Medium and long-term health effects of earthquakes in high-income countries: a systematic review and meta-analysis

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Key Messages

- This systematic review and meta-analysis found increased mortality and morbidity for some health outcomes in the medium and long term, particularly: (i) increased mortality rates for all causes, myocardial infarction, and stroke, and (ii) greater mean levels of glycated haemoglobin
- However, this review also found no evidence of earthquake effects in terms of blood pressure, body mass index, and lipid biomarkers
- Epidemiological surveillance after all major earthquakes is essential to set up public health priorities and advance research
- Whenever possible, future studies should use a cohort design, include both temporal and geographical comparison groups, and assess both physical and mental health indicators
- Post-earthquake epidemiological surveillance should also capture the impact of seismic events on the access and utilization of healthcare services

Keywords: earthquake, health, methods, natural disaster, systematic review, meta-analysis

Abstract

Background. Accurate monitoring of population health is essential to ensure proper recovery after earthquakes. We aimed to summarize the findings and features of post-earthquake epidemiological studies conducted in high-income countries and prompt the development of future surveillance plans.

Methods. Medline, Scopus, and 6 sources of grey literature were systematically searched. Inclusion criteria comprised: observational study conducted in high-income countries with at least one comparison group of unexposed participants, measurement of health outcomes at least one month after the earthquake.

Results. Fifty-two articles were included, assessing the effects of 13 earthquakes occurred in eight countries. Most studies had a time-series (33%) or cross-sectional (29%) design, included temporal comparison groups (63%), used routine data (58%) and focused on patient subgroups rather than the whole population (65%). Individuals exposed to earthquakes presented: 2% higher all-cause mortality rates (95% confidence interval [CI] 1 to 3%), 36% (95%CI 19 to 57%) and 37% (95%CI 29 to 46%) greater mortality rates from myocardial infarction and stroke, 0.16 higher mean percent points of glycated haemoglobin (95%CI 0.07 to 0.25 percent points) and no evidence of earthquake effects for blood pressure, body mass index, and lipid biomarkers.

Conclusion. A more regular and coordinated use of large and routinely-collected datasets would benefit post-earthquake epidemiological surveillance. Whenever possible, a cohort design with geographical and temporal comparison groups should be used, and both communicable and non-communicable diseases should be assessed. Post-earthquake epidemiological surveillance should also capture the impact of seismic events on the access and utilization of healthcare services.

Introduction

Over the last decades, the frequency of natural disasters has risen sharply leading to dramatic consequences and huge economic losses. Only in 2014, 324 natural disasters were reported, resulting in 141 million casualties and in damages for nearly 100 billion dollars.[1] Geophysical disasters, including earthquakes, accounted for circa 10% of these events.

The Sendai Framework for Disaster Risk Reduction promoted by the United Nations fosters a comprehensive approach for disaster prevention, response and recovery, and therefore represents an important step forward to reduce disaster-induced mortality and morbidity. As such, the Sendai Framework highlights that an accurate monitoring of the health status of populations exposed to disasters is essential to identify priority interventions and restore previous health condition.[1,2] Given that earthquakes are non-predictable events, epidemiological surveillance is particularly useful to alleviate the burden of death, disability and disease that often follow these calamities.

Noteworthy is that low-income countries are the most affected by disasters. Regrettably, more pressing political and economic constraints make long-term epidemiological surveillance often impracticable in these settings. By contrast, high-income countries rely on more robust healthcare networks which should allow for the conduction of long-term epidemiological research. However, epidemiological follow-up after earthquakes seems to be often scant and poorly planned also in countries with well-established healthcare systems.[3–5]

Although several approaches for proper epidemiological monitoring after earthquakes have been discussed,[1,6] a comprehensive overview of earthquake-related health effects in the medium or long term is not yet available as most previous studies focused on the immediate health effects of these calamities (i.e., in terms of hours or days).[7,8] Reviews reporting on medium and long-term earthquake effects either focused on specific earthquakes[9,10] or specific sets of health outcomes—particularly in the field of mental health.[11,12]

To our knowledge, no comprehensive systematic research has been conducted on all medium and long-term health effects of earthquakes to date. This study aimed to fill this gap by providing an insight on the methodological approaches and main findings of epidemiological studies assessing the middle and long-term effects of earthquakes in high-income countries.

Methods

We carried out this systematic review and meta-analysis in accordance with the Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) statement.[13]

Search and selection

We searched two electronic databases, Pubmed (MEDLINE) and Scopus, and 6 sources of grey literature including the websites of The World Health Organization, Centers for Disease Control and Prevention – USA, European Centre for Disease Control and Prevention – European Union, National Institutes of Health – USA, EpiCentro Istituto Superiore di Sanità – Italy and Centro di documentazione per la promozione della salute – Italy). **Supplementary Materials 1** lists the search strings used. We included all studies concerning humans and written in either of the following 6 languages: English, Italian, Spanish, French, Portuguese, German. No time restrictions were set. All the reviews found with this search were manually inspected in order to obtain additional studies.

Four authors (ARG, BP, EA, MA) independently screened the titles and abstracts of all papers to exclude those not relevant to the objective of the review; any disagreement was resolved through discussion among these authors. One author (among ARG, DS, GI, MA) read the full-texts of the papers that passed the initial screening to assess compliance with the predefined inclusion and exclusion criteria, and their work was checked independently by another author (either BP or EA).

Inclusion and exclusion criteria

We included studies that: (i) focused on health indicators[14,15] such as mortality and disease incidence, prevalence of risk factors, and access and utilization of healthcare services; (ii) measured indicators occurred at least one month after the main seismic event; (iii) investigated an earthquake that took place in a country classified as a high-income economy by the World Bank;[16] (iv) had an observational design with at least one comparison group, including either a measurement done before the earthquake (from now on, 'temporal comparison group') or obtained from an area that was not affected by the earthquake ('geographical comparison group').

Studies were excluded if: (i) the health effects of the earthquake could not be distinguished from those due to other natural disasters; (ii) some or all of the participants in the comparison group were exposed to the earthquake; (iii) exposure or outcome were not measured objectively (e.g., measurement of self-reported intensity of earthquake damage or use of self-reported pre-earthquake heath status collected during a post-earthquake survey); (iv) the study did not report on quantitative research, was a literature review, or was retracted.

For the specific case of the Great East Japan earthquake of 11 March 2011, which was followed by a tsunami that flooded the area located within 10 km from the coast[17] and a nuclear accident that caused a mass evacuation of the area located in the radius of 20 Km from the Fukushima-Daiichi nuclear power plant,[18] we excluded studies regarding areas located ≤ 10 Km from the coast and ≤ 20 Km from the Fukushima-Daiichi power plant.

Data extraction

For each study, one author (among ARG, MA, DS, GI, BP, EA) extracted data from included papers using a predefined data extraction template and another author (either BP or EA) independently checked their work. Any disagreement was resolved by discussion. We extracted the following study-specific characteristics: earthquake investigated, study design (prospective or retrospective cohort, cross-sectional study, time-series study), study population, sample size, percent of male participants, mean participant age, data source (e.g., hospital records, ad-hoc databases, or both). For each outcome and comparison group, we extracted the following variables as appropriate: number of participants, start and end of follow-up, mean and variance (either standard deviation, standard error, or interquartile range; the latter two were converted to standard deviation as appropriate). Since most studies reported on more than one outcome, the total number of outcomes is greater than the total number of studies. We calculated person-years multiplying group-specific number of participants and length of follow-up. We extracted reported units for all continuous outcomes. In case of multiple publications on the same earthquake, we used the most up-to-date and comprehensive information.

Data synthesis

In descriptive analyses, we used frequencies and proportions to describe categorical variables, and medians and interquartile ranges to summarize continuous variables.

We carried out meta-analyses for all the outcomes assessed. Before carrying out meta-analyses, we harmonised units for continuous outcomes, collapsed within-study subgroups, and dealt with multiple comparison groups as detailed in **Supplementary Materials 2**. For each outcome, within-study summary measures such as incidence rate ratio (IRR), risk ratio (RR), and mean difference (MD) were estimated as appropriate to compare exposed and unexposed participants, using the default settings of the metafor package in R.[19] Outcome-specific summary estimates were then pooled if available for at least two studies having the same type of comparison group (either temporal of geographical) and the same type of summary measure (either IRR, RR, or MD). Owing to heterogeneity in study characteristics and earthquake assessed, we fitted random effects models. We tested evidence of heterogeneity with the Q statistic and quantified the percentage of variability in the effect estimates due to heterogeneity with the I-squared statistic. We plotted both study-specific and pooled effect estimates, including 95% confidence intervals, using Forest plots generated with the metafor package in R.[19] For all meta-analyses including at least 4 studies, we conducted sensitivity analyses to check if the pooled estimates were robust to variations in the following study-level characteristics: maximum duration of follow-up, proportion of males, mean age, study design, and study population. All analysis tests were two-sided.

Results

Search and selection of studies

Overall, we found 2,976 papers (1,549 from Pubmed/MEDLINE and Scopus, and 1,427 from the grey literature – **Figure 1**). The initial screening of titles and abstracts led to inclusion of 377 papers. Fifty-two papers met the eligibility criteria and were included. Among the 325 papers excluded, 122 (38%) either focused on a different natural disaster or the earthquake effects could not be disentangled from those of other natural disasters, 84 (26%) lacked a non-overlapping comparison group, and 49 (15%) did not report on quantitative research (e.g., were case reports, commentary articles, letters, news articles, or editorials).

[Figure 1 here]

Earthquake characteristics

Most studies were conducted in Japan (n=27) and Italy (n=13) (**Table 1**). The most investigated earthquakes, with 10 studies each, occurred in Kobe, (Japan, 17 January 1995), L'Aquila (Italy, 6 April 2009), and Eastern Japan (11 March 2011). The median number of deaths was 143 (interquartile range [IQR] 12 to 2342) and the median earthquake magnitude was 6.6 on the Richter scale (IQR 6.3 to 6.9). The countries that presented the largest cumulative number of deaths were Japan (n=26,467) and Italy (n=3,030).

[Table 1 here]

Study characteristics

We extracted meta-analysis data from 52 studies including 82,479 subjects from studies which analysed individual-level data and 50,015,914 subjects from studies based on aggregated data, in which individual-participant characteristic were not available for the denominator. **Table 2** presents the main characteristics and outcomes assessed by the studies included in this review.

[Table 2 here]

Included studies were published between 1981 and 2015, mostly (58%) between 2010 and 2015. Most studies used time series (n=17) and cross sectional (n=15) study designs, and employed a temporal comparison group, i.e. the outcome of interest was measured at least twice, both before and after the earthquake (n=33). While most studies (n=34) selected participants based on their age or medical condition, 15 studies focused on the general population. Most studies used routinely collected data (n=30), e.g. data from hospital databases (n=18). A considerable number of studies (n=19) used ad-hoc data, mostly obtained from questionnaires (n=13). Only 7 out of 52 studies evaluated whether the effects of earthquakes varied by the intensity of earthquake exposure (e.g., distance from the earthquake epicentre).

Studies had a median sample size of 1,448 subjects (interquartile range [IQR] 175 to 372,253); the largest samples were collected in studies with a time-series design (median 417,900; IQR 301,053 to 4,391,035) and having both temporal and geographical comparison groups (median 163,992; IQR 742 – 845,617). The median number of measurements of was 3 (IQR 2 to 10); the highest number of measurements was observed in studies with a time-series design (median number of measurements 14; IQR 6 to 39) and in studies with temporal comparison group (median number of measurements 4; IQR 2 to 12). Overall, the median length of follow-up was 6 months (IQR 3 to 12); the median length of follow-up was longest for time-series studies (7 months; IRQ

3 to 12) and for studies with both temporal and geographical comparison groups (20 months; IQR 10 to 36).

Earthquake effects on outcomes assessed by 4 or more studies

While accounting for across study heterogeneity, there was strong evidence ($p<0.001$) of 36% greater mortality rates from myocardial infarction after earthquakes compared to measurements carried out before the earthquake (95% confidence interval [CI] 19% to 57%) (**Figure 2A**). In a meta-analysis of 4 studies, there was weak evidence ($p=0.0725$) of 11% lower suicide rates after the earthquakes (95%CI -21% to 1%).

People exposed to earthquakes had higher mean levels of glycated haemoglobin (0.16 percent points, 95%CI 0.07 to 0.25) compared to people unexposed to the earthquake (**Figure 2B**). There was no evidence of earthquake effects in terms of blood pressure, body mass index, and lipid biomarkers.

These findings were generally robust to a number of sensitivity analyses (**Supplementary Materials 3**), with the exception of suicide rates that were higher among people exposed to the earthquake in 1 study using a geographical comparison – an apparent contradiction with the 4 studies using temporal controls.

[Figure 2 here]

Earthquake effects on outcomes assessed by 1 to 3 studies

The full results of earthquake effects for all outcomes from all studies, including effects on several psychometric scales, are available in **Supplementary Materials 4**. In the interest of concision, **Figure 3** presents only findings based on a sample size of at least 1,000 participants and with an effect p-value lower than 0.001.

Although only two studies were available for each meta-analysis, all-cause mortality rates were 2% higher (95%CI 1% to 3%) and stroke mortality rates were 37% higher (95%CI 29% to 46%) among individuals exposed to earthquakes compared to unexposed participants (**Figure 3A**).

In 4 individual studies that could not be pooled together owing to incompatible outcome and comparison-group definitions, individuals exposed to earthquakes had generally higher mortality rates from cardiovascular disease (**Supplementary Materials 4**).

Among people exposed to the Kobe earthquake (Japan, 1995), there was evidence of a general increase in incidence rates of both total and bleeding gastric ulcers.

People exposed to the Irpinia and Naples earthquake (Italy, 1980) had (i) lower incidence rates of German measles and whooping cough, (ii) higher incidence rates of typhoid/paratyphoid and viral hepatitis infections, and (iii) 3% lower hospital discharge rates (95%CI -3% to -2%).

After the L'Aquila earthquake (2009, Italy), there was evidence of a 6% increase in overall antipsychotics consumption (95%CI 4% to 8%), particularly promazine and amilsulpride. Earthquake effects for antidepressants were in different directions. There was evidence of a 2% increase in serotonin reuptake inhibitors consumption rates (95%CI 1% to 2%), but also evidence of a 5% reduction in tricyclics (95%CI -6% to -4%) and a 1% reduction in other antidepressants (95%CI -2% to -1%).

People exposed to L'Aquila earthquake also had a two-fold greater risk of sedentary behaviour (95%CI 1.56 to 2.60) (**Figure 3B**).

After the Great East Japan 2011 earthquake, there was evidence of 0.95 percent point greater average daily prevalence of insomnia compared to daily measurements recorded before the earthquake (95% 0.93 to 0.98 percent points) (**Figure 3C**).

[Figure 3 here]

Discussion

The steep rise in the world population over the past decades and the urbanization of zones with high seismic risk have played a key role in amplifying the impact of earthquakes on human health.[20] Unfortunately, this risk has not triggered a simultaneous improvement of epidemiological surveillance plans in the aftermath of earthquakes. For this reason, a review of the epidemiological studies investigating the chronic health effects of earthquakes can be helpful to guide the development and implementation of future surveillance guidelines.

Discussion of the methodological approaches of the studies included

Out of the 50 seismic events with magnitude ≥ 6.0 that occurred in high-income countries between 1990 and 2012,[21] only 11 were investigated by the studies included in this review (**Supplementary Materials 5**). These 11 events caused a median of 143 deaths (IQR 26 to 421), while the 39 events that were not investigated resulted in a median of 2 deaths (IQR 1 to 7) despite having similar magnitude (6.7 vs 6.6, respectively). This suggests that the studies meeting the inclusion criteria for this review focused mostly on the earthquakes that caused the highest number of casualties. The fact that the earthquakes of Great East Japan (20,896 deaths), Kobe/Hanshin-Awaji (5,530) and L'Aquila (295) were the most frequently investigated supports this hypothesis. However, other deadly seismic events were apparently not investigated, such as the earthquakes of Hokkaido (Japan 1993, 243 deaths) and Georgia (29th April 1991, 114 deaths). Since most of the studies included in this review were published after the year 2000 and the number of studies increased exponentially over time, it is possible that some earthquakes were not investigated either because, at that time, the monitoring of the chronic effects of earthquakes was not deemed a public health priority, or because the epidemiological studies conducted were never published or made available in the institutional websites that we inspected.

The principal reason for exclusion from this review was the difficulty in disentangling the effects of earthquakes from those of other natural disasters occurred simultaneously or as a consequence of the main seismic event (e.g. the Great East Japan earthquake in March 2011 which was followed by a tsunami and a nuclear accident). These studies were excluded based on the assumption that different types of disasters may result in different types of health effects.[22] For example, an isolated nuclear accident can cause immediate mental stress merely on anticipatory basis (fear of cancer, congenital anomalies, etc.) with a greater impact on adult age subgroups (capable of recognizing the risk). By contrast, people exposed to earthquakes appear more likely to suffer from post-traumatic stress disorder, rather than from anticipatory mental stress.[23] Therefore, we excluded a considerable number of studies in order to be able to specifically assess the epidemiological effects of earthquakes.

Most studies used a cross-sectional or time-series design (33% each) and included temporal comparison groups (63%); prospective cohorts were only used in 14 studies (27%). It is well-known that longitudinal studies have a more robust design than cross-sectional studies, enabling the investigation of causal hypotheses when using appropriate methods. However, cohort studies can be resource-consuming, whereas cross-sectional studies with a temporal or geographical comparison group are generally cheaper and can provide timely estimates if a quick response is needed.[24] Since timeliness is usually not a priority for studies assessing medium and long-term health effects, it is possible that the availability of resources may have influenced the choice of the cross-sectional design over the cohort design for some studies.

Furthermore, data sources and their accessibility play an important role in influencing the choice of many study characteristics such as the outcome under study, study design, and timeliness of the investigation. The majority of the studies (58%) used routinely collected data, especially hospital databases (37%). Interestingly, in several studies investigating L'Aquila earthquake (Italy, 2009) there was a lower utilization of routine data compared to studies concerning other earthquakes in high-income countries.[25] The type of outcomes investigated and the study design applied might have been influenced by context-specific factors, namely availability of appropriate resources, human capital, and data sources. A nationally-coordinated and interdisciplinary approach could overcome these limitations by involving epidemiologists and health professionals from both the area hit by the earthquakes and from other centres specialized in disaster epidemiology.

In the case of unpredictable exposures such as some natural disasters, routine data with proper temporal and geographical coverage can provide a good compromise between methodological rigour and economic sustainability. As high-quality routine data are available in many affluent countries, a more widespread linkage between routinely-collected data sources (e.g. primary care records, specialist registries, hospital admission records, mortality registries) would enable systematic assessment of the effects of earthquakes on the most relevant health outcomes while accounting for the most common sources of bias and confounding.

Discussion of the main earthquake effects captured by the studies included

The studies included in this review measured several outcomes comprising: mortality, cardiovascular diseases, mental health and problems related to lifestyle (**Figures 2-3**, **Supplementary Materials 3-4**). Some evidence of a post-earthquake increase was observed for many of these outcomes, suggesting that the long-term assessment of the population's health status is essential to set priorities in resource allocation. Interestingly, in their review on the public health effects of mass traumatic events, Johnson et al. mentioned motor disability and musculoskeletal sequelae as *chief* chronic earthquake-related health problems.[22] On the contrary, our findings suggest that a wide range of physical and mental health endpoints should be monitored several months or years after an earthquake.

This systematic review and meta-analysis found an increased mortality rate for all causes, myocardial infarction, and stroke from the first month to up to 3 years after an earthquake. While these findings have been consistently reproduced in the literature, the reasons at their basis are still unclear. Previous research has underscored the importance of psychological stress as a predictor of coronary heart disease [26,27]; therefore, it is possible that psychological stress and the subsequent sympathetic activation may have played a role in explaining this association. However, a meta-analysis of 7 studies included in this paper showed that earthquakes do not seem to affect clinically measured blood pressure. Additional factors explaining these findings include the destruction of medical records which can lead to one or more consultations/treatments missed, the occurrence of circumstances that can delay self-care such as relocation and unemployment, and reporting bias as some outcomes may have been considered less interesting by researchers and journals.

Regarding the metabolic effects of earthquakes, previous reviews pointed to higher rates of diabetes among disaster-exposed individuals.[22,28] Our meta-analysis confirms that a modest increase of glycated haemoglobin occurs from two to twelve months after earthquakes. Previous literature suggests that at the basis of this phenomenon there could be a combination of various factors such as the disruption of normal routines, emotional stress, change in dietary intake, difficult access to supplies due to the damage of health facilities and pharmacies or interruption in the mobilization of stockpiles to long-term established shelters.

