3. **Incidence and degree of asthma exacerbation** – self-reported, i.e., frequency of daytime/night-time attacks, use of medication, which medication and usual dosage (for short-term exposure, a comparison of the prevalence of asthma would not be appropriate for this study); and
4. **Hospital visits** – self-reported admissions or visits to hospital/clinics/general practitioners, for any reason, but at least focused on respiratory, cardiovascular, and external (burns); cross-checked with hospital records for at least a sample, if feasible, to assess recall bias. Comparison with pre-eruption records would be very useful to assess the possibility that any change in health care utilization may be related to practical problems, such as access to facilities, and/or to increased anxiety ('worried well').

In addition, it would add significant value to the study to include additional health outcome data at a relatively low incremental cost, which has been the practice in other studies[10], including:

1. **Validated health scales** adapted for research purposes, namely:
    - **General Health Questionnaire (GHQ-12),** as a measure of current mental health status[11];

[7] Hansell & Oppenheimer, 2004; Horwell & Baxter, 2006
[8] See, for example, https://www.brit-thoracic.org.uk/document-library/delivery-of-respiratory-care/spirometry/spirometry-in-practice-a-practical-guide-(2005)/
[9] Available here: http://portal.cdisc.org/Questionnaire%20Documentation/Forms/AllItems.aspx?RootFolder=%2FQuestionnaire%20Documentation%2FAirway%20Questionnaire%20%28AQ20%29
[10] Carlsen et al, 2012
[11] Jackson, 2007

- **Depression Anxiety Stress Scale (DASS-21),** a self-report instrument for measuring depression, anxiety and tension/stress[12]

2. **Cardiovascular health** indicators, such as:
    - Blood pressure (systolic & diastolic; mmHg), pulse wave velocity (m/s) and augmentation index (%)[13], measured using a SphygmoCor or Vicorder[14]

5. Demographic and other information

Additional information can be used to determine if any effects are associated with exposures to volcanic ash and whether they are isolated to or heightened in specific sub-groups:

- **Date of birth/age, sex & ethnicity** to assess differences of health impacts by age, sex and ethnicity.
- **Address** details to confirm whether an individual lives in an area exposed to volcanic emissions (if possible, it would be useful if addresses were geocoded, potentially using mobile apps).
- **Place of work**, **smoking status**, and any **pre-existing conditions** could help assess if an individual has additional risk factors, exposures, or underlying illness that might put them at a higher risk of disease. This information could be used to further compare if any groups are more likely to visit healthcare facilities after an eruption. It would also be very useful to collect information on whether individuals wore respiratory protection, such as a facemask.
- **Height & weight using standardized methods.**

These questions should be administered by a trained and qualified interviewer.

6. Statistical Analysis

Some statistical analysis methods which can be used in a cross-sectional study are outlined below. Analyses should be conducted by someone with statistical expertise using appropriate software packages, though it is possible to use MS Excel for simple descriptive statistics.

Statistical analysis allows a comparison of health outcomes of individuals with different levels of estimated exposure. If either differs between groups, e.g., if there are more smokers in a given exposure area, any observed difference in respiratory or cardiovascular health may be as a result of smoking rates, rather than ash exposure; in this example, smoking represents a *confounder*. In this case, the analysis will need to adjust for these confounders, as described below.

Stage 1

Statistical tests, including chi-squared tests, can be used to **evaluate differences in characteristics** between study areas[15]. If a statistically significant difference is detected in a given characteristic, e.g., smoking rates, comparisons of health outcomes between groups should be made after adjustment for these variables e.g., in sub-group analyses of smokers and non-smokers, using multivariable regression methods.

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[12] Osman et al., 2012; for templates, see http://www2.psy.unsw.edu.au/dass/

[13] Sinharay et al., 2017

[14] Shahin et al., 2013

[15] An example of free online statistical software is https://www.medcalc.org/calc/comparison_of_proportions.php. Simple statistics, including t-tests, can also be carried out in MS Excel.

