

# Initial plans for a large-scale investigation into the chronic health effects of earthquakes in Italy: building on Barbara Pacelli's legacy

**Progetto iniziale per uno studio su vasta scala degli effetti cronici dei terremoti in Italia: pianificazione fondata sul lascito scientifico di Barbara Pacelli**

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*The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.*

## ABSTRACT

Barbara Pacelli, a young Italian epidemiologist, passed away unexpectedly in September 2019. During her prolific professional life, she gave several scientific contributions to natural disaster epidemiology, particularly in relation to the medium and long-term health effects of earthquakes. In this opinion paper, we reflect on Barbara's legacy and outline potential actions that could arise from her work. Particularly, availability of electronic health records would enable a systematic and large-scale investigation into the long-term health effects of earthquakes in Italy, a country with high seismic risk. This effort would have high societal value as it would likely enable mitigation of substantial morbidity and mortality in areas affected by earthquakes. In this paper, we define scope, objectives, potential data sources, and analysis methods that could be used to systematically assess the chronic health effects of recent earthquakes in Italy.

**Keywords:** earthquakes, chronic diseases, electronic health records, retrospective cohort, case crossover study

## RIASSUNTO

Barbara Pacelli, una giovane epidemiologa italiana, è scomparsa improvvisamente nel settembre 2019. Durante la sua prolifica vita professionale, Barbara ha dato parecchi contributi all'epidemiologia dei disastri naturali, in particolare riguardo agli effetti a medio e lungo termine dei terremoti. In questo *opinion paper*, riflettiamo su un segmento del lascito scientifico di Barbara e delineiamo potenziali azioni che potrebbero derivare dal suo lavoro. In particolare, la disponibilità di dati sanitari elettronici rende oggi possibile uno studio sistematico e su larga scala degli effetti a lungo termine dei terremoti in Italia, un Paese ad alto rischio sismico. Questa iniziativa avrebbe un alto valore sociale, in quanto potrebbe consentire la riduzione di una notevole quota di morbilità e mortalità nelle zone affette dai terremoti. Nell'articolo definiamo l'ambito di azione, gli obiettivi, le potenziali fonti di dati e i metodi di analisi che si potrebbero utilizzare per valutare sistematicamente gli effetti cronici dei terremoti avvenuti negli ultimi anni in Italia.

**Parole chiave:** terremoti, malattie croniche, dati sanitari elettronici, coorte retrospettiva, studio *case crossover*

## BARBARA PACELLI'S CONTRIBUTION TO EARTHQUAKE EPIDEMIOLOGY

Barbara Pacelli was a talented epidemiologist, a good friend, and a very active member of the Italian Association of Epidemiology. She served as a board member of the Association between 2014-2016, and those of us who were in the same board distinctly remember her exceptional professionalism and kindness. Besides being unusually skilled, Barbara strove to put her in-depth knowledge of epidemiology at the service of society. At the time of her passing, she had already more than 15 years' experience in the field of environmental and health-inequality epidemiology. In the past few years, Barbara also gave several scientific con-

tributions on earthquake epidemiology. In Italy, a nation with high seismic risk, this commitment has high societal value as it aims at a reduction of morbidity and mortality amongst the most vulnerable strata of the population. In the aftermath of earthquakes, assessing the short-term effects of earthquakes is usually prioritized, because a quantification of casualties and deaths is essential to organise the immediate response. Barbara's contribution focused on the long-term effects, an aspect that is still relatively neglected and that is crucial to ensure that the most vulnerable, such as those who were displaced by the earthquakes or had pre-existing medical conditions, are adequately shielded from the indirect, long-term consequences of earthquakes.