Studies reporting on the rates of bleeding and non-bleeding gastric ulcers highlighted an increased probability of these events in the long-term among individuals exposed to earthquakes. Interestingly, this was true regardless of the temporal or geographical nature of the comparison group. This could be attributed to the loss of function of hospitals located in the hardest-hit areas, failure to follow up patients with mild symptoms and mental stress. Of note, the negative impact of the earthquake on the functioning of those health facilities located in the proximity of the epicentre determined, such as in the study by Aoyama et al,[29] a lower number of diagnostic procedures performed; this may have masked an even greater incidence of gastrointestinal ulcer in the areas most affected by earthquakes.

Limited evidence for infectious epidemics after geophysical disasters is available;[30] our results suggest that gastrointestinal infectious agents could be more easily spread in the aftermath of earthquakes while, conversely, airborne infections might decrease. These data are in contradiction with current literature[22] and might be due to the fact that this meta-analysis included only one paper focusing on infectious diseases and that it was restricted to a single country (Italy). Further studies would be useful to appreciate long-term earthquake-related patterns of infectious diseases in high-income countries.

In light of our findings, the role that earthquakes may play in mental health also deserves special attention. While earthquakes seemed to protect from suicide when temporal comparison groups were used, the opposite was found when the comparison group was geographical and when assessing both suicidal ideation and suicide attempts (**Supplementary Materials 3-4**). This highlights the complexity of this phenomenon, which might be heavily influenced by both individual and socio-contextual factors such as gender, earthquake-related experience (e.g. injury, clean-up work activity, loss of family members), sociocultural factors and pre-earthquake mental health. Some studies reported an increase in a vast array of psychiatric and mood disorders, especially in the case of repeated or high-intensity exposure to earthquakes.[31,32] This suggests that earthquakes may be a serious risk factor for mental health disease due to, firstly, the traumatic environmental experience and secondly, the life changes that follow the initial event (e.g. loss of family and friends, unemployment and/or relocation). Unfortunately, differences in terms of outcome definitions and comparison groups prevented further analysis. Altogether, our findings make the case for additional and larger studies including both geographical and temporal comparison groups.

Lastly, it is worth noting that four studies included in our review focussed on health outcomes after the sequence of 4 earthquakes occurred in Christchurch (New Zealand, September 2010-mid-2012).[34–37] Owing to the small numbers of studies available, it is difficult to compare the health effects of repeated events with those of a single earthquake. However, taken together, the effects reported by these studies seem to be broadly in line with those found by investigations concerning a single event (e.g., greater prevalence of mental health disorders among people exposed to multiple seismic events compared to unexposed individuals).

Limitations of this review

Papers written in Japanese were excluded from this review; therefore, some relevant studies may have been missed out. However, this looks unlikely as the most relevant Japanese studies were probably published in English, and our search of six sources of grey literature seems sufficiently broad to capture the most influential epidemiological studies carried out in Japan.

Only two electronic databases (Medline and Scopus) were used in this review. Considering the number and combination of keywords used in this search it would have been unfeasible, with the resources available, to extend the search to other databases. However, these two databases are among the most comprehensive for epidemiological literature. Additionally, grey literature search is likely to have detected initially unretrieved articles.

Some heterogeneity was noted in the meta-analyses we carried out. This is understandable owing to the breadth of our review. Although we attempted to combine studies that were as comparable as possible, this review includes studies conducted in different times, places, and with varying methodology. Between-study heterogeneity was therefore explicitly accounted for, and random-effects meta-analyses were used for all outcomes reported by at least two comparable studies.

It is worth noting that the present review focuses on the studies assessing the independent effects of an earthquake or a series of seismic events. Therefore, the findings of this review should not be generalised to other natural disasters occurring simultaneously with earthquakes or caused by them.

Lastly, this meta-analysis was restricted to earthquakes occurred in high-income countries due to the political and economic barriers that render long-term epidemiological surveillance often impracticable in these settings. While this limitation may be overcome in future updates of this review, it is worth noting that caution should be used when generalised the findings of this review to low-income countries.

Suggestions for the epidemiological surveillance of future earthquakes

From the evidence accrued in the epidemiological studies carried out in the past thirty years, some suggestions emerge that could inform future studies aiming to assess the medium and long-term health effects of earthquakes:

1. Aim: every major earthquake should be investigated for its medium and long-term health effects. In the past, these effects have not been assessed as extensively as for other types of environmental exposure. The numerous health effects reported in the present review suggest that the health needs arising from earthquakes may have been underestimated in many cases, even in high-income countries. Future epidemiological surveillance should be set up to enable timely and in-depth measurement of the medium and long-term health effects of every earthquake.
2. Study design: (a) an intensive and coordinated use of routine data can benefit both epidemiological surveillance and etiological studies in the aftermath of earthquakes; (b) both geographical and temporal comparison groups should be included and both the general population and vulnerable groups (e.g., children and the elderly, patients with chronic disease, healthcare workers involved in the earthquake response) should be considered; (c) a cohort study designs should be preferred whenever possible.
3. Indicators: the complexity in the results obtained in this meta-analysis should prompt epidemiological surveillance studies to capture and report the changes of as many health indicators as possible, e.g. mortality, mental health, vital signs, biomarkers, behavioural

risk factors, and health service utilization. This amount of information will be instrumental to guide practice, by improving efficiency and efficacy of evidence-based public health interventions, and research, by helping to uncover long-term earthquake effects that have not yet been detected.

4. Contributors: a multidisciplinary approach should be preferred, starting from the identification of priority indicators. Contributors should encompass professionals from different and complementary disciplines, including epidemiologists, statisticians, and public health professionals capable of devising and processing standardized protocols for data collection and analysis. The involvement of professionals from various disciplines would also ensure effective communication of key messages to the population at risk, which is also a priority in both recovery and preparedness phases.[38]

Conclusion

Despite the efforts and resources involved to prevent and mitigate the effects of earthquakes, these disasters have still a tremendous health impact even in high-income countries. The Sendai Framework for Disaster Risk Reduction, adopted at the Third United Nations World Conference (Sendai, Japan, March 2015), pursues to achieve a "*substantial reduction of disaster risk and losses in lives, livelihoods and health*"[2]. In order to meet this goal, appropriate preparedness, response and damage mitigation are essential when facing unpredictable events, as in the case of earthquakes.[39]

Epidemiology can play a major role in fostering recovery and preparedness. Considering the numerous earthquake-related health effects reported in this review, all future earthquakes should be investigated to capture their medium and long-term health effects. As earthquakes have been associated to a broad range of health outcomes, rigorous monitoring of their chronic health effects is pivotal to prioritize local and national public health interventions. Allocation of resources matching the health needs of the population affected by the earthquake can alleviate the chronic health effects of these disastrous events. Additionally, regular updates on the health status of the populations would improve future preparedness plans. Already in 1985, De Bruycker and colleagues pointed out "*the need to establish, in each disaster-prone area, a health evaluation system [..] through which data could be collected in view of improving the preparedness and self-reliance of the stricken community itself*".[40]

Over the past 30 years, epidemiology has benefited from great technological advances in many countries, including improvement in computation capabilities and availability of large and integrated electronic datasets. These advances now render feasible planning of epidemiological surveillance capable of providing regular updates on a population's health status in the medium and long-term. We trust that the experience accrued in the past three decades on the epidemiology of earthquakes, and summarized in the present paper, may serve to inform further steps to endure promotion of the population's health in the aftermath of earthquakes.

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Author contributions

ARG, BP, FF and EA contributed to the study concepts. EA ARG, FF, FDC identified the search string; ARG, BP, EA, MA screened the titles and abstracts of all papers to select the studies according to predefined the eligibility criteria and discussed potential disagreement. ARG, DS, GI, MA assessed the full-text of the papers that passed the initial screening; BP and EA reassessed them for compliance with the predefined eligibility criteria. ARG, MA, DS, GI, BP, and EA extracted data for meta-analysis. EA analyzed the data. ARG, BP, MA, FDC, FF, and EA contributed to the interpretation of data. ARG, BP, MA and EA drafted the manuscript. All authors revised critically and edited the manuscript. All authors have seen and approved the final version of the manuscript. ARG, BP, and EA are the guarantors.

Conflicts of interest statement

The authors declare that they do not have conflicts of interest. This study was carried out independently from research groups involved in the assessment of the health effects associated with earthquakes.

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Table 1. Characteristics of the 13 earthquakes investigated by the 52 studies included in this review

Country	Date	Earthquake	Magnitude[a]	N deaths[a]	N studies
Australia	28 December 1989	Newcastle	5.4[b]	12[b]	1
Chile	13 June 2005	Tarapacá	7.8	11	1
	27 February 2010	Maule region	8.8	547	1
Greece	7 September 1999	Athens and Ano Liosia	6.0	143	2
Iceland	17 June 2000	Holt	6.6	0	1
Italy	23 November 1980	Irpinia and Naples	6.5[c]	2,735[c]	3
	6 April 2009	L'Aquila	6.3	295	10
Japan	17 January 1995	Kobe and Hanshin-Awaji	6.9	5,530	10
	23 October 2004	Niigata Prefecture	6.6	40	6
	25 March 2007	Noto Peninsula	6.7	1	1
	11 March 2011	Great East Japan (Higashi-Nihon)	9.0	20,896	10
New Zealand	22 February 2011[d]	Christchurch	6.1	181	5
USA	17 January 1994	Los Angeles / Northridge, California	6.7	60	1

[a] Except where specified otherwise, magnitude and number of deaths are obtained from the United States Geological Survey 1990-2012 archive [21]
[b] Source: National Centers for Environmental Information [41]
[c] Source: United States Geological Survey archive of the earthquakes with >1,000 fatalities 1900-2014 [42]
[d] One study focused on shocks occurred on 4 September 2010; four on shocks occurred both in 2010 and 2011 (22 February, 13 June, 23 December)

Table 2. Main characteristics and outcomes assessed by the 52 studies included in the review

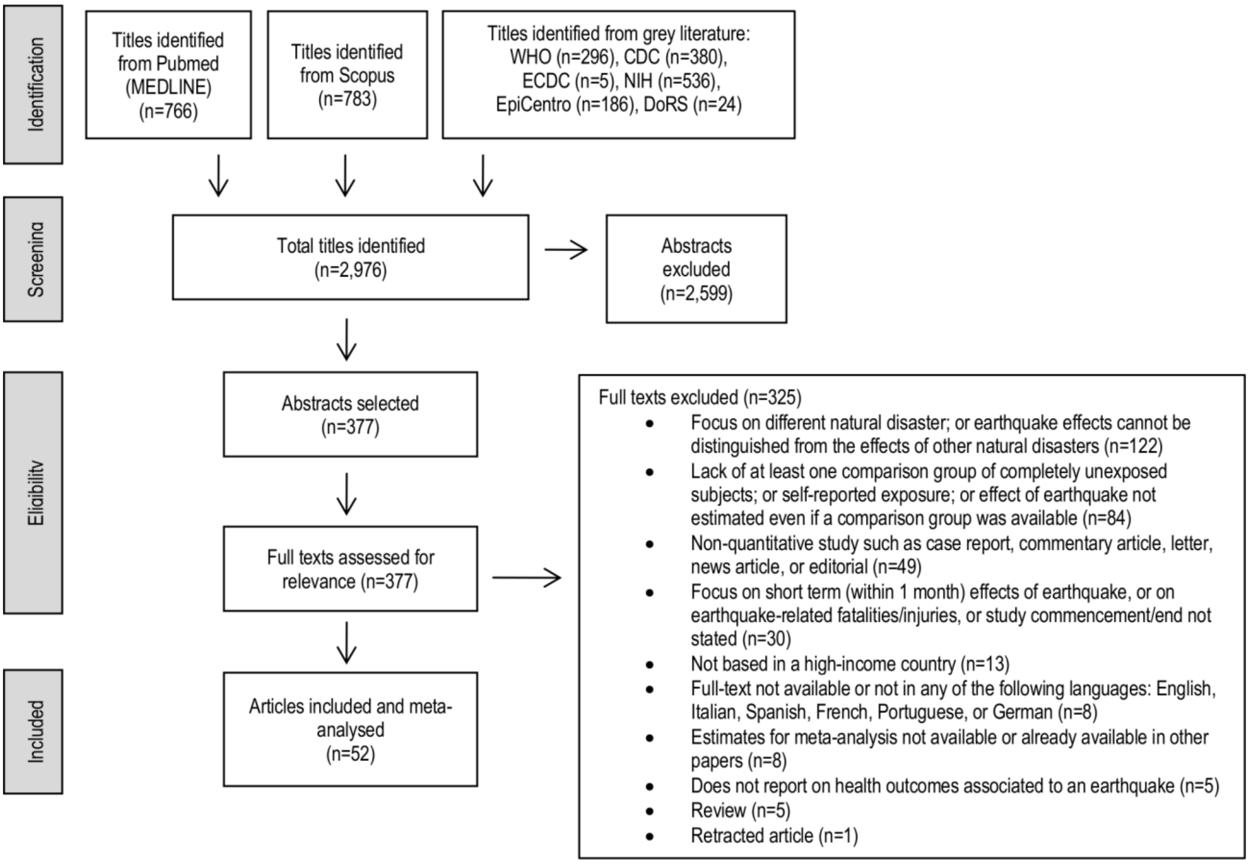
Study	Earthquake (Year)	Study Design (Comparison)	Mean Age (years)	% Males	Follow-up (months)	N Participants	Mortality	Disease: Circulatory	Disease: Nervous system	Disease: Mental health	Disease: Infectious	Disease: Digestive	Disease: Pregnancy, childbirth and puerperium	Disease: Endocrine	Pharmacology	Vital signs & biomarkers	Lifestyle & preventio, screening, healthcare utilization	Psychometric scales	Other outcomes
Alexander 1982 [43]	Irpinia & Naples (1980), Italy	Time-series (T)	-	-	7	6,033,296	-	-	-	✓	✓	-	-	-	-	-	✓	-	-
Aoki 2012 [44]	Great East Japan (2011)	Time-series (T)	-	-	6	4,391,035	-	-	-	✓	-	-	-	-	-	-	-	-	-
Aoyama 1998 [29]	Kobe (1995), Japan	Cross sectional (GT)	-	-	2	26,931	-	-	-	-	-	✓	-	-	-	-	-	-	-
Azuma 2010 [45]	Niigata (2004), Japan	Cohort (T)	41	71	14	4,035	-	✓	-	-	-	-	-	-	-	✓	-	-	-
Bodvarsdottir & Elklit 2004 [46]	Iceland (2000)	Cross sectional (G)	42	47	3	81	-	-	-	✓	-	-	-	-	-	-	-	✓	-
Bourque 2002 [47]	Los Angeles (1994), USA	Time-series (T)	-	-	12	7,676,512	-	-	-	✓	-	-	-	-	-	-	-	-	-
Chan 2013 [34]	Christchurch (2010-2011), New Zealand	Time-series (T)	-	-	1	372,253	-	✓	-	-	-	-	-	-	-	-	-	-	-
D'Argenio 2013 [48]	L'Aquila (2009), Italy	Cross sectional (T)	50	50	19	1,240	-	-	-	✓	-	-	-	-	-	✓	✓	-	✓
Dobson 1991 [49]	Newcastle (1989), Australia	Time-series (T)	-	-	4	417,900	✓	✓	-	-	-	-	-	-	-	-	-	-	-
Fergusson 2014 [35]	Christchurch (2010-2011), New Zealand	Cohort (G)	35	-	24	952	-	-	-	✓	-	-	-	-	-	-	✓	-	-
Fujihara 2012 [50]	Great East Japan (2011)	Cohort (T)	65	63	3	320	-	✓	-	-	-	-	-	-	-	✓	-	-	-
Fukuda 1998 [51]	Kobe (1995), Japan	Time-series (T)	-	-	9	5,395,158	-	-	-	-	-	-	✓	-	-	-	-	-	-
Hata 2012 [52]	Great East Japan (2011)	Cohort (T)	66	100	2	5	-	✓	-	-	-	-	-	-	-	-	-	-	-
Hyodo 2010 [53]	Niigata (2004), Japan	Time-series (GT)	-	48	36	2,426,359	-	-	-	✓	-	-	-	-	-	-	-	-	-
Inui 1998 [54]	Kobe (1995), Japan	Cohort (GT)	59	52	2	434	-	-	-	-	-	-	-	-	-	✓	-	✓	-
Ishii 2014 [55]	Great East Japan (2011)	Cohort (T)	41	6	4	16	-	-	-	✓	-	-	-	-	-	-	-	-	-
ISS 1981 [56]	Irpinia & Naples (1980), Italy	Time-series (T)	-	-	3	1,212,387	✓	-	-	-	-	-	-	-	-	-	-	-	-
Kamoi 2006a [57]	Niigata (2004), Japan	Cohort (T)	67	75	6	222	-	✓	✓	-	-	-	-	✓	✓	✓	-	-	-
Kamoi 2006b [58]	Niigata (2004), Japan	Cohort (T)	59	42	12	65	-	✓	-	-	-	-	-	✓	✓	✓	-	-	-
Kamoi 2006c [59]	Niigata (2004), Japan	Cohort (T)	49	16	2	352	-	-	-	-	-	-	-	-	✓	✓	-	-	-
Kannis-Dymand 2015 [60]	Christchurch (2010), New Zealand	Cross sectional (G)	46	-	2	345	-	-	-	✓	-	-	-	-	-	-	-	✓	-
Kario 2001 [61]	Kobe (1995), Japan	Cohort (T)	69	34	2	124	-	✓	-	-	-	-	-	-	-	-	-	-	-
Kario and Ohashi 1997 [62]	Kobe (1995), Japan	Time-series (T)	-	-	3	64,082	✓	✓	-	-	-	-	-	-	-	-	-	-	-
Kato 2014 [63]	Great East Japan (2011)	Cross sectional (T)	41	33	6	600,000	-	-	-	✓	-	-	-	-	-	-	-	-	-
Kolaitis 2003 [64]	Athens (1999), Greece	Cross sectional (G)	11	47	6	163	-	-	-	✓	-	-	-	-	-	-	-	✓	-
Kotozaki 2012 [65]	Great East Japan (2011)	Cohort (T)	21	50	3	30	-	-	-	-	-	-	-	-	-	✓	-	✓	✓
Nakagawa 2009 [66]	Niigata (2004), Japan	Cross sectional (GT)	-	-	36	2,426,359	✓	-	-	-	-	-	-	-	-	-	-	-	-
Nakano 2012 [67]	Great East Japan (2011)	Cohort (T)	56	71	6	170	-	✓	-	-	-	-	-	-	-	-	-	-	-
Nishio 2009 [68]	Kobe (1995), Japan	Time-series (T)	-	-	36	1,273,333	-	-	-	✓	-	-	-	-	-	-	-	-	-
Pearson 2013 [37]	Christchurch (2010-2011), New Zealand	Time-series (T)	-	-	16	372,253	-	-	-	-	✓	-	-	-	-	-	-	-	-
Pollice 2012 [69]	L'Aquila (2009), Italy	Cohort (T)	32	62	3	117	-	-	-	-	-	-	-	-	-	-	-	✓	-
Rossi 2012 [70]	L'Aquila (2009), Italy	Cross sectional (T)	18	42	10	1,476	-	-	-	-	-	-	-	-	-	-	-	✓	-
Roussos 2005 [71]	Athens (1999), Greece	Cross sectional (G)	-	44	3	1,937	-	-	-	-	-	-	-	-	-	-	-	✓	-
Sofia 2012 [72]	L'Aquila (2009), Italy	Cross sectional (T)	75	52	4	102,669	-	✓	-	-	-	-	-	-	-	-	-	-	-
Sokejima 2004 [31]	Kobe (1995), Japan	Time-series (T)	-	45	24	17,651	-	-	✓	-	-	-	-	-	-	-	-	-	-
Stratta 2012 [73]	L'Aquila (2009), Italy	Cross sectional (G)	33	44	12	948	-	-	-	✓	-	-	-	-	-	-	-	✓	-
Sugiura 2013 [74]	Great East Japan (2011)	Time-series (T)	-	50	2	10,106	-	-	-	✓	-	-	-	-	-	-	-	-	-
Takegami 2015 [75]	Great East Japan (2011); Kobe (1995), Japan	Time-series (T)	-	-	12	16,545,012	✓	-	-	-	-	-	-	-	-	-	-	-	-
Tanaka 2014 [76]	Great East Japan (2011)	Cohort (T)	66	80	2	25	-	✓	-	-	-	-	-	-	✓	✓	-	-	-
Tani 2014 [77]	Great East Japan (2011)	Cohort (T)	67	52	2	205	-	✓	-	-	-	-	-	-	-	✓	-	-	-
Tempesta 2013 [32]	L'Aquila (2009), Italy	Cross sectional (GT)	-	50	24	1,419	-	-	-	-	-	-	-	-	-	-	-	✓	-
Torche and Kleinhaus 2012 [78]	Chile (2005), Chile	Cohort (GT)	-	0	9	7,035	-	-	-	-	-	-	✓	-	-	-	-	-	-

Study	Earthquake (Year)	Study Design (Comparison)	Mean Age (years)	% Males	Follow-up (months)	N Participants	Mortality	Disease							Pharmacology	Vital signs & biomarkers	Lifestyle & preventio, screening, healthcare utilization	Psychometric scales	Other outcomes
								Circulatory	Nervous system	Mental health	Infectious	Digestive	Pregnancy, childbirth and puerperium	Endocrine					
Trevisan 1992 [79]	Irpinia & Naples (1980), Italy	Cohort (T)	41	100	79	505	-	✓	-	-	-	-	-	-	-	✓	-	-	-
Trifirò 2013 [80]	L'Aquila (2009), Italy	Time-series (T)	-	-	11	301,053	-	-	-	-	-	-	-	-	✓	-	-	-	-
Tsuchida 2009 [81]	Japan Noto Peninsula (2007), Japan	Time-series (T)	-	-	1	34,000	-	✓	✓	-	-	-	-	-	-	-	-	-	-
Valenti 2012a [82]	L'Aquila (2009), Italy	Cohort (GT)	-	-	12	36	-	-	-	-	-	-	-	-	-	-	-	✓	-
Valenti 2012b [83]	L'Aquila (2009), Italy	Cohort (T)	-	49	11	179	-	-	-	-	-	-	-	-	-	-	-	✓	-
Valenti 2014 [84]	L'Aquila (2009), Italy	Cohort (GT)	-	11	24	64	-	-	-	-	-	-	-	-	-	-	-	✓	-
Wu 2014 [36]	Christchurch (2010-2011), New Zealand	Time-series (T)	-	-	1	372,253	-	✓	✓	-	-	-	-	-	-	-	-	-	-
Yamamoto 1997 [85]	Kobe (1995), Japan	Cross sectional (T)	-	53	6	221	-	-	-	-	-	-	-	-	-	-	-	-	✓
Yashiro 2000 [86]	Kobe (1995), Japan	Cross sectional (G)	67	63	36	30	✓	-	-	-	-	-	-	-	✓	✓	-	-	✓
Zubizarreta 2013 [87]	Chile (2010), Chile	Cross sectional (T)	48	33	4	5,040	-	-	-	-	-	-	-	-	-	-	-	✓	-

Comparison groups: T, temporal; G, geographical; GT, geographical and temporal

ISS is the Italian National Institute of Health (Istituto Superiore di Sanità)

Figure 1. Paper selection and reasons for exclusion

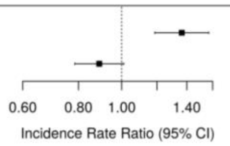


WHO, World Health Organization. CDC, Centers for Disease Control and Prevention (USA). ECDC, European Centre for Disease Control and Prevention (EU). NIH, National Institutes of Health (USA). EpiCentro, Istituto superiore di sanità (Italy). DoRS, Centro di documentazione per la promozione della salute (Italy).