Stage 2

For each health outcome, t-tests for two exposure groups, or analysis of variance (ANOVA) tests for more than two exposure groups, with a continuous health outcome e.g., lung function, or a chi-squared test for the proportionate outcomes e.g., those experiencing symptoms, should be employed to **assess mean differences in health outcomes by exposure group**[16]. Areas of individuals without significantly different age and sex structures and smoking rates could be compared across whole exposure groups. However, if differences are identified in Step 1, sub-groups should be adjusted for using regression methods. For this analysis, a higher overall sample size would be needed to ensure sufficient numbers (i.e., >50) in each subgroup to detect differences.

If more detailed exposure data are used (for instance, if comprehensive exposure data are available to assign individual exposures), there are two analysis options, depending on the availability of statistical software: (1) individuals can be grouped into tertiles (or other suitable quantiles) based on exposures to low/medium/high (or other categories) levels of ash or, as a more sophisticated approach, (2) regression methods can be used to assess the significance of different explanatory variables, e.g., age, and include exposure as a continuous variable; each health outcome should be included as the dependent variable in separate models.

7. Interpretation & Follow-up

The results of a cross-sectional study can show whether there is a statistically significant association between exposure groups/levels and health but these findings, alone, would not be able to prove a causal[17] link, because health is being examined at a point in time, rather than before and after an eruption (i.e., the exposure of interest). Nevertheless, study findings would be useful to identify health needs of the population and deploy resources.

If there appears to be deleterious health effects in the more exposed group(s), continued follow-up study may be warranted. Even if this follow-up does not take place, the results of the cross-sectional study would provide baseline information that could be used in the event of a subsequent eruption; the continued study of these individuals would represent longitudinal data and would significantly strengthen the interpretation of study findings and, ultimately, whether exposure to volcanic ash, and at what concentration, is hazardous to respiratory health.

Study findings and interpretations should be made available to the public, for transparency and clear communication, and also to the wider research community, who may benefit from the research methods and results.

8. Protocol

The figure below presents a step-by-step protocol for the basic epidemiological study, which should be used with reference to the information in sections 1-7, above.

[16] Carlsen et al., 2012

[17] Establishing a causal link typically requires a number of studies and considerations. A good discussion is presented in Bradford Hill's seminal paper: '*The environment and disease; association or causation?'*.

1. **Study Area**
    - Identify the target study area, including, if possible, a range of areas exposed to ashfall.

2. **Study Recruitment**
    - Identify the most appropriate method for sampling all individuals (or a representative sample of individuals) within that area.
    - Recruit individuals from target study population ensuring the required sample size for each exposure level. Use non-exposed population as a reference if exposure levels were similar across the target population.

3. **Exposure Assessment**
    - Assign area-level exposures using quantitative ambient concentrations of ash (PM_{10}) or gases (SO_2) or ash on the ground (g/m^2), otherwise use qualitative estimates (e.g., high/medium/low or exposed [yes/no]).
    - Track the period of exposure based on volcanic emissions and clean-up activities.

4. **Health Outcomes**
    - Collect (at a minimum) respiratory health data from each individual, namely:
        - Symptoms, asthma exacerbation, hospital visits, lung function
    - If possible, also record data on cardiovascular health and validated mental health scales, including:
        - General Health Questionnaire, Depression Anxiety Stress Scale

5. **Demographic and other information**
    - Record other data from each participant, such as:
        - Age, sex, ethnicity, smoking habits, and address
    - Exposure history – location of residence and work, exposure duration, relevant activities and their frequency, use of respiratory protection, e.g. facemasks

6. **Analysis & Interpretation**
    1. Assess similarity of characteristics in exposure groups (Stage 1)
    2. Use chi-squared tests to compare proportions with each health outcome between different exposure groups (Stage 2). Perform regression analysis if exposure groups differ, i.e., compare separately health in smokers and non-smokers.
    3. If feasible, carry out statistical modelling of exposure and health outcome
    4. Interpret statistical tests and decide whether to continue study.

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