As a board member of the Italian Association of Epidemiology, Barbara liaised with local authorities, academics and public health professionals to raise awareness about the scarceness of investigations about the long-term consequences of earthquakes. This advocacy work was conducted with particular interest for L'Aquila earthquake (Abruzzo Region, Southern Italy), a major seismic event that occurred in central Italy in 2009, costing the lives of 308 people and the displacement of several thousands. These initiatives culminated in a well-attended spring meeting of the Italian Association of Epidemiology held in L'Aquila in April 2016, which Barbara contributed to organising and moderating. Barbara also contributed to assembling an open-access monographic issue of the Association's journal, *Epidemiologia&Prevenzione*, in which Barbara co-authored 3 papers.<sup>1-3</sup> In this monographic issue (available from: <https://www.epiprev.it/publicazione/epidemiol-prev-2016-40-2-suppl-1>) Barbara's main paper focused on a systematic comparison between studies assessing the long-term health effects of the L'Aquila earthquake and studies assessing other major seismic events. This review found that the L'Aquila earthquake was the most investigated (along with the Kobe/Hanshin-Awaji earthquake, occurred in 1995 in Japan) and its effects were estimated mostly in terms of mental health outcomes. These findings suggested that there was scope for a more comprehensive investigation into the long-term health effects in L'Aquila by using electronic health records, which would have enabled more in-depth assessment of its health effects. However, at the time, a meta-analysis of long-term earthquake effects had not yet been conducted, and therefore the relevance of this kind of new investigation was not yet clear.

Barbara was instrumental, together with her co-lead author (Dr. Alba Ripoll-Gallardo) and other investigators, to ensure that this initial review was expanded to include a meta-analysis of published studies on long-term health effects of earthquakes in affluent countries. In 2018, this work was published in the *International Journal of Epidemiology*<sup>4</sup> and an extract was posted on the journal's blog.<sup>5</sup> This meta-analysis of 52 studies showed that populations exposed to one of 13 major earthquakes (occurred in 8 countries between 1980 and 2011) had on average 36% and 37% higher mortality rate for myocardial infarction and stroke after the first month from the main shock, as well as higher mean concentration of glycated haemoglobin. Several other long-term effects were found in relation to psychiatric disorders and other chronic diseases. This work suggested that a new systematic investigation into the long-term effects in Italy would not only be scientifically innovative, but also essential to reduce a preventable and sizeable burden of mortality and morbidity. Finally, in a recent editorial, Barbara and others outlined the features required to a such comprehensive investigation into the health effects of earthquakes.<sup>6</sup>

Because Italy is a country at a high seismic risk, establishing a post-earthquake epidemiological study would enable early detection of many deleterious effects and damage mitigation. Barbara and others proposed that this study should:

- capitalise on routinely collected health data, rendering the study relatively inexpensive;
- be coordinated centrally by a multidisciplinary team to enable harmonised procedures and analysis;
- capture both physical and mental health diseases;
- consider a follow-up of at least 7 years, based on the effects found in the meta-analysis;<sup>4</sup>
- gather sufficient data to enable stratified analysis and identify at-risk subgroups that may need targeted interventions.

### PLANS FOR A LARGE-SCALE STUDY INTO THE CHRONIC HEALTH EFFECTS OF EARTHQUAKES IN ITALY

Barbara's and others' work has been crucial to reliably formulate the rationale and outline the features of a comprehensive study of the medium and long-term effects of earthquakes in Italy.<sup>1-4,6-8</sup> We think that it is now time to continue this work and devise the research plan for an investigation into the subject. On average, Italy experienced a major earthquake every three years in the past ten years. Taken together, the L'Aquila (2009), Emilia-Romagna (2012), and Amatrice (2016) earthquakes resulted in 679 deaths, displacement of more than 120,000 people, and cumulative economic losses of more than 20 billion euros.<sup>9</sup> However, their medium and long-term health effects are largely unknown. A comprehensive and rigorous investigation is long-overdue and crucial to ensure that at-risk populations will be adequately protected in the event of a future disaster. In addition, to having high public health value, this study would be highly innovative, as a systematic investigation of the health effects of earthquakes has never been performed. Finally, using a large-scale approach (i.e., including the whole population of individuals likely exposed to the earthquake of interest and matching controls) would enable detection of small effects and assessment of potential interactions between earthquakes and sociodemographic characteristics such as age and socioeconomic status; thus, enabling greater precision in mitigation and prevention measures.

### OBJECTIVES

This study will have two main objectives:

1. to ascertain the medium and long-term effects of earthquakes on pre-specified endpoints;
2. to conduct exploratory analyses to capture additional health effects (e.g., arising from an agnostic, phenome-wide association study into the health effects of earthquakes) and interactions with relevant subgroups (e.g., defined by age and socioeconomic status).