Figure 2. Earthquake effects for all outcomes assessed by 4 or more independent studies

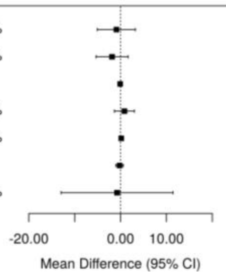
A. Binary outcomes

	Comparison	Follow-up (months)	Studies	Exposed Events/Person-years	Unexposed Events/Person-years	I²	
Myocardial infarction mortality	Temporal	3 to 36	4	11,054/24,632,550	8,102/25,893,326	94.0%	1.36 [1.19, 1.57]
Suicides	Temporal	3 to 36	4	2,075/14,838,090	1,710/19,685,589	56.7%	0.89 [0.79, 1.01]



B. Continuous outcome

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	
Clinically measured diastolic blood pressure	mmHg	Temporal	2 to 79	7	5,568	5,476	98.2%	-0.91 [-5.06, 3.24]
Clinically measured systolic blood pressure	mmHg	Temporal	2 to 79	7	5,568	5,476	93.7%	-1.86 [-5.35, 1.64]
Body mass index	Kg/m²	Temporal	3 to 79	5	4,743	5,147	3.2%	-0.08 [-0.23, 0.06]
Total cholesterol	mg/dL	Temporal	3 to 79	5	4,743	5,147	21.9%	0.83 [-1.35, 3.02]
Glycated haemoglobin	%	Temporal	2 to 12	4	716	717	33.3%	0.16 [0.07, 0.25]
HDL cholesterol	mg/dL	Temporal	3 to 14	4	4,641	4,642	5.8%	-0.21 [-1.01, 0.58]
Triglycerides	mg/dL	Temporal	3 to 79	4	708	1,112	58.8%	-0.77 [-12.98, 11.44]

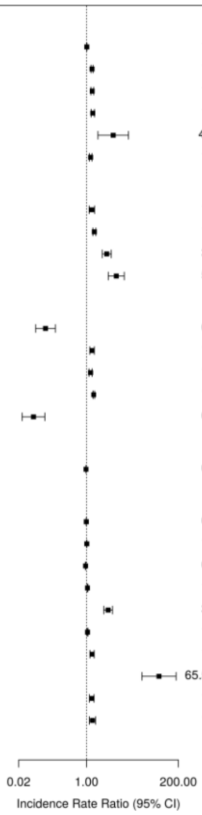


HDL is high-density lipoprotein. I² is percentage of variation across studies due to heterogeneity. Follow-up refers to the latest post-earthquake measurement.

Figure 3. Earthquake effects for outcomes assessed by 1-3 studies based on at least 1,000 participants and with effect p-value < 0.001[a]

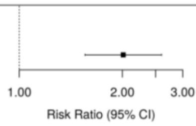
A. Binary outcomes, Incidence Rate Ratio

	Comparison	Follow-up (months)	Studies	Exposed Events/Person-years	Unexposed Events/Person-years	I²	Incidence Rate Ratio (95% CI)
Mortality							
All-cause mortality	Temporal	12	2	179,502/22,316,146	176,741/22,316,146	49.9%	1.02 [1.01, 1.03]
Stroke mortality	Temporal	12	2	24,429/22,316,146	17,987/22,316,146	89.6%	1.37 [1.29, 1.46]
Death for cardiocirculatory cause	Temporal	3	1	2,167/325,295	845/175,925	-	1.39 [1.28, 1.50]
Death for cardiocirculatory cause (onset < 1 week)	Temporal	3	1	1,482/325,295	560/175,925	-	1.43 [1.30, 1.58]
Death for coronary heart disease, including sudden death	Temporal	3	1	28/18,071	6/18,071	-	4.67 [1.93, 11.27]
Myocardial infarction mortality	Geographical	36	1	1,074/1,991,109	2,254/5,287,968	-	1.27 [1.18, 1.36]
Diseases of the digestive system							
Gastric ulcer	Geographical	2	1	335/466	302/571	-	1.36 [1.16, 1.59]
Gastric ulcer	Temporal	2	1	960/1,666	909/2,477	-	1.57 [1.43, 1.72]
Gastric ulcer, with bleeding	Temporal	2	1	180/1,666	83/2,477	-	3.22 [2.49, 4.18]
Gastric ulcer, with bleeding	Geographical	2	1	100/466	22/571	-	5.57 [3.51, 8.83]
Infectious and parasitic diseases							
German measles	Temporal	2	1	12/1,009,738	760/6,000,386	-	0.09 [0.05, 0.17]
Paratyphoid and other salmonellosis	Temporal	7	1	377/2,813,615	548/5,627,230	-	1.38 [1.21, 1.57]
Typhoid fever	Temporal	7	1	599/2,411,670	2,217/11,254,460	-	1.26 [1.15, 1.38]
Viral hepatitis	Temporal	7	1	2,511/2,411,670	7,753/11,254,460	-	1.51 [1.44, 1.58]
Whooping cough (pertussis)	Temporal	2	1	9/1,009,738	1,141/6,000,386	-	0.05 [0.02, 0.09]
Healthcare quality and costs							
Hospital discharges	Temporal	6	1	399,263/3,029,213	948,532/7,000,450	-	0.97 [0.97, 0.98]
Pharmacology							
Anti-depressants, other	Temporal	11	1	194,732/275,590	215,030/300,818	-	0.99 [0.98, 0.99]
Anti-depressants, serotonin reuptake inhibitors	Temporal	11	1	518,236/275,590	556,427/300,818	-	1.02 [1.01, 1.02]
Anti-depressants, tryciclics	Temporal	11	1	81,998/275,590	94,447/300,818	-	0.95 [0.94, 0.96]
Anti-psychotics	Temporal	11	1	17,445/275,590	18,012/300,819	-	1.06 [1.04, 1.08]
Anti-psychotics, Amilsulpride	Temporal	1	1	268/25,054	77/25,068	-	3.48 [2.70, 4.49]
Anti-psychotics, atypical	Temporal	11	1	11,923/275,590	12,261/300,818	-	1.06 [1.04, 1.09]
Anti-psychotics, Haloperidol	Temporal	1	1	596/25,054	433/25,068	-	1.38 [1.22, 1.56]
Anti-psychotics, Promazine	Temporal	1	1	262/25,054	4/25,068	-	65.54 [24.41, 175.93]
Anti-psychotics, Quetiapine	Temporal	1	1	508/25,054	376/25,068	-	1.35 [1.18, 1.54]
Anti-psychotics, Risperidone	Temporal	1	1	297/25,054	211/25,068	-	1.41 [1.18, 1.68]



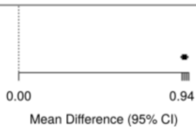
B. Binary outcomes, Risk Ratio

	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I²	Risk Ratio (95% CI)
Lifestyle & prevention							
Physical activity, sedentaty behaviour	Temporal	19	1	364/943	52/271	-	2.01 [1.56, 2.60]



C. Continuous outcomes

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Mean Difference (95% CI)
Mental, behavioral and neurodevelopmental disorders								
Insomnia, average daily prevalence	%	Temporal	2	1	5,053	5,053	-	0.95 [0.93, 0.98]



[a] Sample size and p-value thresholds were set in the interest of concision. The full results are available in Supplementary Materials 4.

I² is percentage of variation across studies due to heterogeneity. Follow-up refers to the latest post-earthquake measurement.

Supplementary Materials 1. Search strings

Pubmed (MEDLINE)

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Scopus

TITLE-ABS-KEY((earthquake* OR quake* OR seismic upheaval* OR seism* OR aftershock*) **AND** ("Andorra" OR "Antigua and Barbuda" OR "Antigua" OR "Barbuda" OR "Aruba" OR "Australia" OR "Austria" OR "Bahamas" OR "Bahrain" OR "Barbados" OR "Belgium" OR "Bermuda" OR "Brunei" OR "Brunei Darussalam" OR "Canada" OR "Cayman Islands" OR "Cayman" OR "Channel Islands" OR "Chile" OR "Croatia" OR "Curaçao" OR "Cyprus" OR "Czech Republic" OR "Denmark" OR "Equatorial Guinea" OR "Estonia" OR "Faeroe Islands" OR "Finland" OR "France" OR "Polynesia" OR "French Polynesia" OR "Germany" OR "Greece" OR "Greenland" OR "Guam" OR "Hong Kong SAR, China" OR "Hong Kong" OR "Iceland" OR "Ireland" OR "Isle of Man" OR "Israel" OR "Italy" OR "Japan" OR "Korea, Rep." OR "Korea" OR "Kuwait" OR "Latvia" OR "Liechtenstein" OR "Lithuania" OR "Luxembourg" OR "Macao SAR, China" OR "Macao" OR "Malta" OR "Monaco" OR "Netherlands" OR "New Caledonia" OR "New Zealand" OR "Northern Mariana Islands" OR "Norway" OR "Oman" OR "Poland" OR "Portugal" OR "Puerto Rico" OR "Qatar" OR "Republic" OR "Russian Federation" OR "Russia" OR "San Marino" OR "Saudi Arabia" OR "Singapore" OR "Sint Maarten" OR "Slovak" OR "Slovenia" OR "Spain" OR "St. Kitts and Nevis" OR "St. Martin" OR "Sweden" OR "Switzerland" OR "Trinidad and Tobago" OR "Turks and Caicos Islands" OR "United Arab Emirates" OR "UAE" OR "U.A.E." OR "United Kingdom" OR "UK"

OR "U.K." OR "United States" OR "USA" OR "U.S.A." OR "Uruguay" OR "Virgin Islands (U.S.)" OR "Virgin Islands")) **AND** (LIMIT-TO(DOCTYPE,"ar") OR LIMIT-TO(DOCTYPE,"re") OR LIMIT-TO(DOCTYPE,"ip")) **AND** (LIMIT-TO(LANGUAGE,"English") OR LIMIT-TO(LANGUAGE,"French") OR LIMIT-TO(LANGUAGE,"Spanish") OR LIMIT-TO(LANGUAGE,"German") OR LIMIT-TO(LANGUAGE,"Italian") OR LIMIT-TO(LANGUAGE,"Portuguese")) **AND** (LIMIT-TO(SUBJAREA,"MULT") OR LIMIT-TO(SUBJAREA,"MEDI") OR LIMIT-TO(SUBJAREA,"BIOC") OR LIMIT-TO(SUBJAREA,"PSYC") OR LIMIT-TO(SUBJAREA,"NURS") OR LIMIT-TO(SUBJAREA,"NEUR") OR LIMIT-TO(SUBJAREA,"HEAL") OR LIMIT-TO(SUBJAREA,"PHAR") OR LIMIT-TO(SUBJAREA,"IMMU"))

WHO

allintitle: earthquake OR earthquakes OR quake OR quakes OR seism OR seismic OR aftershock OR aftershocks

allintitle: seismic upheaval

allintitle: seismic upheavals

CDC

earthquake OR earthquakes OR quake OR quakes OR seism OR seismic OR aftershock OR aftershocks OR (seismic AND upheaval) OR (seismic AND upheavals)

NIH

earthquake OR earthquakes OR quake OR quakes OR seism OR seismic OR aftershock OR aftershocks OR (seismic AND upheaval) OR (seismic AND upheavals)

ECDC

earthquake earthquakes quake quakes seism seismic aftershock aftershocks

seismic upheaval

seismic upheavals

Epicentro

"terremoto" OR "sisma" OR "sismico" OR "scossa" OR "scossa di assestamento"

DORS

"terremoto" OR "sisma" OR "sismico" OR "scossa" OR "scossa di assestamento"

Supplementary Materials 2. Further details on data synthesis

Unit conversions

We harmonised units of continuous outcome by giving priority to the units used in the majority of the included studies. For example, we converted mmol/L to mg/dL multiplying cholesterol measurements by 38.7 and triglycerides measurements by 88.6. We also converted µmol/L of uric acid to mg/dL multiplying estimates by 0.0168.

Collapsing of within-study subgroups

Fifteen studies reported estimates stratified not only by exposure status, but also by sex, age categories or other subgroups. We pooled within-study subgroup estimates to enable comparison of estimates between all exposed and unexposed participants for each outcome reported. For binary outcomes, we pooled estimates by summing subgroup-specific numerators and subgroup-specific denominators. For continuous outcomes, we used the formulae below as per Cochrane Collaboration recommendations [1]. If there were more than two groups to combine, we applied the formulae sequentially.

	Group 1	Group 2	Combined groups
Sample size	n_1	n_2	$n_1 + n_2$
Mean	$\bar{x}_1$	$\bar{x}_2$	$\frac{n_1\bar{x}_1 + n_2\bar{x}_2}{n_1 + n_2}$
Standard deviation	SD_1	SD_2	$\sqrt{\frac{(n_1 - 1)SD_1{}^2 + (n_2 - 1)SD_2{}^2}{n_1 + n_2 - 1}}$

Dealing with multiple comparison groups

In studies reporting on more than two temporal comparison groups, such as multiple measurements carried out before and/or after the earthquake, we selected the latest pre-earthquake and the latest post-earthquake data points.

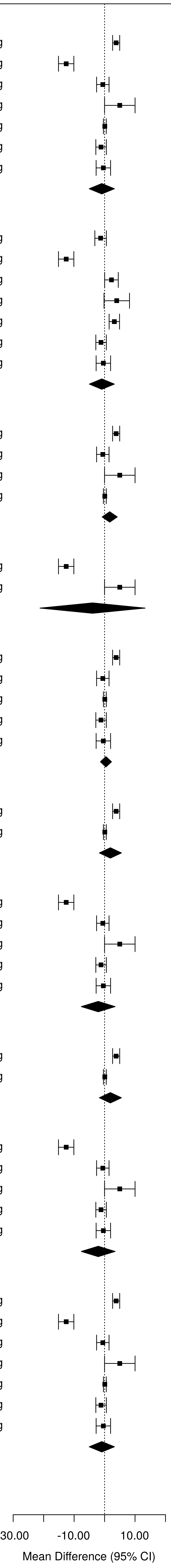
In studies reporting on more than two geographical comparison groups, we selected the group of individuals living closest to the earthquake epicentre and the group of residents furthest away from the epicentre.

Reference

1. Higgins J, Green S. Cochrane Handbook for Systematic Reviews of Interventions [Internet]. 2011. Available from: www.cochrane-handbook.org

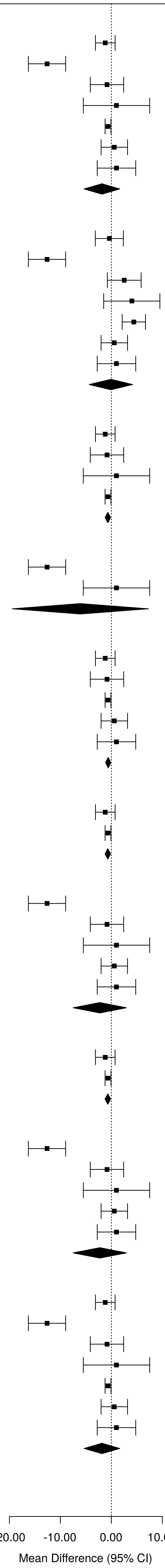
Clinically measured diastolic blood pressure