## ENDPOINTS

Based on previous evidence,<sup>4</sup> we will consider the following endpoints:

- all-cause mortality;
- cardiometabolic disease incidence and mortality (i.e., coronary heart disease, stroke, diabetes and subtypes);
- psychiatric disorder incidence and mortality (i.e., intentional self-harm, major depression, psychotic events);
- gastro-enterological disease incidence and mortality (i.e., gastric ulcers).

## PARTICIPANTS

To ensure adequate power, the study should gather data from:

- Populations exposed to recent major earthquakes in Italy (~2.7 million people):
  - L'Aquila, 6<sup>th</sup> April 2009: the province most exposed was L'Aquila (309,131 individuals);<sup>10</sup>
  - Emilia, 20<sup>th</sup> May 2012: the provinces most exposed were Modena (685,822) and Ferrara (352,856);<sup>11</sup>
  - Amatrice, 24<sup>th</sup> August 2016: the provinces most exposed were Rieti (158,467), Ascoli-Piceno (210,066), Perugia (662,110), Teramo (310,339);<sup>12</sup>
- populations unexposed to earthquakes: control Italian provinces will be selected amongst those which were not exposed to major natural disasters in the previous 20 years and will be matched to exposed provinces based on their:
  - size;
  - sociodemographic characteristics (proportion of men and women, people with ≥65 years, sociodemographic status, population density);
  - prevalence of behavioural risk factors (smoking, alcohol drinking, obesity);
  - indicators of healthcare quality and efficiency measured before the earthquake of interest.

This approach is expected to ensure that exposed and unexposed areas are as balanced as possible in terms of a range of baseline covariates.

An anticipated sample size of ~5 million participants from exposed and unexposed provinces will enable an unparalleled range of analyses, including ascertainment of potential subgroup effects that would enable more tailored and efficient public health intervention and an agnostic investigation of smaller (and therefore previously undetected) associations.

## PROPOSED STUDY DESIGN

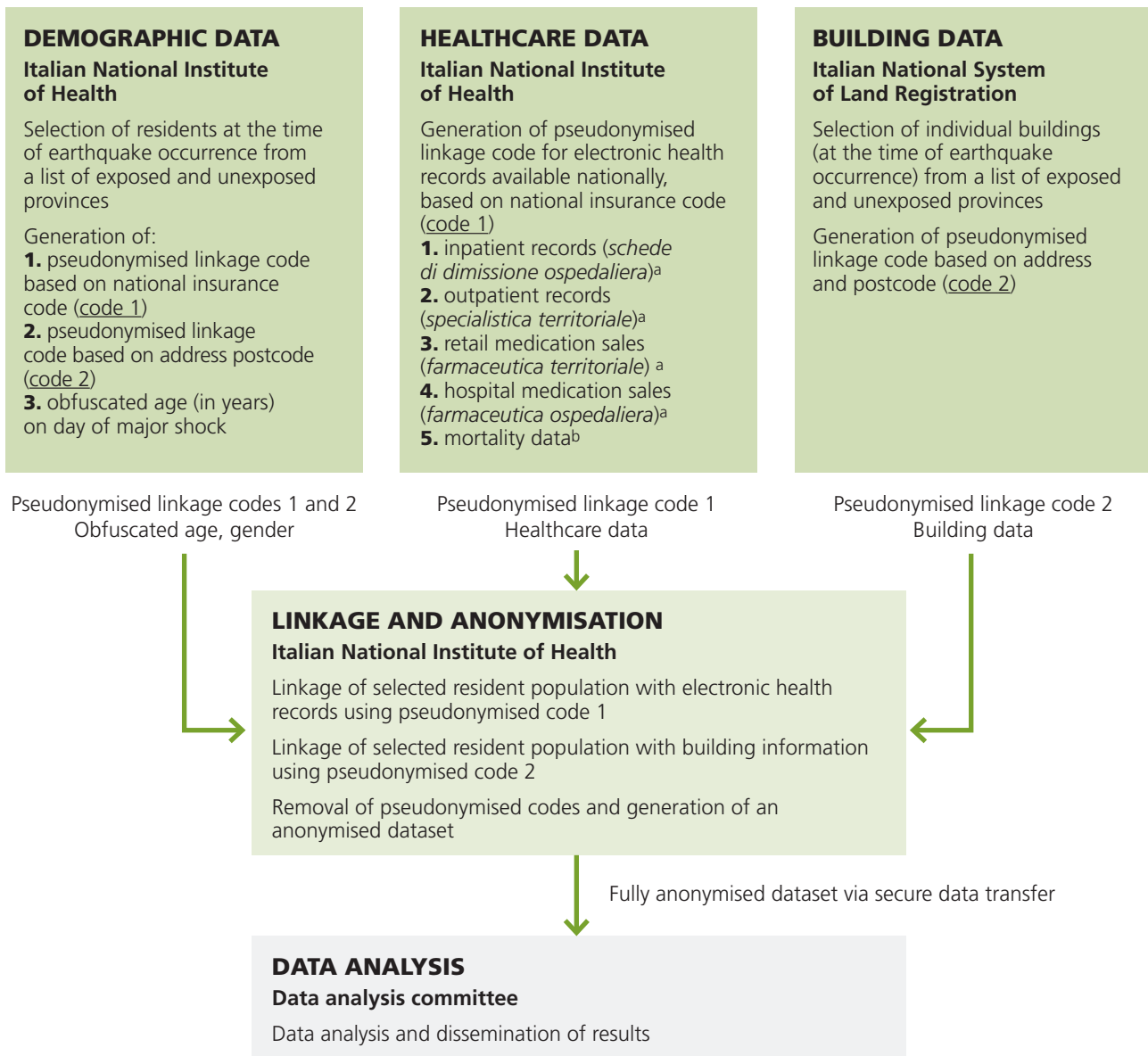
A retrospective cohort design would enable detailed ascertainment of the effects of earthquakes whilst including individuals who moved beyond their usual residential province. As several thousand people were displaced due to earthquakes, requesting electronic health records only from the exposed provinces would likely result in right censoring of the data, which would bias associations towards the null and therefore lead to likely underestimation of earthquake effects.

The proposed design requires individual-level data of the resident population to collect sociodemographic composition of the at-risk population and matched controls before each earthquake; subsequent linkage with electronic health records and, potentially, linkage with individual building characteristics to assess potential effect modification.

A cohort design in disaster epidemiology is not new,<sup>13</sup> but the idea of linking resident data with e-health data and building characteristics is novel and particularly attractive when investigating the health effects of earthquakes. While building characteristics are known to have an impact on earthquake-related immediate injury and death,<sup>14-17</sup> their impact on chronic health outcomes is unclear. It is possible that living in at-risk buildings may indirectly increase long-term morbidity and mortality, for example via an increased duration of displacement. A better understanding of the potential effect modification arising from building characteristics might further support the need for preparedness efforts related to building-related risk factors. In line with the information analysed in previous short-term studies, building characteristics should comprise essential features that may affect the building's response to seismic shocks, such as configuration (e.g., single building or storey), frame (e.g., reinforced concrete or stones/bricks), and period of construction.<sup>14-17</sup> At the time of writing, it is not yet clear whether individual building characteristics data will be available from the Italian National System of Land Registration (*catasto*). If confidentiality concerns render such a linkage difficult, a possible solution could consist in obfuscating building characteristics (e.g., by categorising building construction year) or in generating area-level, aggregated datasets. The latter approach, while practical, has however the disadvantage of being prone to bias due to potential contextual effects of neighbourhood environments on health outcomes (independent of individual building characteristics). Disagreement between individual and area-level socioeconomic status has been shown in previous publications,<sup>18-20</sup> and it is possible that a similar distortion might occur when using aggregated data of building characteristics.

Further details about the proposed linkage process is available in figure 1.

An important requirement is that the linkage of individual-level data should occur while preserving the confidentiality of participants. As such, measures will be applied to pseudonymise participant information and retain only the data that are essential for analysis (e.g., after linkage, day of birth, and death could be obfuscated to prevent re-identification). We feel that, ideally, this process should be managed by the Italian National Institute of Health (*Istituto Superiore di Sanità*, ISS). The purpose of this study would fall within their institutional mission to protect national public health, as reflected by their previous involvement in studies assessing the health impact of the L'Aquila earthquake.<sup>21-24</sup> Furthermore, ISS have access to demo-



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b. Istat. Decessi e cause di morte: cosa produce l'ISTAT. Istat 2020. Available from: <https://www.istat.it/it/archivio/240401> (last accessed: 30.04.2020).