	Follow-up (months)	Study design	Exposed Participants	Unexposed Participants	Exposed Mean (SD)	Unexposed Mean (SD)	Unit	Mean Difference (95% CI)
Main analysis: All studies (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	606	505	88.2 (10.39)	84.4 (9.40)	mmHg	3.80 [2.64, 4.97]
Kobe 1995 (Kario 2001)	2	Cohort	116	124	80.4 (2.92)	93.0 (14.00)	mmHg	-12.61 [-15.13, -10.09]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	75.4 (10.97)	76.0 (11.00)	mmHg	-0.58 [-2.62, 1.47]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	77.0 (15.00)	72.0 (14.00)	mmHg	5.00 [-0.01, 10.01]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	74.4 (10.65)	74.3 (10.70)	mmHg	0.09 [-0.38, 0.56]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	73.9 (11.29)	75.0 (11.00)	mmHg	-1.14 [-2.87, 0.58]
Great East Japan 2011 (Tani 2014)	2	Cohort	205	205	77.1 (11.70)	77.5 (12.80)	mmHg	-0.40 [-2.77, 1.97]
RE model (Heterog. p-value=2.7638e-28; I²=98.2%)								*-0.91 [-5.06, 3.24]*
Sensitivity analysis: Follow-up duration < 6 months (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	2	Cohort	102	505	83.1 (8.80)	84.4 (9.40)	mmHg	-1.30 [-3.19, 0.59]
Kobe 1995 (Kario 2001)	2	Cohort	116	124	80.4 (2.92)	93.0 (14.00)	mmHg	-12.61 [-15.13, -10.09]
Niigata 2004 (Kamoi 2006a)	3	Cohort	222	222	78.3 (12.95)	76.0 (11.00)	mmHg	2.26 [0.03, 4.50]
Niigata 2004 (Kamoi 2006b)	3	Cohort	65	65	76.0 (10.00)	72.0 (14.00)	mmHg	4.00 [-0.18, 8.18]
Niigata 2004 (Azuma 2010)	5	Cohort	279	279	78.1 (10.30)	74.9 (10.30)	mmHg	3.20 [1.49, 4.91]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	73.9 (11.29)	75.0 (11.00)	mmHg	-1.14 [-2.87, 0.58]
Great East Japan 2011 (Tani 2014)	2	Cohort	205	205	77.1 (11.70)	77.5 (12.80)	mmHg	-0.40 [-2.77, 1.97]
RE model (Heterog. p-value=4.2986e-23; I²=96.0%)								*-0.90 [-5.01, 3.22]*
Sensitivity analysis: Follow-up duration >= 6 months (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	606	505	88.2 (10.39)	84.4 (9.40)	mmHg	3.80 [2.64, 4.97]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	75.4 (10.97)	76.0 (11.00)	mmHg	-0.58 [-2.62, 1.47]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	77.0 (15.00)	72.0 (14.00)	mmHg	5.00 [-0.01, 10.01]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	74.4 (10.65)	74.3 (10.70)	mmHg	0.09 [-0.38, 0.56]
RE model (Heterog. p-value=3.0156e-08; I²=92.0%)								*1.68 [-0.81, 4.17]*
Sensitivity analysis: % males < 50% (temporal comparison)								
Kobe 1995 (Kario 2001)	2	Cohort	116	124	80.4 (2.92)	93.0 (14.00)	mmHg	-12.61 [-15.13, -10.09]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	77.0 (15.00)	72.0 (14.00)	mmHg	5.00 [-0.01, 10.01]
RE model (Heterog. p-value=7.5374e-10; I²=97.4%)								*-3.94 [-21.20, 13.31]*
Sensitivity analysis: % males >= 50% (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	606	505	88.2 (10.39)	84.4 (9.40)	mmHg	3.80 [2.64, 4.97]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	75.4 (10.97)	76.0 (11.00)	mmHg	-0.58 [-2.62, 1.47]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	74.4 (10.65)	74.3 (10.70)	mmHg	0.09 [-0.38, 0.56]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	73.9 (11.29)	75.0 (11.00)	mmHg	-1.14 [-2.87, 0.58]
Great East Japan 2011 (Tani 2014)	2	Cohort	205	205	77.1 (11.70)	77.5 (12.80)	mmHg	-0.40 [-2.77, 1.97]
RE model (Heterog. p-value=7.5383e-08; I²=89.7%)								*0.45 [-1.37, 2.27]*
Sensitivity analysis: Mean age < 50 years (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	606	505	88.2 (10.39)	84.4 (9.40)	mmHg	3.80 [2.64, 4.97]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	74.4 (10.65)	74.3 (10.70)	mmHg	0.09 [-0.38, 0.56]
RE model (Heterog. p-value=6.6472e-09; I²=97.0%)								*1.91 [-1.73, 5.54]*
Sensitivity analysis: Mean age >= 50 years (temporal comparison)								
Kobe 1995 (Kario 2001)	2	Cohort	116	124	80.4 (2.92)	93.0 (14.00)	mmHg	-12.61 [-15.13, -10.09]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	75.4 (10.97)	76.0 (11.00)	mmHg	-0.58 [-2.62, 1.47]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	77.0 (15.00)	72.0 (14.00)	mmHg	5.00 [-0.01, 10.01]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	73.9 (11.29)	75.0 (11.00)	mmHg	-1.14 [-2.87, 0.58]
Great East Japan 2011 (Tani 2014)	2	Cohort	205	205	77.1 (11.70)	77.5 (12.80)	mmHg	-0.40 [-2.77, 1.97]
RE model (Heterog. p-value=2.6452e-16; I²=96.3%)								*-2.09 [-7.65, 3.47]*
Sensitivity analysis: Occupational subgroups (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	606	505	88.2 (10.39)	84.4 (9.40)	mmHg	3.80 [2.64, 4.97]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	74.4 (10.65)	74.3 (10.70)	mmHg	0.09 [-0.38, 0.56]
RE model (Heterog. p-value=6.6472e-09; I²=97.0%)								*1.91 [-1.73, 5.54]*
Sensitivity analysis: Patient subgroups (temporal comparison)								
Kobe 1995 (Kario 2001)	2	Cohort	116	124	80.4 (2.92)	93.0 (14.00)	mmHg	-12.61 [-15.13, -10.09]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	75.4 (10.97)	76.0 (11.00)	mmHg	-0.58 [-2.62, 1.47]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	77.0 (15.00)	72.0 (14.00)	mmHg	5.00 [-0.01, 10.01]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	73.9 (11.29)	75.0 (11.00)	mmHg	-1.14 [-2.87, 0.58]
Great East Japan 2011 (Tani 2014)	2	Cohort	205	205	77.1 (11.70)	77.5 (12.80)	mmHg	-0.40 [-2.77, 1.97]
RE model (Heterog. p-value=2.6452e-16; I²=96.3%)								*-2.09 [-7.65, 3.47]*
Sensitivity analysis: Cohort (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	606	505	88.2 (10.39)	84.4 (9.40)	mmHg	3.80 [2.64, 4.97]
Kobe 1995 (Kario 2001)	2	Cohort	116	124	80.4 (2.92)	93.0 (14.00)	mmHg	-12.61 [-15.13, -10.09]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	75.4 (10.97)	76.0 (11.00)	mmHg	-0.58 [-2.62, 1.47]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	77.0 (15.00)	72.0 (14.00)	mmHg	5.00 [-0.01, 10.01]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	74.4 (10.65)	74.3 (10.70)	mmHg	0.09 [-0.38, 0.56]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	73.9 (11.29)	75.0 (11.00)	mmHg	-1.14 [-2.87, 0.58]
Great East Japan 2011 (Tani 2014)	2	Cohort	205	205	77.1 (11.70)	77.5 (12.80)	mmHg	-0.40 [-2.77, 1.97]
RE model (Heterog. p-value=2.7638e-28; I²=98.2%)								*-0.91 [-5.06, 3.24]*



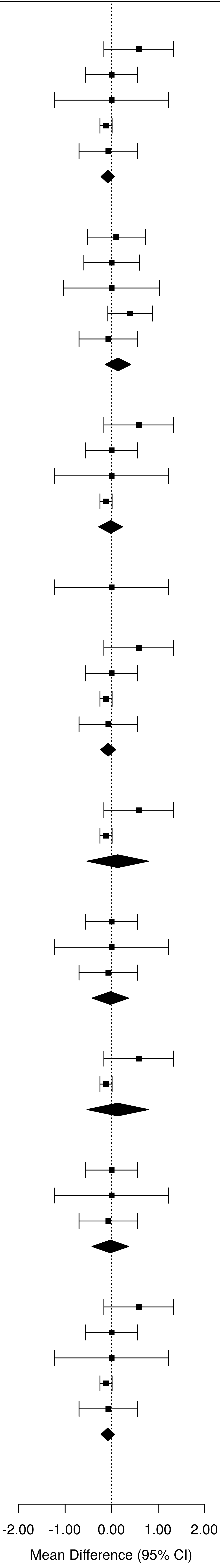
Clinically measured systolic blood pressure

	Follow-up (months)	Study design	Exposed Participants	Unexposed Participants	Exposed Mean (SD)	Unexposed Mean (SD)	Unit	
Main analysis: All studies (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	606	505	129.4 (17.85)	130.6 (14.90)	mmHg	-1.20 [-3.12, 0.73]
Kobe 1995 (Kario 2001)	2	Cohort	116	124	149.4 (5.37)	162.0 (20.00)	mmHg	-12.63 [-16.28, -8.97]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	132.1 (17.16)	133.0 (18.00)	mmHg	-0.87 [-4.14, 2.41]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	127.0 (22.00)	126.0 (15.00)	mmHg	1.00 [-5.51, 7.51]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	120.1 (14.75)	120.8 (11.32)	mmHg	-0.66 [-1.23, -0.09]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	131.6 (17.43)	131.0 (16.00)	mmHg	0.57 [-2.02, 3.17]
Great East Japan 2011 (Tani 2014)	2	Cohort	205	205	149.6 (19.00)	148.6 (20.00)	mmHg	1.00 [-2.78, 4.78]
RE model (Heterog. p-value=1.2482e-07; I²=93.7%)								*-1.86 [-5.35, 1.64]*
Sensitivity analysis: Follow-up duration < 6 months (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	2	Cohort	102	505	130.2 (12.50)	130.6 (14.90)	mmHg	-0.40 [-3.15, 2.35]
Kobe 1995 (Kario 2001)	2	Cohort	116	124	149.4 (5.37)	162.0 (20.00)	mmHg	-12.63 [-16.28, -8.97]
Niigata 2004 (Kamoi 2006a)	3	Cohort	222	222	135.5 (17.59)	133.0 (18.00)	mmHg	2.52 [-0.79, 5.83]
Niigata 2004 (Kamoi 2006b)	3	Cohort	65	65	130.0 (17.00)	126.0 (15.00)	mmHg	4.00 [-1.51, 9.51]
Niigata 2004 (Azuma 2010)	5	Cohort	279	279	125.2 (14.20)	120.8 (13.30)	mmHg	4.40 [2.12, 6.68]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	131.6 (17.43)	131.0 (16.00)	mmHg	0.57 [-2.02, 3.17]
Great East Japan 2011 (Tani 2014)	2	Cohort	205	205	149.6 (19.00)	148.6 (20.00)	mmHg	1.00 [-2.78, 4.78]
RE model (Heterog. p-value=6.0876e-12; I²=92.1%)								*-0.09 [-4.35, 4.17]*
Sensitivity analysis: Follow-up duration >= 6 months (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	606	505	129.4 (17.85)	130.6 (14.90)	mmHg	-1.20 [-3.12, 0.73]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	132.1 (17.16)	133.0 (18.00)	mmHg	-0.87 [-4.14, 2.41]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	127.0 (22.00)	126.0 (15.00)	mmHg	1.00 [-5.51, 7.51]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	120.1 (14.75)	120.8 (11.32)	mmHg	-0.66 [-1.23, -0.09]
RE model (Heterog. p-value=0.9085; I²=0.0%)								*-0.70 [-1.24, -0.16]*
Sensitivity analysis: % males < 50% (temporal comparison)								
Kobe 1995 (Kario 2001)	2	Cohort	116	124	149.4 (5.37)	162.0 (20.00)	mmHg	-12.63 [-16.28, -8.97]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	127.0 (22.00)	126.0 (15.00)	mmHg	1.00 [-5.51, 7.51]
RE model (Heterog. p-value=0.0003; I²=92.2%)								*-6.09 [-19.43, 7.25]*
Sensitivity analysis: % males >= 50% (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	606	505	129.4 (17.85)	130.6 (14.90)	mmHg	-1.20 [-3.12, 0.73]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	132.1 (17.16)	133.0 (18.00)	mmHg	-0.87 [-4.14, 2.41]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	120.1 (14.75)	120.8 (11.32)	mmHg	-0.66 [-1.23, -0.09]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	131.6 (17.43)	131.0 (16.00)	mmHg	0.57 [-2.02, 3.17]
Great East Japan 2011 (Tani 2014)	2	Cohort	205	205	149.6 (19.00)	148.6 (20.00)	mmHg	1.00 [-2.78, 4.78]
RE model (Heterog. p-value=0.7522; I²=0.0%)								*-0.62 [-1.15, -0.10]*
Sensitivity analysis: Mean age < 50 years (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	606	505	129.4 (17.85)	130.6 (14.90)	mmHg	-1.20 [-3.12, 0.73]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	120.1 (14.75)	120.8 (11.32)	mmHg	-0.66 [-1.23, -0.09]
RE model (Heterog. p-value=0.6003; I²=0.0%)								*-0.70 [-1.25, -0.16]*
Sensitivity analysis: Mean age >= 50 years (temporal comparison)								
Kobe 1995 (Kario 2001)	2	Cohort	116	124	149.4 (5.37)	162.0 (20.00)	mmHg	-12.63 [-16.28, -8.97]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	132.1 (17.16)	133.0 (18.00)	mmHg	-0.87 [-4.14, 2.41]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	127.0 (22.00)	126.0 (15.00)	mmHg	1.00 [-5.51, 7.51]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	131.6 (17.43)	131.0 (16.00)	mmHg	0.57 [-2.02, 3.17]
Great East Japan 2011 (Tani 2014)	2	Cohort	205	205	149.6 (19.00)	148.6 (20.00)	mmHg	1.00 [-2.78, 4.78]
RE model (Heterog. p-value=4.3522e-08; I²=90.3%)								*-2.27 [-7.50, 2.97]*
Sensitivity analysis: Occupational subgroups (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	606	505	129.4 (17.85)	130.6 (14.90)	mmHg	-1.20 [-3.12, 0.73]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	120.1 (14.75)	120.8 (11.32)	mmHg	-0.66 [-1.23, -0.09]
RE model (Heterog. p-value=0.6003; I²=0.0%)								*-0.70 [-1.25, -0.16]*
Sensitivity analysis: Patient subgroups (temporal comparison)								
Kobe 1995 (Kario 2001)	2	Cohort	116	124	149.4 (5.37)	162.0 (20.00)	mmHg	-12.63 [-16.28, -8.97]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	132.1 (17.16)	133.0 (18.00)	mmHg	-0.87 [-4.14, 2.41]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	127.0 (22.00)	126.0 (15.00)	mmHg	1.00 [-5.51, 7.51]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	131.6 (17.43)	131.0 (16.00)	mmHg	0.57 [-2.02, 3.17]
Great East Japan 2011 (Tani 2014)	2	Cohort	205	205	149.6 (19.00)	148.6 (20.00)	mmHg	1.00 [-2.78, 4.78]
RE model (Heterog. p-value=4.3522e-08; I²=90.3%)								*-2.27 [-7.50, 2.97]*
Sensitivity analysis: Cohort (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	606	505	129.4 (17.85)	130.6 (14.90)	mmHg	-1.20 [-3.12, 0.73]
Kobe 1995 (Kario 2001)	2	Cohort	116	124	149.4 (5.37)	162.0 (20.00)	mmHg	-12.63 [-16.28, -8.97]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	132.1 (17.16)	133.0 (18.00)	mmHg	-0.87 [-4.14, 2.41]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	127.0 (22.00)	126.0 (15.00)	mmHg	1.00 [-5.51, 7.51]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	120.1 (14.75)	120.8 (11.32)	mmHg	-0.66 [-1.23, -0.09]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	131.6 (17.43)	131.0 (16.00)	mmHg	0.57 [-2.02, 3.17]
Great East Japan 2011 (Tani 2014)	2	Cohort	205	205	149.6 (19.00)	148.6 (20.00)	mmHg	1.00 [-2.78, 4.78]
RE model (Heterog. p-value=1.2482e-07; I²=93.7%)								*-1.86 [-5.35, 1.64]*



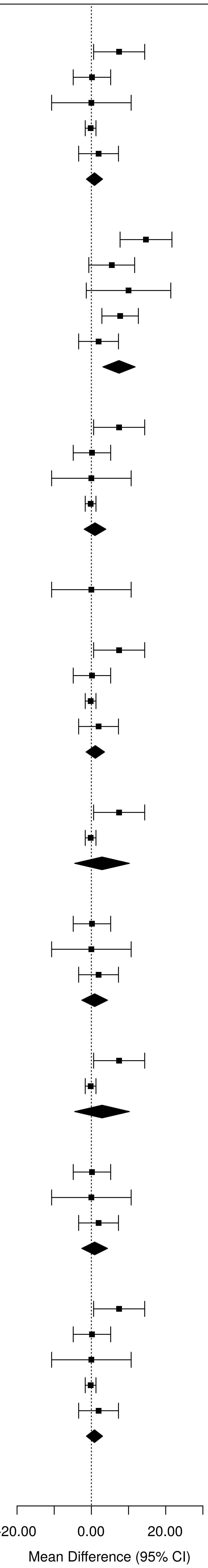
Body mass index

	Follow-up (months)	Study design	Exposed Participants	Unexposed Participants	Exposed Mean (SD)	Unexposed Mean (SD)	Unit	
Main analysis: All studies (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	26.5 (3.60)	25.9 (3.10)	Kg/m²	0.58 [-0.17, 1.33]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	24.0 (2.99)	24.0 (3.00)	Kg/m²	0.00 [-0.56, 0.56]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	22.0 (4.00)	22.0 (3.00)	Kg/m²	0.00 [-1.22, 1.22]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	22.5 (2.95)	22.7 (3.00)	Kg/m²	-0.12 [-0.25, 0.01]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	24.2 (4.04)	24.3 (4.10)	Kg/m²	-0.07 [-0.70, 0.56]
RE model (Heterog. p-value=0.4870; I²=3.2%)								*-0.08 [-0.23, 0.06]*
Sensitivity analysis: Follow-up duration < 6 months (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	2	Cohort	102	505	26.0 (2.90)	25.9 (3.10)	Kg/m²	0.10 [-0.52, 0.72]
Niigata 2004 (Kamoi 2006a)	3	Cohort	222	222	24.0 (3.40)	24.0 (3.00)	Kg/m²	0.00 [-0.60, 0.60]
Niigata 2004 (Kamoi 2006b)	3	Cohort	65	65	22.0 (3.00)	22.0 (3.00)	Kg/m²	0.00 [-1.03, 1.03]
Niigata 2004 (Azuma 2010)	5	Cohort	279	279	23.4 (2.90)	23.0 (2.90)	Kg/m²	0.40 [-0.08, 0.88]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	24.2 (4.04)	24.3 (4.10)	Kg/m²	-0.07 [-0.70, 0.56]
RE model (Heterog. p-value=0.7637; I²=0.0%)								*0.14 [-0.14, 0.41]*
Sensitivity analysis: Follow-up duration >= 6 months (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	26.5 (3.60)	25.9 (3.10)	Kg/m²	0.58 [-0.17, 1.33]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	24.0 (2.99)	24.0 (3.00)	Kg/m²	0.00 [-0.56, 0.56]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	22.0 (4.00)	22.0 (3.00)	Kg/m²	0.00 [-1.22, 1.22]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	22.5 (2.95)	22.7 (3.00)	Kg/m²	-0.12 [-0.25, 0.01]
RE model (Heterog. p-value=0.3293; I²=22.2%)								*-0.02 [-0.28, 0.24]*
Sensitivity analysis: % males < 50% (temporal comparison)								
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	22.0 (4.00)	22.0 (3.00)	Kg/m²	0.00 [-1.22, 1.22]
Sensitivity analysis: % males >= 50% (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	26.5 (3.60)	25.9 (3.10)	Kg/m²	0.58 [-0.17, 1.33]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	24.0 (2.99)	24.0 (3.00)	Kg/m²	0.00 [-0.56, 0.56]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	22.5 (2.95)	22.7 (3.00)	Kg/m²	-0.12 [-0.25, 0.01]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	24.2 (4.04)	24.3 (4.10)	Kg/m²	-0.07 [-0.70, 0.56]
RE model (Heterog. p-value=0.3316; I²=6.9%)								*-0.08 [-0.24, 0.09]*
Sensitivity analysis: Mean age < 50 years (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	26.5 (3.60)	25.9 (3.10)	Kg/m²	0.58 [-0.17, 1.33]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	22.5 (2.95)	22.7 (3.00)	Kg/m²	-0.12 [-0.25, 0.01]
RE model (Heterog. p-value=0.0696; I²=69.6%)								*0.13 [-0.53, 0.79]*
Sensitivity analysis: Mean age >= 50 years (temporal comparison)								
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	24.0 (2.99)	24.0 (3.00)	Kg/m²	0.00 [-0.56, 0.56]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	22.0 (4.00)	22.0 (3.00)	Kg/m²	0.00 [-1.22, 1.22]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	24.2 (4.04)	24.3 (4.10)	Kg/m²	-0.07 [-0.70, 0.56]
RE model (Heterog. p-value=0.9855; I²=0.0%)								*-0.03 [-0.42, 0.37]*
Sensitivity analysis: Occupational subgroups (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	26.5 (3.60)	25.9 (3.10)	Kg/m²	0.58 [-0.17, 1.33]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	22.5 (2.95)	22.7 (3.00)	Kg/m²	-0.12 [-0.25, 0.01]
RE model (Heterog. p-value=0.0696; I²=69.6%)								*0.13 [-0.53, 0.79]*
Sensitivity analysis: Patient subgroups (temporal comparison)								
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	24.0 (2.99)	24.0 (3.00)	Kg/m²	0.00 [-0.56, 0.56]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	22.0 (4.00)	22.0 (3.00)	Kg/m²	0.00 [-1.22, 1.22]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	24.2 (4.04)	24.3 (4.10)	Kg/m²	-0.07 [-0.70, 0.56]
RE model (Heterog. p-value=0.9855; I²=0.0%)								*-0.03 [-0.42, 0.37]*
Sensitivity analysis: Cohort (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	26.5 (3.60)	25.9 (3.10)	Kg/m²	0.58 [-0.17, 1.33]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	24.0 (2.99)	24.0 (3.00)	Kg/m²	0.00 [-0.56, 0.56]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	22.0 (4.00)	22.0 (3.00)	Kg/m²	0.00 [-1.22, 1.22]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	22.5 (2.95)	22.7 (3.00)	Kg/m²	-0.12 [-0.25, 0.01]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	24.2 (4.04)	24.3 (4.10)	Kg/m²	-0.07 [-0.70, 0.56]
RE model (Heterog. p-value=0.4870; I²=3.2%)								*-0.08 [-0.23, 0.06]*