**Figure 1.** Proposed linkage procedures for a retrospective cohort study of the long-term health effects of recent earthquakes in Italy.

**Figura 1.** Procedure di linkage proposte per uno studio di coorte retrospettivo degli effetti sulla salute a lungo termine dei terremoti recenti avvenuti in Italia.

graphic and healthcare data needed for this study, which would likely facilitate generation of an anonymised analytic dataset. However, alternative options should be explored if this solution is not viable. For example, investigators could consider a decentralised approach similar to the one used in a large-scale investigation of factors associated with Covid-19 prognosis in 17 million UK participants.<sup>25</sup> In this approach, a standardised software would be provided to regional authorities which would perform linkage and analyses locally, and only summary association statistics would be shared with the data analysis committee. This method would likely reduce confidentiality problems, but would have the disadvantage of not enabling linkage of participants that used healthcare facilities outside of their region of residence.

## ALTERNATIVE STUDY DESIGN

If the above-described design is not feasible, e.g., due to the difficulty in linking resident data with healthcare data and building characteristics, we will only request anonymised healthcare data from provinces exposed and unexposed to earthquakes (as defined in the «Participants» paragraph). This will enable quantification of disease events and deaths occurred both before and after the earthquake in exposed provinces and in matched unexposed provinces. While this approach does not need linkage with demographic data, it is worth noting that, due to the high numbers of displaced people, a sizeable proportion of participants will likely not be captured by electronics health records. This unfortunately might bias associations towards the null due to right censoring, thus underestimating earthquake effects.



## INVESTIGATION INTO POTENTIAL INTERMEDIATE TRAITS

As a complement, a parallel study could be conducted analysing variation in risk behaviours from the 'PASSI' national surveillance, active since 2006.<sup>26</sup> In the meta-analysis that Barbara co-led, a two-fold increase in sedentary behaviour was noted, suggesting that a thorough investigation into behavioural determinants of health and intermediate traits of cardiometabolic diseases would be useful to complement analyses on health outcomes.

## ADDITIONAL EXPLORATORY ANALYSES

Given its large scale, we envision that this study should also attempt to assess the effects of earthquakes on all outcomes available from electronic health records via a phenome-wide, agnostic assessment (while conducting appropriate adjustment for potential false-discovery rate). Ideally, this study should also attempt investigation of potential subgroup effects by sociodemographic characteristics (e.g., gender, age, socioeconomic status) and geographical region (as some heterogeneity in damage and damage mitigation is expected owing to broad socioeconomic inequalities).

## PUBLIC ENGAGEMENT AND INVOLVEMENT

Using electronic health records for public health research is within the scope of the General Data Protection Regulation (GDPR) (EU Regulation 2016/679), which in Articles 6(1) and 9(2) allows data processing in the public interest and for scientific research purposes.<sup>27</sup>

We feel that it would be useful to be transparent about this plan and confer with the general public, including (but not limited to) associations of earthquake victims and their relatives. This will hopefully ensure that the purposes and methods of this study are aligned with the public's priorities and expectations.

## CONCLUSIONS

In this opinion paper, we summarised the contributions to earthquake epidemiology by Barbara Pacelli, a talented epidemiologist who passed away unexpectedly last year. Based on her work, we feel that there is a strong rationale for a large-scale investigation into the long-term health effects of earthquakes in Italy. We propose a retrospective cohort study design that would enable follow-up of displaced populations, thus resulting in reliable estimation of earthquake effects. The investigation will be led by a consortium of centres with expertise in disaster medicine and preparedness (CRIMEDIM WHO Collaborating Centre, Italy), earthquake epidemiology (University of L'Aquila, Italy), and analysis of large-scale datasets (University of Cambridge, UK). If successful, this effort would be the first to reliably assess the long-term health effects of earthquakes at an unprecedented scale and detail.

**Conflict of interest:** none declared.

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