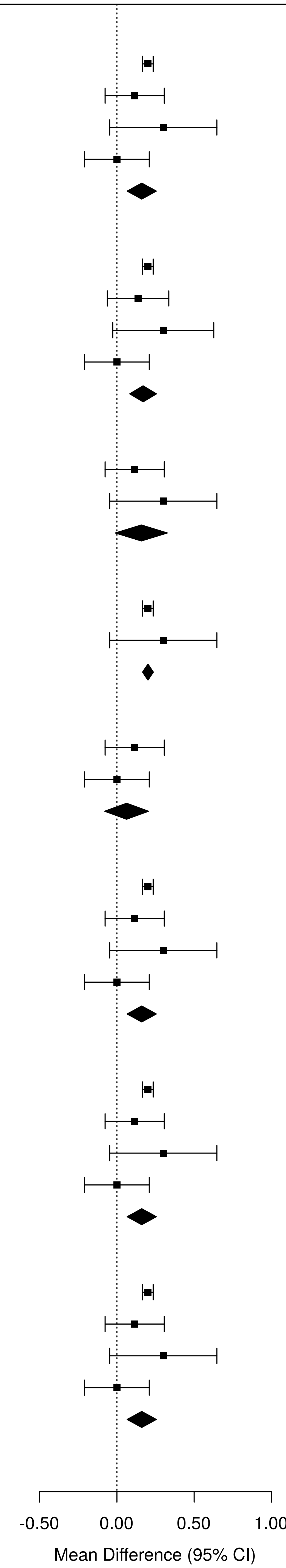
Total cholesterol

Study	Follow-up (months)	Study design	Exposed Participants	Unexposed Participants	Exposed Mean (SD)	Unexposed Mean (SD)	Unit	Mean Difference (95% CI)
Main analysis: All studies (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	202.3 (32.19)	194.8 (32.80)	mg/dL	7.47 [0.60, 14.34]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	197.2 (19.40)	197.0 (33.00)	mg/dL	0.15 [-4.88, 5.19]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	195.0 (31.00)	195.0 (31.00)	mg/dL	0.00 [-10.70, 10.70]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	198.5 (32.95)	198.7 (33.16)	mg/dL	-0.21 [-1.65, 1.23]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	194.1 (33.98)	192.2 (35.19)	mg/dL	1.93 [-3.43, 7.29]
RE model (Heterog. p-value=0.2860; I²=21.9%)								*0.83 [-1.35, 3.02]*
Sensitivity analysis: Follow-up duration < 6 months (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	2	Cohort	102	505	209.5 (32.80)	194.8 (32.80)	mg/dL	14.70 [7.72, 21.68]
Niigata 2004 (Kamoi 2006a)	3	Cohort	222	222	202.5 (33.30)	197.0 (33.00)	mg/dL	5.48 [-0.69, 11.64]
Niigata 2004 (Kamoi 2006b)	3	Cohort	65	65	205.0 (35.00)	195.0 (31.00)	mg/dL	10.00 [-1.37, 21.37]
Niigata 2004 (Azuma 2010)	5	Cohort	279	279	200.3 (30.16)	192.6 (29.00)	mg/dL	7.73 [2.82, 12.64]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	194.1 (33.98)	192.2 (35.19)	mg/dL	1.93 [-3.43, 7.29]
RE model (Heterog. p-value=0.0691; I²=55.9%)								*7.44 [3.08, 11.79]*
Sensitivity analysis: Follow-up duration >= 6 months (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	202.3 (32.19)	194.8 (32.80)	mg/dL	7.47 [0.60, 14.34]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	197.2 (19.40)	197.0 (33.00)	mg/dL	0.15 [-4.88, 5.19]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	195.0 (31.00)	195.0 (31.00)	mg/dL	0.00 [-10.70, 10.70]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	198.5 (32.95)	198.7 (33.16)	mg/dL	-0.21 [-1.65, 1.23]
RE model (Heterog. p-value=0.2037; I²=35.3%)								*0.98 [-1.95, 3.90]*
Sensitivity analysis: % males < 50% (temporal comparison)								
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	195.0 (31.00)	195.0 (31.00)	mg/dL	0.00 [-10.70, 10.70]
Sensitivity analysis: % males >= 50% (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	202.3 (32.19)	194.8 (32.80)	mg/dL	7.47 [0.60, 14.34]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	197.2 (19.40)	197.0 (33.00)	mg/dL	0.15 [-4.88, 5.19]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	198.5 (32.95)	198.7 (33.16)	mg/dL	-0.21 [-1.65, 1.23]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	194.1 (33.98)	192.2 (35.19)	mg/dL	1.93 [-3.43, 7.29]
RE model (Heterog. p-value=0.1710; I²=34.5%)								*1.05 [-1.44, 3.55]*
Sensitivity analysis: Mean age < 50 years (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	202.3 (32.19)	194.8 (32.80)	mg/dL	7.47 [0.60, 14.34]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	198.5 (32.95)	198.7 (33.16)	mg/dL	-0.21 [-1.65, 1.23]
RE model (Heterog. p-value=0.0320; I²=78.2%)								*2.87 [-4.51, 10.24]*
Sensitivity analysis: Mean age >= 50 years (temporal comparison)								
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	197.2 (19.40)	197.0 (33.00)	mg/dL	0.15 [-4.88, 5.19]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	195.0 (31.00)	195.0 (31.00)	mg/dL	0.00 [-10.70, 10.70]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	194.1 (33.98)	192.2 (35.19)	mg/dL	1.93 [-3.43, 7.29]
RE model (Heterog. p-value=0.8805; I²=0.0%)								*0.88 [-2.59, 4.36]*
Sensitivity analysis: Occupational subgroups (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	202.3 (32.19)	194.8 (32.80)	mg/dL	7.47 [0.60, 14.34]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	198.5 (32.95)	198.7 (33.16)	mg/dL	-0.21 [-1.65, 1.23]
RE model (Heterog. p-value=0.0320; I²=78.2%)								*2.87 [-4.51, 10.24]*
Sensitivity analysis: Patient subgroups (temporal comparison)								
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	197.2 (19.40)	197.0 (33.00)	mg/dL	0.15 [-4.88, 5.19]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	195.0 (31.00)	195.0 (31.00)	mg/dL	0.00 [-10.70, 10.70]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	194.1 (33.98)	192.2 (35.19)	mg/dL	1.93 [-3.43, 7.29]
RE model (Heterog. p-value=0.8805; I²=0.0%)								*0.88 [-2.59, 4.36]*
Sensitivity analysis: Cohort (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	202.3 (32.19)	194.8 (32.80)	mg/dL	7.47 [0.60, 14.34]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	197.2 (19.40)	197.0 (33.00)	mg/dL	0.15 [-4.88, 5.19]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	195.0 (31.00)	195.0 (31.00)	mg/dL	0.00 [-10.70, 10.70]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	198.5 (32.95)	198.7 (33.16)	mg/dL	-0.21 [-1.65, 1.23]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	194.1 (33.98)	192.2 (35.19)	mg/dL	1.93 [-3.43, 7.29]
RE model (Heterog. p-value=0.2860; I²=21.9%)								*0.83 [-1.35, 3.02]*



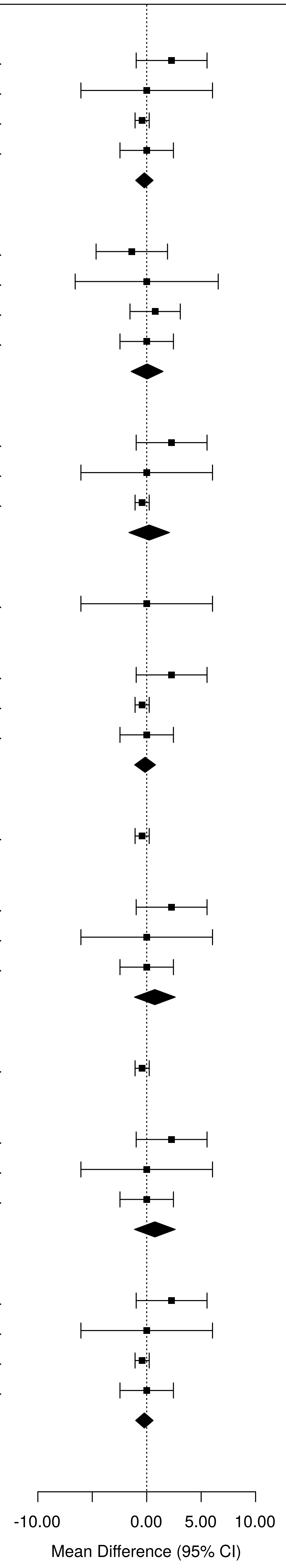
Glycated haemoglobin

	Follow-up (months)	Study design	Exposed Participants	Unexposed Participants	Exposed Mean (SD)	Unexposed Mean (SD)	Unit	Mean Difference (95% CI)
Main analysis: All studies (temporal comparison)								
Kobe 1995 (Inui 1998)	2	Cohort	110	110	7.6 (0.11)	7.4 (0.15)	%	0.20 [0.17, 0.23]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	6.9 (1.06)	6.8 (1.00)	%	0.12 [-0.08, 0.31]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	7.0 (1.10)	6.7 (0.90)	%	0.30 [-0.05, 0.65]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	7.7 (1.40)	7.7 (1.30)	%	0.00 [-0.21, 0.21]
RE model (Heterog. p-value=0.2193; I²=33.3%)								*0.16 [0.07, 0.25]*
Sensitivity analysis: Follow-up duration < 6 months (temporal comparison)								
Kobe 1995 (Inui 1998)	2	Cohort	110	110	7.6 (0.11)	7.4 (0.15)	%	0.20 [0.17, 0.23]
Niigata 2004 (Kamoi 2006a)	3	Cohort	222	222	6.9 (1.14)	6.8 (1.00)	%	0.14 [-0.06, 0.34]
Niigata 2004 (Kamoi 2006b)	3	Cohort	65	65	7.0 (1.00)	6.7 (0.90)	%	0.30 [-0.03, 0.63]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	7.7 (1.40)	7.7 (1.30)	%	0.00 [-0.21, 0.21]
RE model (Heterog. p-value=0.2475; I²=27.2%)								*0.17 [0.08, 0.26]*
Sensitivity analysis: Follow-up duration >= 6 months (temporal comparison)								
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	6.9 (1.06)	6.8 (1.00)	%	0.12 [-0.08, 0.31]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	7.0 (1.10)	6.7 (0.90)	%	0.30 [-0.05, 0.65]
RE model (Heterog. p-value=0.3605; I²=0.0%)								*0.16 [-0.01, 0.33]*
Sensitivity analysis: % males < 50% (temporal comparison)								
Kobe 1995 (Inui 1998)	2	Cohort	110	110	7.6 (0.11)	7.4 (0.15)	%	0.20 [0.17, 0.23]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	7.0 (1.10)	6.7 (0.90)	%	0.30 [-0.05, 0.65]
RE model (Heterog. p-value=0.5742; I²=0.0%)								*0.20 [0.17, 0.24]*
Sensitivity analysis: % males >= 50% (temporal comparison)								
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	6.9 (1.06)	6.8 (1.00)	%	0.12 [-0.08, 0.31]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	7.7 (1.40)	7.7 (1.30)	%	0.00 [-0.21, 0.21]
RE model (Heterog. p-value=0.4270; I²=0.0%)								*0.06 [-0.08, 0.20]*
Sensitivity analysis: Mean age >= 50 years (temporal comparison)								
Kobe 1995 (Inui 1998)	2	Cohort	110	110	7.6 (0.11)	7.4 (0.15)	%	0.20 [0.17, 0.23]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	6.9 (1.06)	6.8 (1.00)	%	0.12 [-0.08, 0.31]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	7.0 (1.10)	6.7 (0.90)	%	0.30 [-0.05, 0.65]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	7.7 (1.40)	7.7 (1.30)	%	0.00 [-0.21, 0.21]
RE model (Heterog. p-value=0.2193; I²=33.3%)								*0.16 [0.07, 0.25]*
Sensitivity analysis: Patient subgroups (temporal comparison)								
Kobe 1995 (Inui 1998)	2	Cohort	110	110	7.6 (0.11)	7.4 (0.15)	%	0.20 [0.17, 0.23]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	6.9 (1.06)	6.8 (1.00)	%	0.12 [-0.08, 0.31]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	7.0 (1.10)	6.7 (0.90)	%	0.30 [-0.05, 0.65]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	7.7 (1.40)	7.7 (1.30)	%	0.00 [-0.21, 0.21]
RE model (Heterog. p-value=0.2193; I²=33.3%)								*0.16 [0.07, 0.25]*
Sensitivity analysis: Cohort (temporal comparison)								
Kobe 1995 (Inui 1998)	2	Cohort	110	110	7.6 (0.11)	7.4 (0.15)	%	0.20 [0.17, 0.23]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	6.9 (1.06)	6.8 (1.00)	%	0.12 [-0.08, 0.31]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	7.0 (1.10)	6.7 (0.90)	%	0.30 [-0.05, 0.65]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	7.7 (1.40)	7.7 (1.30)	%	0.00 [-0.21, 0.21]
RE model (Heterog. p-value=0.2193; I²=33.3%)								*0.16 [0.07, 0.25]*



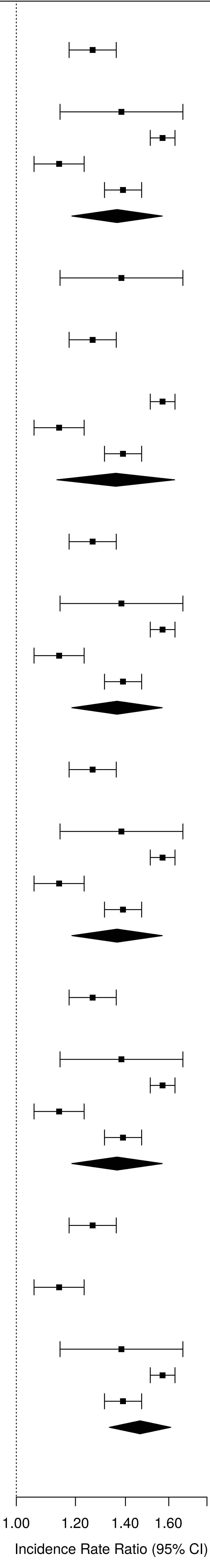
HDL cholesterol

	Follow-up (months)	Study design	Exposed Participants	Unexposed Participants	Exposed Mean (SD)	Unexposed Mean (SD)	Unit	Mean Difference (95% CI)
Main analysis: All studies (temporal comparison)								
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	58.3 (16.96)	56.0 (18.00)	mg/dL	2.29 [-0.97, 5.54]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	68.0 (18.00)	68.0 (17.00)	mg/dL	0.00 [-6.04, 6.04]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	59.8 (13.95)	60.2 (15.75)	mg/dL	-0.42 [-1.07, 0.23]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	54.1 (15.83)	54.1 (15.85)	mg/dL	0.00 [-2.45, 2.45]
RE model (Heterog. p-value=0.4530; I²=5.8%)								*-0.21 [-1.01, 0.58]*
Sensitivity analysis: Follow-up duration < 6 months (temporal comparison)								
Niigata 2004 (Kamoi 2006a)	3	Cohort	222	222	54.6 (17.25)	56.0 (18.00)	mg/dL	-1.37 [-4.65, 1.91]
Niigata 2004 (Kamoi 2006b)	3	Cohort	65	65	68.0 (21.00)	68.0 (17.00)	mg/dL	0.00 [-6.57, 6.57]
Niigata 2004 (Azuma 2010)	5	Cohort	279	279	57.6 (13.92)	56.8 (13.92)	mg/dL	0.77 [-1.54, 3.08]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	54.1 (15.83)	54.1 (15.85)	mg/dL	0.00 [-2.45, 2.45]
RE model (Heterog. p-value=0.7777; I²=0.0%)								*0.04 [-1.42, 1.50]*
Sensitivity analysis: Follow-up duration >= 6 months (temporal comparison)								
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	58.3 (16.96)	56.0 (18.00)	mg/dL	2.29 [-0.97, 5.54]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	68.0 (18.00)	68.0 (17.00)	mg/dL	0.00 [-6.04, 6.04]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	59.8 (13.95)	60.2 (15.75)	mg/dL	-0.42 [-1.07, 0.23]
RE model (Heterog. p-value=0.2770; I²=35.0%)								*0.23 [-1.63, 2.09]*
Sensitivity analysis: % males < 50% (temporal comparison)								
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	68.0 (18.00)	68.0 (17.00)	mg/dL	0.00 [-6.04, 6.04]
Sensitivity analysis: % males >= 50% (temporal comparison)								
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	58.3 (16.96)	56.0 (18.00)	mg/dL	2.29 [-0.97, 5.54]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	59.8 (13.95)	60.2 (15.75)	mg/dL	-0.42 [-1.07, 0.23]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	54.1 (15.83)	54.1 (15.85)	mg/dL	0.00 [-2.45, 2.45]
RE model (Heterog. p-value=0.2703; I²=14.9%)								*-0.15 [-1.10, 0.80]*
Sensitivity analysis: Mean age < 50 years (temporal comparison)								
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	59.8 (13.95)	60.2 (15.75)	mg/dL	-0.42 [-1.07, 0.23]
Sensitivity analysis: Mean age >= 50 years (temporal comparison)								
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	58.3 (16.96)	56.0 (18.00)	mg/dL	2.29 [-0.97, 5.54]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	68.0 (18.00)	68.0 (17.00)	mg/dL	0.00 [-6.04, 6.04]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	54.1 (15.83)	54.1 (15.85)	mg/dL	0.00 [-2.45, 2.45]
RE model (Heterog. p-value=0.5283; I²=0.0%)								*0.75 [-1.11, 2.62]*
Sensitivity analysis: Occupational subgroups (temporal comparison)								
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	59.8 (13.95)	60.2 (15.75)	mg/dL	-0.42 [-1.07, 0.23]
Sensitivity analysis: Patient subgroups (temporal comparison)								
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	58.3 (16.96)	56.0 (18.00)	mg/dL	2.29 [-0.97, 5.54]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	68.0 (18.00)	68.0 (17.00)	mg/dL	0.00 [-6.04, 6.04]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	54.1 (15.83)	54.1 (15.85)	mg/dL	0.00 [-2.45, 2.45]
RE model (Heterog. p-value=0.5283; I²=0.0%)								*0.75 [-1.11, 2.62]*
Sensitivity analysis: Cohort (temporal comparison)								
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	58.3 (16.96)	56.0 (18.00)	mg/dL	2.29 [-0.97, 5.54]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	68.0 (18.00)	68.0 (17.00)	mg/dL	0.00 [-6.04, 6.04]
Niigata 2004 (Azuma 2010)	14	Cohort	4,035	4,035	59.8 (13.95)	60.2 (15.75)	mg/dL	-0.42 [-1.07, 0.23]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	54.1 (15.83)	54.1 (15.85)	mg/dL	0.00 [-2.45, 2.45]
RE model (Heterog. p-value=0.4530; I²=5.8%)								*-0.21 [-1.01, 0.58]*



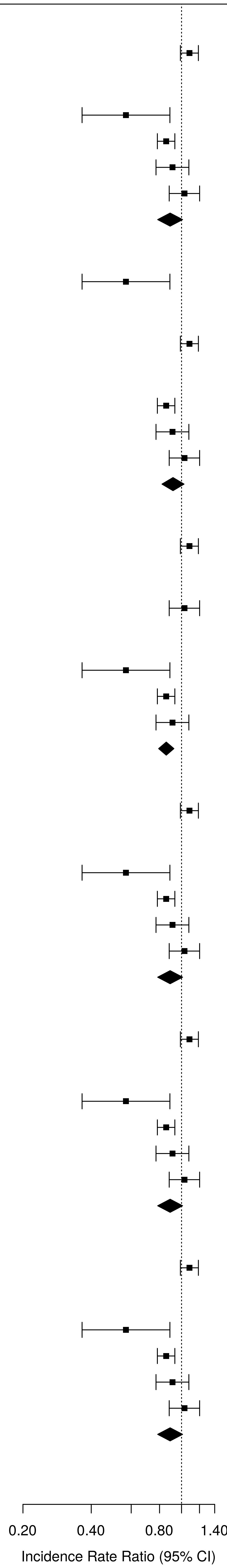
Myocardial infarction mortality

	Follow-up (months)	Study design	Exposed Events/Person-years	Unexposed Events/Person-years	
Main analysis: All studies (geographical comparison)					
Niigata 2004 (Nakagawa 2009)	36	Cross sectional	1,074/1,991,109	2,254/5,287,968	1.27 [1.18, 1.36]
Main analysis: All studies (temporal comparison)					
Irpinia & Naples 1980 (ISS 1981)	3	Time series	381/325,295	149/175,925	1.38 [1.14, 1.67]
Kobe 1995 (Takegami 2015)	12	Time series	6,800/16,545,012	4,331/16,545,012	1.57 [1.51, 1.63]
Niigata 2004 (Nakagawa 2009)	36	Cross sectional	1,074/1,991,109	1,608/3,401,255	1.14 [1.06, 1.23]
Great East Japan 2011 (Takegami 2015)	12	Time series	2,799/5,771,134	2,014/5,771,134	1.39 [1.31, 1.47]
RE model (Heterog. p-value=4.0059e-12; I²=94.0%)					*1.36 [1.19, 1.57]*
Sensitivity analysis: Follow-up duration < 6 months (temporal comparison)					
Irpinia & Naples 1980 (ISS 1981)	3	Time series	381/325,295	149/175,925	1.38 [1.14, 1.67]
Sensitivity analysis: Follow-up duration >= 6 months (geographical comparison)					
Niigata 2004 (Nakagawa 2009)	36	Cross sectional	1,074/1,991,109	2,254/5,287,968	1.27 [1.18, 1.36]
Sensitivity analysis: Follow-up duration >= 6 months (temporal comparison)					
Kobe 1995 (Takegami 2015)	12	Time series	6,800/16,545,012	4,331/16,545,012	1.57 [1.51, 1.63]
Niigata 2004 (Nakagawa 2009)	36	Cross sectional	1,074/1,991,109	1,608/3,401,255	1.14 [1.06, 1.23]
Great East Japan 2011 (Takegami 2015)	12	Time series	2,799/5,771,134	2,014/5,771,134	1.39 [1.31, 1.47]
RE model (Heterog. p-value=7.4630e-13; I²=96.9%)					*1.36 [1.13, 1.63]*
Sensitivity analysis: % males not specified (geographical comparison)					
Niigata 2004 (Nakagawa 2009)	36	Cross sectional	1,074/1,991,109	2,254/5,287,968	1.27 [1.18, 1.36]
Sensitivity analysis: % males not specified (temporal comparison)					
Irpinia & Naples 1980 (ISS 1981)	3	Time series	381/325,295	149/175,925	1.38 [1.14, 1.67]
Kobe 1995 (Takegami 2015)	12	Time series	6,800/16,545,012	4,331/16,545,012	1.57 [1.51, 1.63]
Niigata 2004 (Nakagawa 2009)	36	Cross sectional	1,074/1,991,109	1,608/3,401,255	1.14 [1.06, 1.23]
Great East Japan 2011 (Takegami 2015)	12	Time series	2,799/5,771,134	2,014/5,771,134	1.39 [1.31, 1.47]
RE model (Heterog. p-value=4.0059e-12; I²=94.0%)					*1.36 [1.19, 1.57]*
Sensitivity analysis: Mean age not specified (geographical comparison)					
Niigata 2004 (Nakagawa 2009)	36	Cross sectional	1,074/1,991,109	2,254/5,287,968	1.27 [1.18, 1.36]
Sensitivity analysis: Mean age not specified (temporal comparison)					
Irpinia & Naples 1980 (ISS 1981)	3	Time series	381/325,295	149/175,925	1.38 [1.14, 1.67]
Kobe 1995 (Takegami 2015)	12	Time series	6,800/16,545,012	4,331/16,545,012	1.57 [1.51, 1.63]
Niigata 2004 (Nakagawa 2009)	36	Cross sectional	1,074/1,991,109	1,608/3,401,255	1.14 [1.06, 1.23]
Great East Japan 2011 (Takegami 2015)	12	Time series	2,799/5,771,134	2,014/5,771,134	1.39 [1.31, 1.47]
RE model (Heterog. p-value=4.0059e-12; I²=94.0%)					*1.36 [1.19, 1.57]*
Sensitivity analysis: General population (geographical comparison)					
Niigata 2004 (Nakagawa 2009)	36	Cross sectional	1,074/1,991,109	2,254/5,287,968	1.27 [1.18, 1.36]
Sensitivity analysis: General population (temporal comparison)					
Irpinia & Naples 1980 (ISS 1981)	3	Time series	381/325,295	149/175,925	1.38 [1.14, 1.67]
Kobe 1995 (Takegami 2015)	12	Time series	6,800/16,545,012	4,331/16,545,012	1.57 [1.51, 1.63]
Niigata 2004 (Nakagawa 2009)	36	Cross sectional	1,074/1,991,109	1,608/3,401,255	1.14 [1.06, 1.23]
Great East Japan 2011 (Takegami 2015)	12	Time series	2,799/5,771,134	2,014/5,771,134	1.39 [1.31, 1.47]
RE model (Heterog. p-value=4.0059e-12; I²=94.0%)					*1.36 [1.19, 1.57]*
Sensitivity analysis: Cross sectional (geographical comparison)					
Niigata 2004 (Nakagawa 2009)	36	Cross sectional	1,074/1,991,109	2,254/5,287,968	1.27 [1.18, 1.36]
Sensitivity analysis: Cross sectional (temporal comparison)					
Niigata 2004 (Nakagawa 2009)	36	Cross sectional	1,074/1,991,109	1,608/3,401,255	1.14 [1.06, 1.23]
Sensitivity analysis: Time series (temporal comparison)					
Irpinia & Naples 1980 (ISS 1981)	3	Time series	381/325,295	149/175,925	1.38 [1.14, 1.67]
Kobe 1995 (Takegami 2015)	12	Time series	6,800/16,545,012	4,331/16,545,012	1.57 [1.51, 1.63]
Great East Japan 2011 (Takegami 2015)	12	Time series	2,799/5,771,134	2,014/5,771,134	1.39 [1.31, 1.47]
RE model (Heterog. p-value=0.0016; I²=81.6%)					*1.46 [1.33, 1.61]*



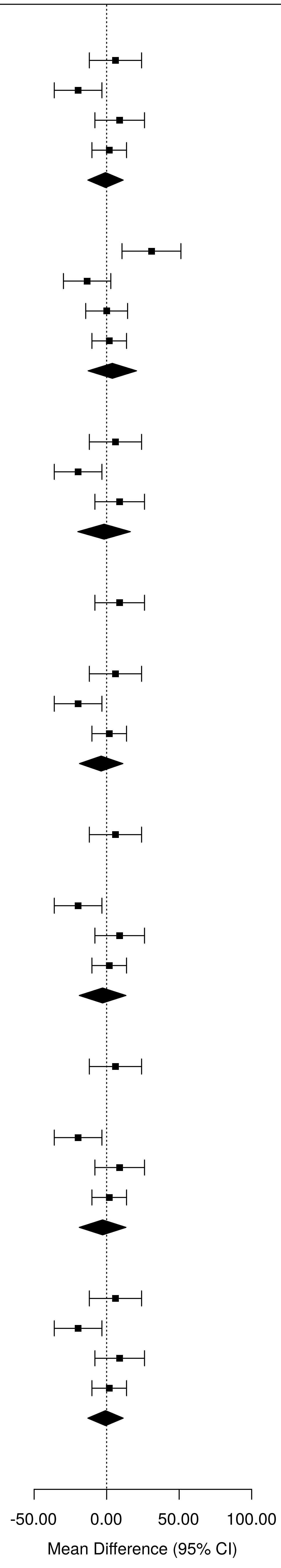
Suicides

	Follow-up (months)	Study design	Exposed Events/Person-years	Unexposed Events/Person-years	Incidence Rate Ratio (95% CI)
Main analysis: All studies (geographical comparison)					
Niigata 2004 (Hyodo 2010)	36	Time series	648/1,991,109	1,589/5,287,968	1.08 [0.99, 1.19]
Main analysis: All studies (temporal comparison)					
Irpinia & Naples 1980 (Alexander 1982)	3	Time series	21/1,514,606	245/10,055,493	0.57 [0.36, 0.89]
Los Angeles 1994 (Bourque 2002)	12	Time series	906/7,676,512	1,059/7,676,512	0.86 [0.78, 0.93]
Kobe 1995 (Nishio 2009)	36	Time series	500/3,655,863	191/1,273,333	0.91 [0.77, 1.08]
Niigata 2004 (Hyodo 2010)	36	Time series	648/1,991,109	215/680,251	1.03 [0.88, 1.20]
RE model (Heterog. p-value=0.0428; I²=56.7%)					*0.89 [0.79, 1.01]*
Sensitivity analysis: Follow-up duration < 6 months (temporal comparison)					
Irpinia & Naples 1980 (Alexander 1982)	3	Time series	21/1,514,606	245/10,055,493	0.57 [0.36, 0.89]
Sensitivity analysis: Follow-up duration >= 6 months (geographical comparison)					
Niigata 2004 (Hyodo 2010)	36	Time series	648/1,991,109	1,589/5,287,968	1.08 [0.99, 1.19]
Sensitivity analysis: Follow-up duration >= 6 months (temporal comparison)					
Los Angeles 1994 (Bourque 2002)	12	Time series	906/7,676,512	1,059/7,676,512	0.86 [0.78, 0.93]
Kobe 1995 (Nishio 2009)	36	Time series	500/3,655,863	191/1,273,333	0.91 [0.77, 1.08]
Niigata 2004 (Hyodo 2010)	36	Time series	648/1,991,109	215/680,251	1.03 [0.88, 1.20]
RE model (Heterog. p-value=0.1208; I²=52.5%)					*0.92 [0.82, 1.03]*
Sensitivity analysis: % males < 50% (geographical comparison)					
Niigata 2004 (Hyodo 2010)	36	Time series	648/1,991,109	1,589/5,287,968	1.08 [0.99, 1.19]
Sensitivity analysis: % males < 50% (temporal comparison)					
Niigata 2004 (Hyodo 2010)	36	Time series	648/1,991,109	215/680,251	1.03 [0.88, 1.20]
Sensitivity analysis: % males not specified (temporal comparison)					
Irpinia & Naples 1980 (Alexander 1982)	3	Time series	21/1,514,606	245/10,055,493	0.57 [0.36, 0.89]
Los Angeles 1994 (Bourque 2002)	12	Time series	906/7,676,512	1,059/7,676,512	0.86 [0.78, 0.93]
Kobe 1995 (Nishio 2009)	36	Time series	500/3,655,863	191/1,273,333	0.91 [0.77, 1.08]
RE model (Heterog. p-value=0.1514; I²=0.1%)					*0.86 [0.79, 0.93]*
Sensitivity analysis: Mean age not specified (geographical comparison)					
Niigata 2004 (Hyodo 2010)	36	Time series	648/1,991,109	1,589/5,287,968	1.08 [0.99, 1.19]
Sensitivity analysis: Mean age not specified (temporal comparison)					
Irpinia & Naples 1980 (Alexander 1982)	3	Time series	21/1,514,606	245/10,055,493	0.57 [0.36, 0.89]
Los Angeles 1994 (Bourque 2002)	12	Time series	906/7,676,512	1,059/7,676,512	0.86 [0.78, 0.93]
Kobe 1995 (Nishio 2009)	36	Time series	500/3,655,863	191/1,273,333	0.91 [0.77, 1.08]
Niigata 2004 (Hyodo 2010)	36	Time series	648/1,991,109	215/680,251	1.03 [0.88, 1.20]
RE model (Heterog. p-value=0.0428; I²=56.7%)					*0.89 [0.79, 1.01]*
Sensitivity analysis: General population (geographical comparison)					
Niigata 2004 (Hyodo 2010)	36	Time series	648/1,991,109	1,589/5,287,968	1.08 [0.99, 1.19]
Sensitivity analysis: General population (temporal comparison)					
Irpinia & Naples 1980 (Alexander 1982)	3	Time series	21/1,514,606	245/10,055,493	0.57 [0.36, 0.89]
Los Angeles 1994 (Bourque 2002)	12	Time series	906/7,676,512	1,059/7,676,512	0.86 [0.78, 0.93]
Kobe 1995 (Nishio 2009)	36	Time series	500/3,655,863	191/1,273,333	0.91 [0.77, 1.08]
Niigata 2004 (Hyodo 2010)	36	Time series	648/1,991,109	215/680,251	1.03 [0.88, 1.20]
RE model (Heterog. p-value=0.0428; I²=56.7%)					*0.89 [0.79, 1.01]*
Sensitivity analysis: Time series (geographical comparison)					
Niigata 2004 (Hyodo 2010)	36	Time series	648/1,991,109	1,589/5,287,968	1.08 [0.99, 1.19]
Sensitivity analysis: Time series (temporal comparison)					
Irpinia & Naples 1980 (Alexander 1982)	3	Time series	21/1,514,606	245/10,055,493	0.57 [0.36, 0.89]
Los Angeles 1994 (Bourque 2002)	12	Time series	906/7,676,512	1,059/7,676,512	0.86 [0.78, 0.93]
Kobe 1995 (Nishio 2009)	36	Time series	500/3,655,863	191/1,273,333	0.91 [0.77, 1.08]
Niigata 2004 (Hyodo 2010)	36	Time series	648/1,991,109	215/680,251	1.03 [0.88, 1.20]
RE model (Heterog. p-value=0.0428; I²=56.7%)					*0.89 [0.79, 1.01]*



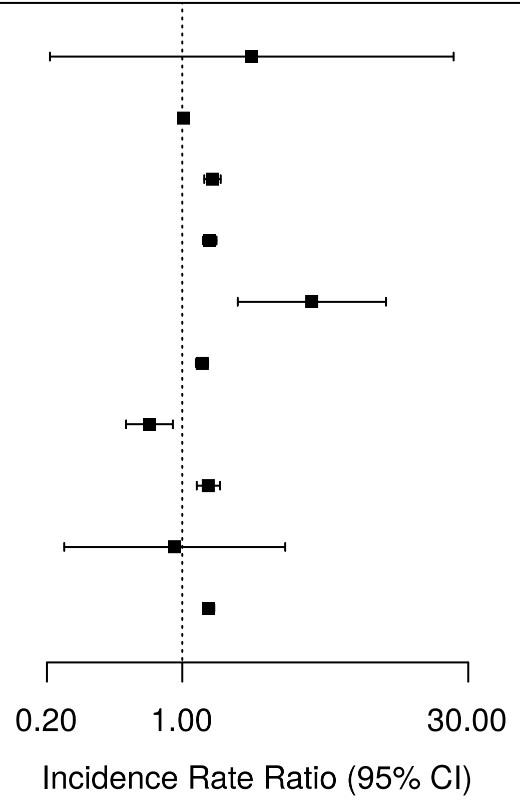
Triglycerides

	Follow-up (months)	Study design	Exposed Participants	Unexposed Participants	Exposed Mean (SD)	Unexposed Mean (SD)	Unit	Mean Difference (95% CI)
Main analysis: All studies (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	133.6 (86.74)	127.5 (73.70)	mg/dL	6.08 [-11.94, 24.09]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	125.3 (69.14)	145.0 (104.00)	mg/dL	-19.69 [-36.12, -3.27]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	96.0 (56.00)	87.0 (42.00)	mg/dL	9.00 [-8.10, 26.10]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	132.9 (77.82)	131.1 (76.17)	mg/dL	1.77 [-10.16, 13.70]
RE model (Heterog. p-value=0.0694; I²=58.8%)								*-0.77 [-12.98, 11.44]*
Sensitivity analysis: Follow-up duration < 6 months (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	2	Cohort	102	505	158.4 (99.30)	127.5 (73.70)	mg/dL	30.90 [10.59, 51.21]
Niigata 2004 (Kamoi 2006a)	3	Cohort	222	222	131.5 (67.78)	145.0 (104.00)	mg/dL	-13.46 [-29.79, 2.87]
Niigata 2004 (Kamoi 2006b)	3	Cohort	65	65	87.0 (42.00)	87.0 (42.00)	mg/dL	0.00 [-14.44, 14.44]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	132.9 (77.82)	131.1 (76.17)	mg/dL	1.77 [-10.16, 13.70]
RE model (Heterog. p-value=0.0102; I²=78.8%)								*3.91 [-12.78, 20.61]*
Sensitivity analysis: Follow-up duration >= 6 months (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	133.6 (86.74)	127.5 (73.70)	mg/dL	6.08 [-11.94, 24.09]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	125.3 (69.14)	145.0 (104.00)	mg/dL	-19.69 [-36.12, -3.27]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	96.0 (56.00)	87.0 (42.00)	mg/dL	9.00 [-8.10, 26.10]
RE model (Heterog. p-value=0.0331; I²=70.1%)								*-1.76 [-19.89, 16.36]*
Sensitivity analysis: % males < 50% (temporal comparison)								
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	96.0 (56.00)	87.0 (42.00)	mg/dL	9.00 [-8.10, 26.10]
Sensitivity analysis: % males >= 50% (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	133.6 (86.74)	127.5 (73.70)	mg/dL	6.08 [-11.94, 24.09]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	125.3 (69.14)	145.0 (104.00)	mg/dL	-19.69 [-36.12, -3.27]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	132.9 (77.82)	131.1 (76.17)	mg/dL	1.77 [-10.16, 13.70]
RE model (Heterog. p-value=0.0622; I²=65.1%)								*-3.78 [-18.75, 11.19]*
Sensitivity analysis: Mean age < 50 years (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	133.6 (86.74)	127.5 (73.70)	mg/dL	6.08 [-11.94, 24.09]
Sensitivity analysis: Mean age >= 50 years (temporal comparison)								
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	125.3 (69.14)	145.0 (104.00)	mg/dL	-19.69 [-36.12, -3.27]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	96.0 (56.00)	87.0 (42.00)	mg/dL	9.00 [-8.10, 26.10]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	132.9 (77.82)	131.1 (76.17)	mg/dL	1.77 [-10.16, 13.70]
RE model (Heterog. p-value=0.0402; I²=70.8%)								*-2.80 [-18.90, 13.30]*
Sensitivity analysis: Occupational subgroups (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	133.6 (86.74)	127.5 (73.70)	mg/dL	6.08 [-11.94, 24.09]
Sensitivity analysis: Patient subgroups (temporal comparison)								
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	125.3 (69.14)	145.0 (104.00)	mg/dL	-19.69 [-36.12, -3.27]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	96.0 (56.00)	87.0 (42.00)	mg/dL	9.00 [-8.10, 26.10]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	132.9 (77.82)	131.1 (76.17)	mg/dL	1.77 [-10.16, 13.70]
RE model (Heterog. p-value=0.0402; I²=70.8%)								*-2.80 [-18.90, 13.30]*
Sensitivity analysis: Cohort (temporal comparison)								
Irpinia & Naples 1980 (Trevisan 1992)	79	Cohort	102	505	133.6 (86.74)	127.5 (73.70)	mg/dL	6.08 [-11.94, 24.09]
Niigata 2004 (Kamoi 2006a)	6	Cohort	222	222	125.3 (69.14)	145.0 (104.00)	mg/dL	-19.69 [-36.12, -3.27]
Niigata 2004 (Kamoi 2006b)	12	Cohort	64	65	96.0 (56.00)	87.0 (42.00)	mg/dL	9.00 [-8.10, 26.10]
Great East Japan 2011 (Fujihara 2012)	3	Cohort	320	320	132.9 (77.82)	131.1 (76.17)	mg/dL	1.77 [-10.16, 13.70]
RE model (Heterog. p-value=0.0694; I²=58.8%)								*-0.77 [-12.98, 11.44]*



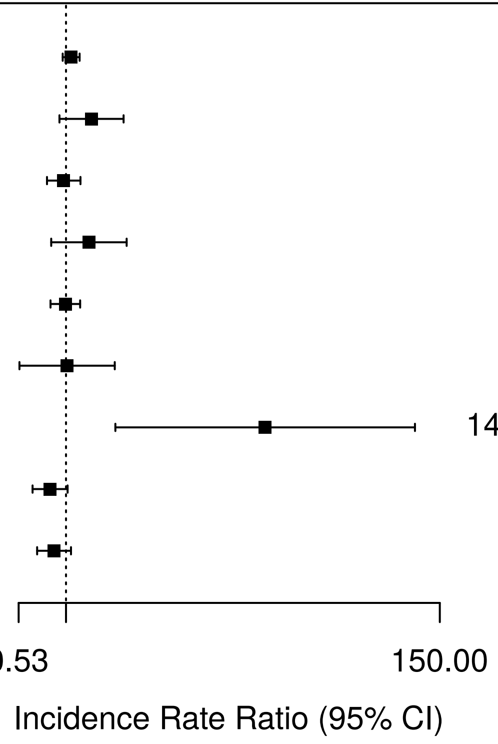
Mortality

	Comparison	Follow-up (months)	Studies	Exposed Events/Person-years	Unexposed Events/Person-years	I^2	Effect p-value	
All-cause mortality	Geographical	36	1	2/42	1/48	-	0.4997	2.29 [0.21, 25.21]
All-cause mortality	Temporal	12	2	179,502/22,316,146	176,741/22,316,146	49.9%	0.0009	1.02 [1.01, 1.03]
Death for cardiocirculatory cause (onset < 1 week)	Temporal	3	1	1,482/325,295	560/175,925	-	4.8991e-13	1.43 [1.30, 1.58]
Death for cardiocirculatory cause	Temporal	3	1	2,167/325,295	845/175,925	-	7.3359e-16	1.39 [1.28, 1.50]
Death for coronary heart disease, including sudden death	Temporal	3	1	28/18,071	6/18,071	-	0.0006	4.67 [1.93, 11.27]
Myocardial infarction mortality	Geographical	36	1	1,074/1,991,109	2,254/5,287,968	-	2.1597e-10	1.27 [1.18, 1.36]
Myocardial infarction mortality (including sudden death)	Temporal	4	1	58/142,933	334/557,200	-	0.0061	0.68 [0.51, 0.89]
Myocardial infarction mortality	Temporal	3 to 36	4	11,054/24,632,550	8,102/25,893,326	94.0%	1.2610e-05	1.36 [1.19, 1.57]
Renal mortality	Geographical	36	1	4/42	5/48	-	0.8937	0.91 [0.25, 3.40]
Stroke mortality	Temporal	12	2	24,429/22,316,146	17,987/22,316,146	89.6%	3.5259e-22	1.37 [1.29, 1.46]



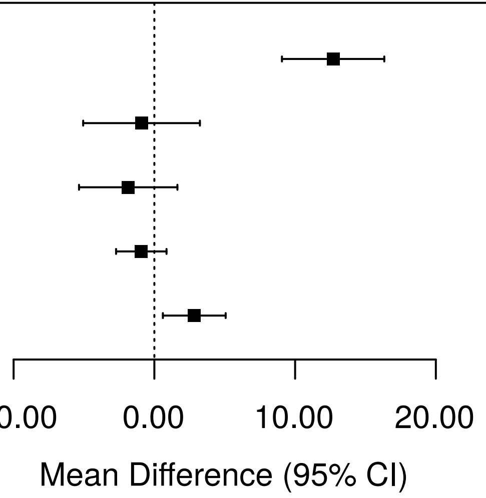
Diseases of the circulatory system (Incidence Rate Ratio)

	Comparison	Follow-up (months)	Studies	Exposed Events/Person-years	Unexposed Events/Person-years	I²	Effect p-value	Incidence Rate Ratio (95% CI)
Acute admissions to cardiology department	Temporal	1	2	834/71,371	468/42,909	0.0%	0.2332	1.07 [0.96, 1.20]
Atrial fibrillation	Temporal	1	2	46/20	38/23	0.0%	0.1191	1.41 [0.92, 2.16]
Cerebrovascular disease	Temporal	4	1	148/31,491	158/32,607	-	0.7894	0.97 [0.78, 1.21]
Coronary heart disease	Temporal	1 to 4	2	350/34,751	299/42,399	27.9%	0.2336	1.36 [0.82, 2.25]
Myocardial infarction, possible, nonfatal	Temporal	4	1	122/142,933	480/557,200	-	0.9276	0.99 [0.81, 1.21]
Myocardial infarction	Temporal	3 to 4	2	128/161,004	460/575,271	83.9%	0.9641	1.01 [0.54, 1.92]
Stress cardiomyopathy	Temporal	1	2	27/71,371	0/42,909	0.0%	0.0092	14.43 [1.94, 107.48]
Supraventricular tachycardia and ventricular arrhythmia	Temporal	6	1	126/85	156/85	-	0.0746	0.81 [0.64, 1.02]
Ventricular arrhythmia	Temporal	6	1	138/85	162/85	-	0.1663	0.85 [0.68, 1.07]



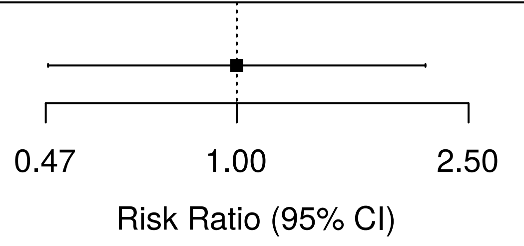
Diseases of the circulatory system (Mean Difference)

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I^2	Effect p-value	
Aortic diameter, maximum	mm	Temporal	2	1	5	5	-	7.5214e-12	12.70 [9.06, 16.34]
Clinically measured diastolic blood pressure	mmHg	Temporal	2 to 79	7	5,568	5,476	98.2%	0.6670	-0.91 [-5.06, 3.24]
Clinically measured systolic blood pressure	mmHg	Temporal	2 to 79	7	5,568	5,476	93.7%	0.2978	-1.86 [-5.35, 1.64]
Morning home diastolic blood pressure	mmHg	Temporal	1 to 6	2	247	247	0.0%	0.3102	-0.93 [-2.72, 0.86]
Morning home systolic blood pressure	mmHg	Temporal	1 to 6	2	247	247	0.0%	0.0127	2.84 [0.61, 5.07]



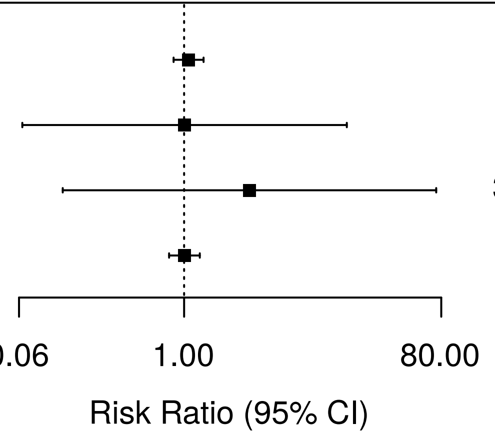
Diseases of the circulatory system (Risk Ratio)

	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I²	Effect p-value	Risk Ratio (95% CI)
Coronary heart disease	Temporal	6	1	13/222	13/222	-	1.0000	1.00 [0.47, 2.11]



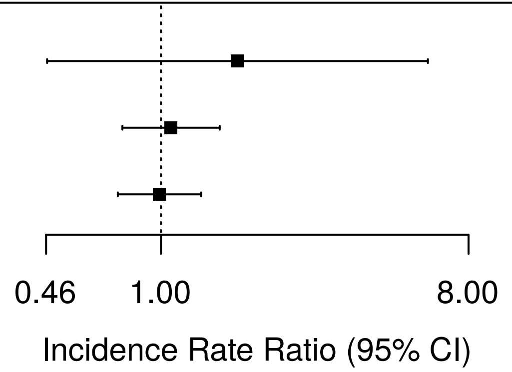
Endocrine, nutritional and metabolic diseases

	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I²	Effect p-value	Risk Ratio (95% CI)
Diabetes complications, nephropathy	Temporal	6 to 12	2	86/286	80/287	0.0%	0.5591	1.08 [0.84, 1.39]
Diabetes complications, neuropathy	Temporal	6 to 12	2	0/286	0/287	0.0%	0.9957	1.01 [0.06, 16.00]
Diabetes complications, others	Temporal	12	1	1/64	0/65	-	0.4927	3.05 [0.13, 73.41]
Diabetes complications, retinopathy	Temporal	6 to 12	2	79/286	79/287	0.0%	0.9663	1.01 [0.77, 1.31]

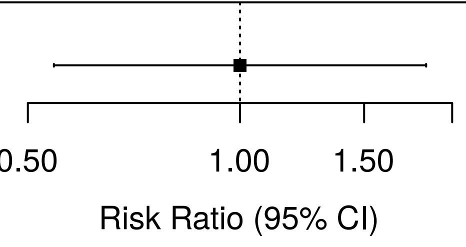


Diseases of the nervous system (Incidence Rate Ratio)

	Comparison	Follow-up (months)	Studies	Exposed Events/Person-years	Unexposed Events/Person-years	I^2	Effect p-value	Incidence Rate Ratio (95% CI)
Stroke, haemorrhagic	Temporal	1 to 24	2	32/20,863	20/18,550	77.8%	0.4307	1.68 [0.46, 6.08]
Stroke, ischaemic	Temporal	1 to 24	3	236/103,248	183/94,576	62.1%	0.6834	1.07 [0.77, 1.49]
Stroke	Temporal	1 to 24	3	295/103,248	245/94,576	60.8%	0.9446	0.99 [0.75, 1.31]

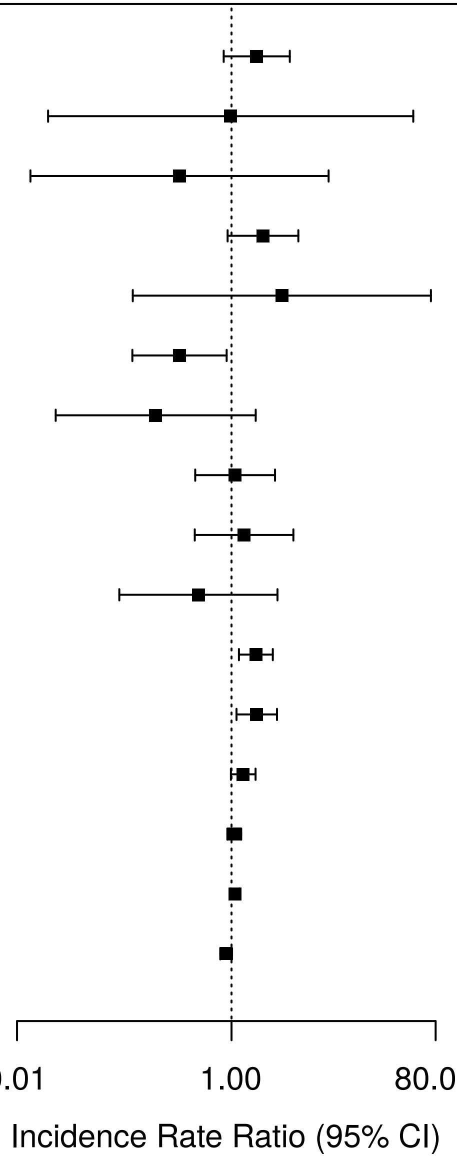


Diseases of the nervous system (Risk Ratio)

	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I²	Effect p-value		
Stroke	Temporal	6	1	19/222	19/222	-	1.0000		1.00 [0.54, 1.84]

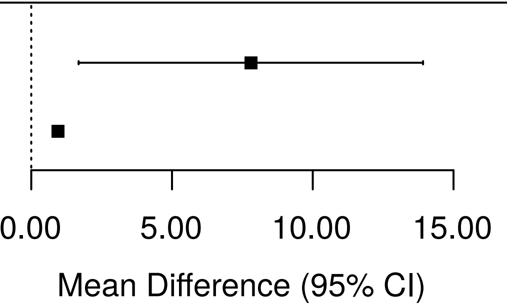
Mental, behavioral and neurodevelopmental disorders (Incidence Rate Ratio)

	Comparison	Follow-up (months)	Studies	Exposed Events/Person-years	Unexposed Events/Person-years	I^2	Effect p-value	
Psychiatric emergency hospitalization, acute transient psychotic disorders	Temporal	6	1	21/2,217,410	12/2,177,472	-	0.1346	1.72 [0.85, 3.49]
Psychiatric emergency hospitalization, behavioural and emotional disorders with onset usually occurring in childhood and adolescence	Temporal	6	1	0/2,217,410	0/2,177,472	-	0.9927	0.98 [0.02, 49.49]
Psychiatric emergency hospitalization, behavioural syndromes associated with physiological disturbances and physical factors	Temporal	6	1	0/2,217,410	1/2,177,472	-	0.4940	0.33 [0.01, 8.04]
Psychiatric emergency hospitalization, disorders of adult personality and behaviour	Temporal	6	1	20/2,217,410	10/2,177,472	-	0.0814	1.96 [0.92, 4.20]
Psychiatric emergency hospitalization, disorders of psychological development	Temporal	6	1	1/2,217,410	0/2,177,472	-	0.5082	2.95 [0.12, 72.32]
Psychiatric emergency hospitalization, mental disorders due to psychoactive substance use	Temporal	6	1	5/2,217,410	15/2,177,472	-	0.0306	0.33 [0.12, 0.90]
Psychiatric emergency hospitalization, mental retardation	Temporal	6	1	1/2,217,410	5/2,177,472	-	0.1373	0.20 [0.02, 1.68]
Psychiatric emergency hospitalization, mood/affective disorders	Temporal	6	1	11/2,217,410	10/2,177,472	-	0.8599	1.08 [0.46, 2.54]
Psychiatric emergency hospitalization, neurotic/stress-related/somatoform disorders	Temporal	6	1	8/2,217,410	6/2,177,472	-	0.6178	1.31 [0.45, 3.77]
Psychiatric emergency hospitalization, organic mental disorders	Temporal	6	1	2/2,217,410	4/2,177,472	-	0.4114	0.49 [0.09, 2.68]
Psychiatric emergency hospitalization, schizophrenia/schizotypal/delusional disorders	Temporal	6	1	79/2,217,410	46/2,177,472	-	0.0048	1.69 [1.17, 2.43]
Psychiatric emergency hospitalization, schizophrenia	Temporal	6	1	56/2,217,410	32/2,177,472	-	0.0146	1.72 [1.11, 2.65]
Psychiatric emergency hospitalization	Temporal	6	1	127/2,217,410	97/2,177,472	-	0.0624	1.29 [0.99, 1.67]
Suicides, attempted	Temporal	3 to 6	2	336/1,814,606	483/10,355,493	0.0%	0.4357	1.06 [0.91, 1.23]
Suicides	Geographical	36	1	648/1,991,109	1,589/5,287,968	-	0.0870	1.08 [0.99, 1.19]
Suicides	Temporal	3 to 36	4	2,075/14,838,090	1,710/19,685,589	56.7%	0.0725	0.89 [0.79, 1.01]



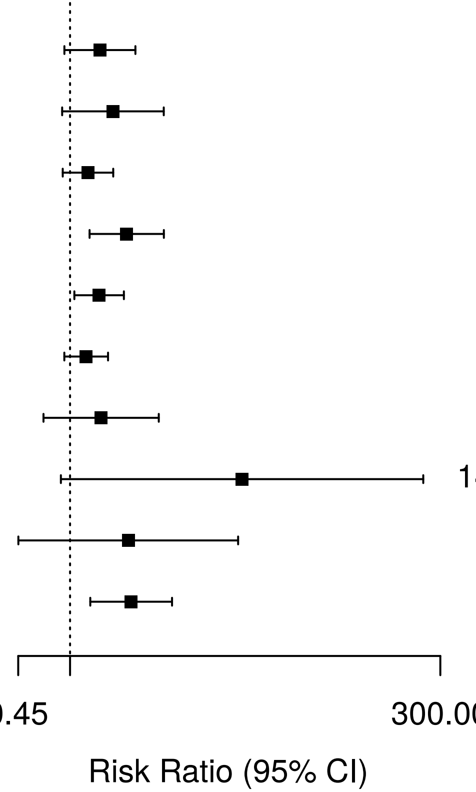
Mental, behavioral and neurodevelopmental disorders (Mean Difference)

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	Mean Difference (95% CI)
Frequency of headaches	days/month	Temporal	4	1	12	16	-	0.0125	7.80 [1.68, 13.92]
Insomnia, average daily prevalence	%	Temporal	2	1	5,053	5,053	-	0.0000	0.95 [0.93, 0.98]



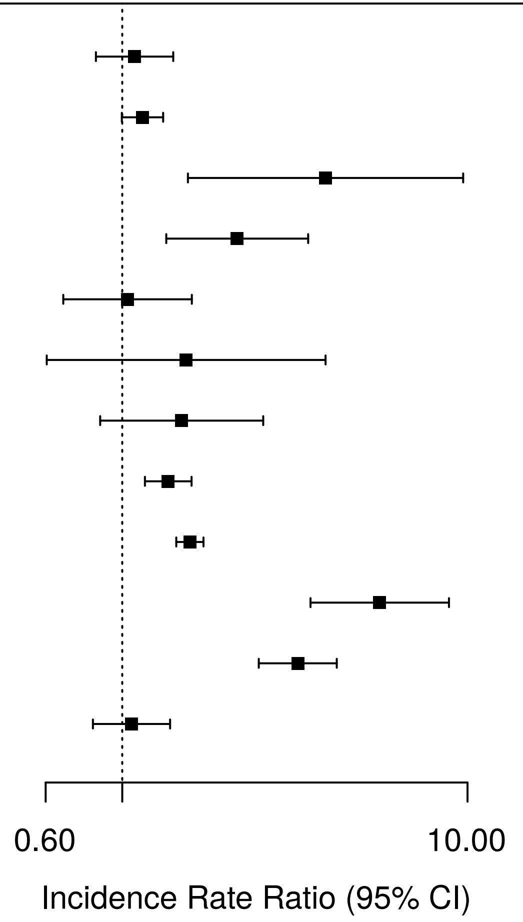
Mental, behavioral and neurodevelopmental disorders (Risk Ratio)

	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I^2	Effect p-value	Risk Ratio (95% CI)
Acute stress disorder, probable	Geographical	2	1	23/61	15/63	-	0.0995	1.58 [0.92, 2.74]
Generalized anxiety disorder, probable	Geographical	2	1	15/61	8/63	-	0.0979	1.94 [0.89, 4.24]
Major depressive disorder	Geographical	24	1	63/543	36/409	-	0.1639	1.32 [0.89, 1.94]
Major depressive disorder, probable	Geographical	2 to 6	2	52/176	13/111	0.0%	0.0028	2.39 [1.35, 4.24]
Major depressive disorder, probable	Temporal	19	1	147/936	28/279	-	0.0214	1.56 [1.07, 2.29]
Other anxiety disorder	Geographical	24	1	80/543	47/409	-	0.1479	1.28 [0.92, 1.80]
Post-traumatic stress disorder	Geographical	24	1	15/543	7/409	-	0.2906	1.61 [0.66, 3.92]
Post-traumatic stress disorder, probable	Geographical	3	1	12/52	0/29	-	0.0628	14.15 [0.87, 230.62]
Suicides, attempted	Geographical	12	1	4/426	2/522	-	0.2993	2.45 [0.45, 13.32]
Suicides, attempted or ideated	Geographical	12 to 24	2	36/969	14/931	5.6%	0.0034	2.56 [1.37, 4.81]



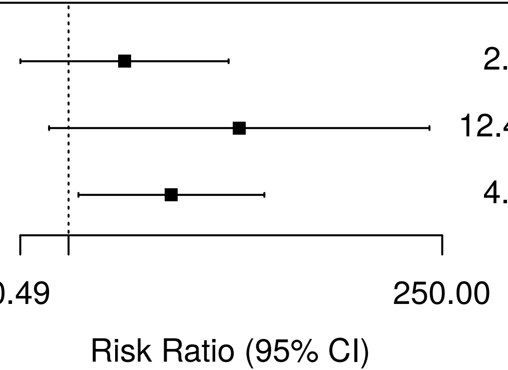
Diseases of the digestive system

	Comparison	Follow-up (months)	Studies	Exposed Events/Person-years	Unexposed Events/Person-years	I²	Effect p-value	Incidence Rate Ratio (95% CI)
Duodenal ulcer	Geographical	2	1	109/466	123/571	-	0.5322	1.09 [0.84, 1.40]
Duodenal ulcer	Temporal	2	1	358/1,666	465/2,477	-	0.0550	1.14 [1.00, 1.31]
Duodenal ulcer, with bleeding	Geographical	2	1	19/466	6/571	-	0.0038	3.88 [1.55, 9.71]
Duodenal ulcer, with bleeding	Temporal	2	1	42/1,666	29/2,477	-	0.0015	2.15 [1.34, 3.46]
Duodenal ulcer, with serum H. Pylori IgG	Geographical	2	1	33/6	57/10	-	0.8715	1.04 [0.67, 1.59]
Gastric and duodenal ulcer	Geographical	2	1	10/466	8/571	-	0.3690	1.53 [0.60, 3.88]
Gastric and duodenal ulcer	Temporal	2	1	26/1,666	26/2,477	-	0.1529	1.49 [0.86, 2.56]
Gastric ulcer	Geographical	2	1	335/466	302/571	-	0.0001	1.36 [1.16, 1.59]
Gastric ulcer	Temporal	2	1	960/1,666	909/2,477	-	1.9366e-22	1.57 [1.43, 1.72]
Gastric ulcer, with bleeding	Geographical	2	1	100/466	22/571	-	3.0579e-13	5.57 [3.51, 8.83]
Gastric ulcer, with bleeding	Temporal	2	1	180/1,666	83/2,477	-	1.1222e-18	3.22 [2.49, 4.18]
Gastric ulcer, with serum H. Pylori IgG	Geographical	2	1	99/19	140/28	-	0.6385	1.06 [0.82, 1.38]



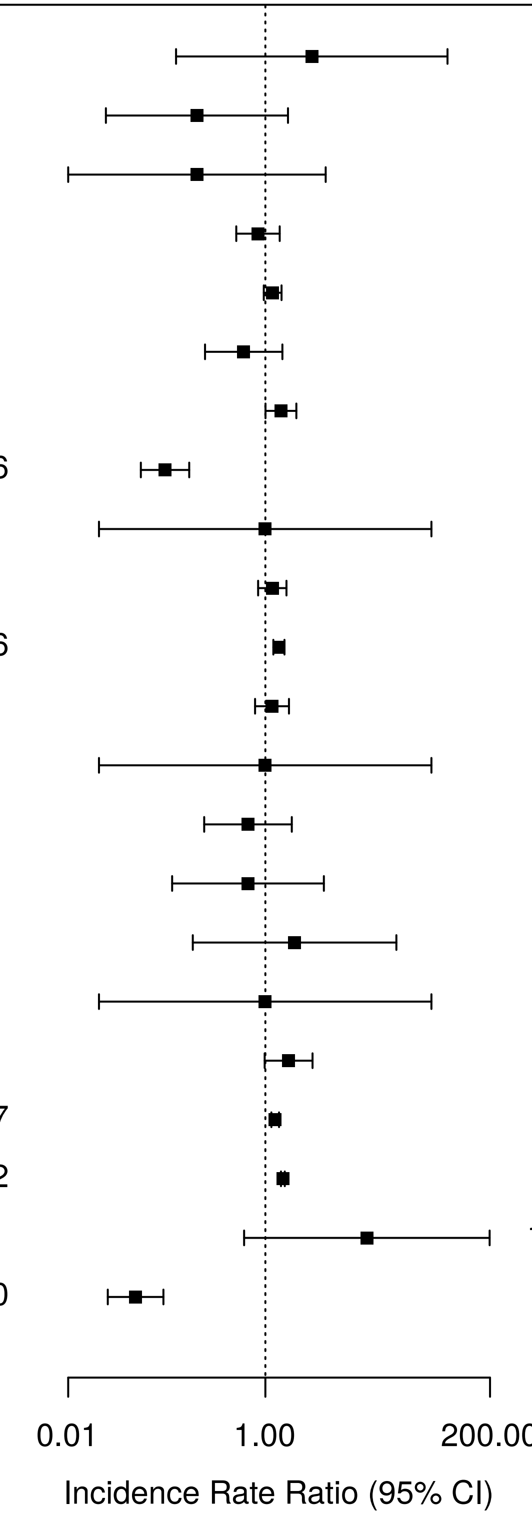
Diseases of the respiratory system

	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I²	Effect p-value	Risk Ratio (95% CI)
Interstitial pneumonitis	Geographical	36	1	4/14	2/16	-	0.2922	2.29 [0.49, 10.64]
Pulmonary haemorrhage	Geographical	36	1	5/14	0/16	-	0.0785	12.47 [0.75, 207.19]
Upper respitatory tract inflammation, as initial symptom	Geographical	36	1	8/14	2/16	-	0.0301	4.57 [1.16, 18.05]

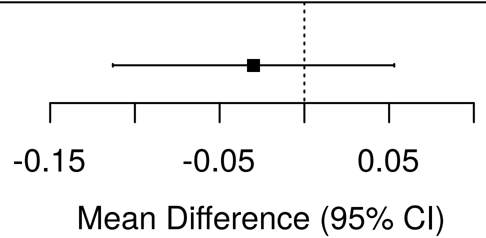


Infectious and parasitic diseases

	Comparison	Follow-up (months)	Studies	Exposed Events/Person-years	Unexposed Events/Person-years	I²	Effect p-value	Incidence Rate Ratio (95% CI)
Bacillary dysentery	Temporal	2	1	1/1,009,738	0/1,005,549	-	0.5027	2.99 [0.12, 73.34]
Blennorrhoea	Temporal	2	1	1/1,009,738	5/1,005,549	-	0.1408	0.20 [0.02, 1.70]
Botulism	Temporal	2	1	0/1,009,738	2/1,005,549	-	0.2976	0.20 [0.01, 4.15]
Brucellosis	Temporal	2	1	27/1,009,738	32/1,005,549	-	0.5054	0.84 [0.50, 1.40]
Chicken pox (Varicella)	Temporal	2	1	192/1,009,738	161/1,005,549	-	0.1076	1.19 [0.96, 1.46]
Dyphtheria	Temporal	7	1	6/2,813,615	20/5,627,230	-	0.2725	0.60 [0.24, 1.49]
Endemic parotitis (Mumps)	Temporal	2	1	71/1,009,738	49/1,005,549	-	0.0483	1.44 [1.00, 2.08]
German measles	Temporal	2	1	12/1,009,738	760/6,000,386	-	4.1854e-16	0.09 [0.05, 0.17]
Leptospirosis	Temporal	2	1	0/1,009,738	0/1,005,549	-	0.9983	1.00 [0.02, 50.19]
Meningococcal meningitis	Temporal	7	1	45/3,534,082	146/13,500,868	-	0.3380	1.18 [0.84, 1.64]
Paratyphoid and other salmonellosis	Temporal	7	1	377/2,813,615	548/5,627,230	-	1.8501e-06	1.38 [1.21, 1.57]
Pneumococcal pneumonia	Temporal	16	1	44/495,339	53/697,974	-	0.4419	1.17 [0.78, 1.74]
Poliomyelitis	Temporal	2	1	0/1,009,738	0/1,005,549	-	0.9983	1.00 [0.02, 50.19]
Roseola infantum	Temporal	2	1	6/1,009,738	9/1,005,549	-	0.4370	0.66 [0.24, 1.87]
Scarlettina (Scarlet fever)	Temporal	2	1	2/1,009,738	3/1,005,549	-	0.6536	0.66 [0.11, 3.97]
Tetanus	Temporal	2	1	2/1,009,738	1/1,005,549	-	0.5737	1.99 [0.18, 21.96]
Tuberculosis: extra-pulmonary	Temporal	2	1	0/1,009,738	0/1,005,549	-	0.9983	1.00 [0.02, 50.19]
Tuberculosis: pulmonary	Temporal	2	1	33/1,009,738	19/1,005,549	-	0.0571	1.73 [0.98, 3.04]
Typhoid fever	Temporal	7	1	599/2,411,670	2,217/11,254,460	-	4.8112e-07	1.26 [1.15, 1.38]
Viral hepatitis	Temporal	7	1	2,511/2,411,670	7,753/11,254,460	-	2.3910e-72	1.51 [1.44, 1.58]
Viral neuritis	Temporal	2	1	5/1,009,738	0/1,005,549	-	0.1051	10.95 [0.61, 198.11]
Whooping cough (pertussis)	Temporal	2	1	9/1,009,738	1,141/6,000,386	-	5.9679e-20	0.05 [0.02, 0.09]

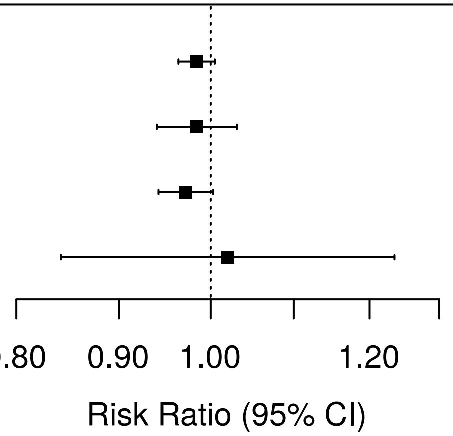


Pregnancy, childbirth and the puerperium (Mean Difference)

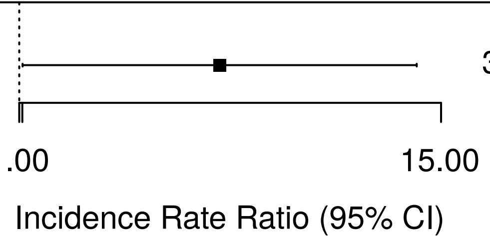
	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I^2	Effect p-value		
Gestational age	weeks	Temporal	9	1	3,447	3,427	-	0.4788		-0.03 [-0.11, 0.05]

Pregnancy, childbirth and the puerperium (Risk Ratio)

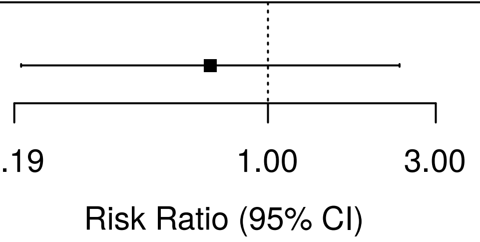
	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I^2	Effect p-value		
All newborns (fertility)	Temporal	9	1	17,411/5,395,158	17,695/5,395,158	-	0.1290		0.98 [0.96, 1.00]
Male newborns	Geographical	9	1	1,737/3,447	1,837/3,588	-	0.4987		0.98 [0.94, 1.03]
Male newborns	Temporal	9	2	3,705/7,375	3,942/7,627	0.0%	0.0755		0.97 [0.94, 1.00]
Preterm	Temporal	9	1	200/3,447	195/3,427	-	0.8418		1.02 [0.84, 1.23]



Other diseases (Incidence Rate Ratio)

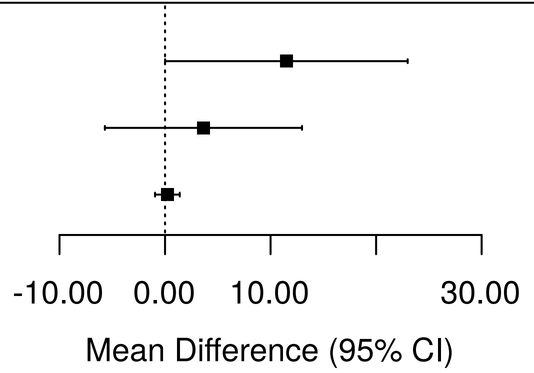
	Comparison	Follow-up (months)	Studies	Exposed Events/Person-years	Unexposed Events/Person-years	I²	Effect p-value		
Recurrence of endogenous uveitis	Temporal	6	1	12/58	3/52	-	0.0462		3.62 [1.02, 12.83]

Other diseases (Risk Ratio)

	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I²	Effect p-value		
Renal failure, no recover after haemodialisis	Geographical	36	1	3/14	5/16	-	0.5505		0.69 [0.20, 2.37]

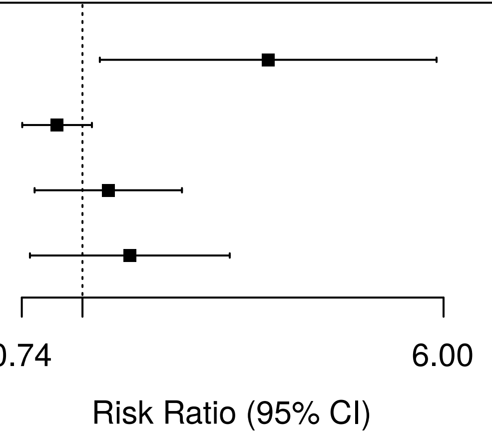
Health status and quality of life (Mean Difference)

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I^2	Effect p-value	Mean Difference (95% CI)
Cornell Medical Index, emotion status score	-	Temporal	3	1	14	15	-	0.0498	11.50 [0.01, 22.99]
Cornell Medical Index, somatic status score	-	Temporal	3	1	14	15	-	0.4449	3.64 [-5.70, 12.98]
Unhealthy days, continuous	days	Temporal	19	1	957	283	-	0.7087	0.22 [-0.95, 1.39]

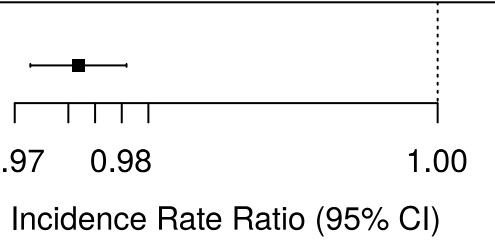


Health status and quality of life (Risk Ratio)

	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I²	Effect p-value	Risk Ratio (95% CI)
Health status, functional limitations, binary	Temporal	19	1	51/957	6/283	-	0.0306	2.51 [1.09, 5.80]
Health status, low, binary	Temporal	19	1	322/957	108/283	-	0.1535	0.88 [0.74, 1.05]
Health status, low mental, binary	Temporal	19	1	123/957	32/283	-	0.4923	1.14 [0.79, 1.64]
Health status, low physical, binary	Temporal	19	1	77/957	18/283	-	0.3526	1.27 [0.77, 2.08]

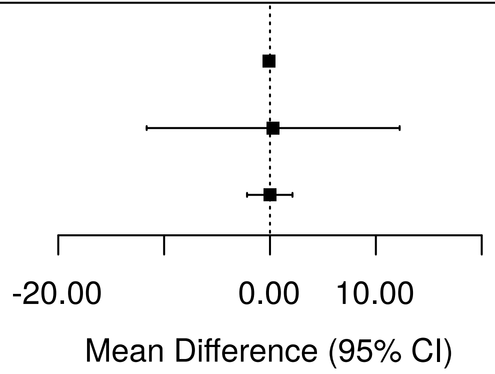


Healthcare quality and costs

	Comparison	Follow-up (months)	Studies	Exposed Events/Person-years	Unexposed Events/Person-years	I^2	Effect p-value		
Hospital discharges	Temporal	6	1	399,263/3,029,213	948,532/7,000,450	-	1.4985e-48		0.97 [0.97, 0.98]

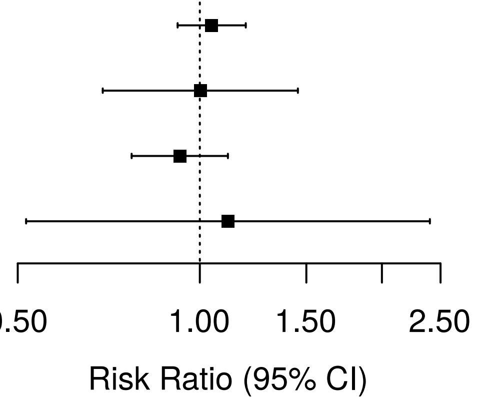
Vital signs (Mean Difference)

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	Mean Difference (95% CI)
Body mass index	Kg/m²	Temporal	3 to 79	5	4,743	5,147	3.2%	0.2675	-0.08 [-0.23, 0.06]
Cardiotoracic ratio	%	Temporal	2	1	25	25	-	0.9607	0.30 [-11.65, 12.25]
Weight	Kg	Temporal	2	2	230	230	0.0%	0.9849	-0.02 [-2.17, 2.12]



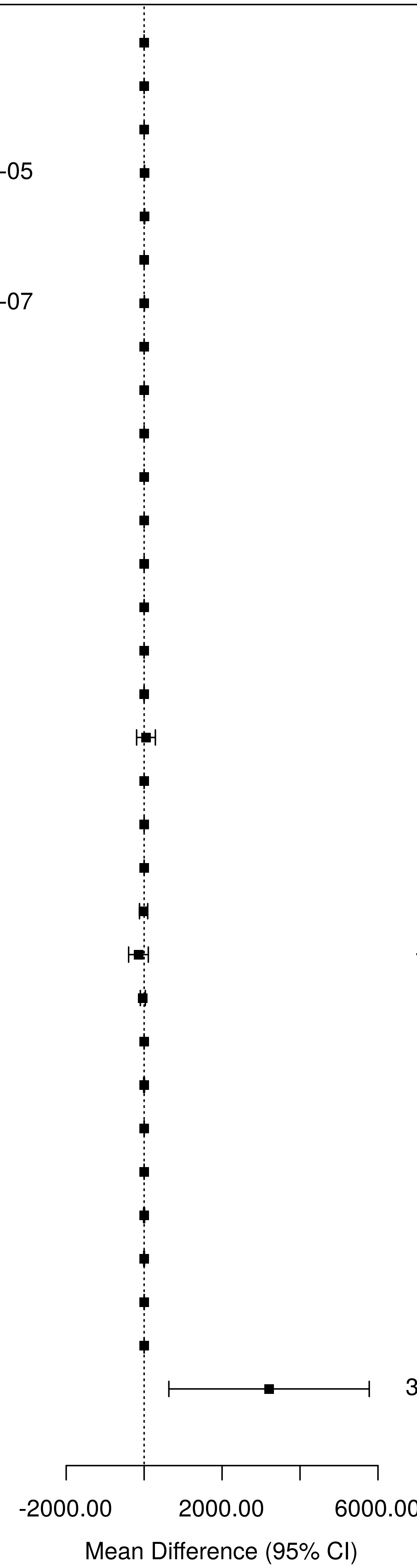
Vital signs (Risk Ratio)

	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I²	Effect p-value	Risk Ratio (95% CI)
Body mass index, normal	Temporal	19	1	504/950	143/282	-	0.4948	1.05 [0.92, 1.19]
Body mass index, obese	Temporal	19	1	108/950	32/282	-	0.9923	1.00 [0.69, 1.45]
Body mass index, overweight	Temporal	19	1	309/950	99/282	-	0.4142	0.93 [0.77, 1.11]
Body mass index, underweight	Temporal	19	1	30/950	8/282	-	0.7845	1.11 [0.52, 2.40]



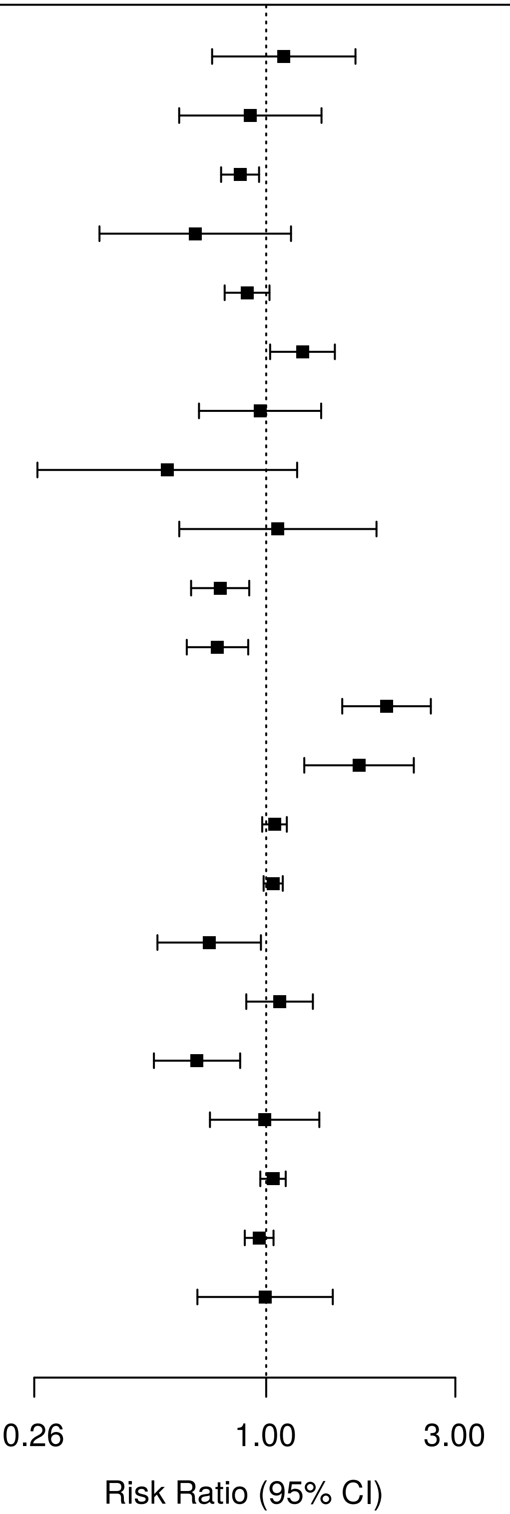
Biomarkers

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	Mean Difference (95% CI)
Albumin	g/dL	Temporal	2	1	25	25	-	0.4795	-0.10 [-0.38, 0.18]
Calcium	mg/dL	Temporal	1 to 2	2	230	230	0.0%	0.0765	-0.09 [-0.19, 0.01]
Chloride	mEq/L	Temporal	1	1	205	205	-	1.0000	0.00 [-0.59, 0.59]
Cortisol, salivary	-	Temporal	3	1	28	30	-	5.8733e-05	7.54 [3.86, 11.21]
C-reactive protein	mg/dL	Geographical	36	1	14	16	-	0.0651	7.00 [-0.44, 14.44]
Creatinine, declining rate of 1/Cr	dL/mg/week	Geographical	36	1	14	16	-	0.0042	0.24 [0.08, 0.40]
Creatinine	mg/dL	Geographical	36	1	14	16	-	8.0622e-07	5.30 [3.19, 7.41]
Creatinine	mg/dL	Temporal	1 to 6	3	452	452	0.0%	0.9887	0.00 [-0.04, 0.04]
Free T3	pg/mL	Temporal	2	1	207	207	-	0.8567	-0.04 [-0.52, 0.43]
Free T4	ng/mL	Temporal	2	1	207	207	-	0.3250	-0.07 [-0.22, 0.07]
Glucose, plasma, random	mmol/L	Temporal	3	1	320	320	-	0.0933	0.53 [-0.09, 1.15]
Glycated haemoglobin	%	Temporal	2 to 12	4	716	717	33.3%	0.0008	0.16 [0.07, 0.25]
Haemoglobin	g/dL	Temporal	1 to 2	2	230	230	0.0%	0.0352	-0.19 [-0.37, -0.01]
HDL cholesterol	mg/dL	Temporal	3 to 14	4	4,641	4,642	5.8%	0.5993	-0.21 [-1.01, 0.58]
Heart rate	beats/min	Temporal	2 to 79	2	307	710	0.0%	0.2684	-0.92 [-2.55, 0.71]
LDL cholesterol	mg/dL	Temporal	3 to 12	3	606	607	0.0%	0.4697	-1.19 [-4.42, 2.04]
Myeloperoxidase-antineutrophil cytoplasmic autoantibody	U/mL	Geographical	36	1	14	16	-	0.6960	48.00 [-192.77, 288.77]
Phosphorus	mg/dL	Temporal	1 to 2	2	230	230	0.0%	0.0424	0.20 [0.01, 0.39]
Potassium	mEq/L	Temporal	1	1	205	205	-	0.1204	0.10 [-0.03, 0.23]
Sodium	mEq/L	Temporal	1	1	205	205	-	1.0000	0.00 [-0.51, 0.51]
Thyroglobulin antibody	U/mL	Temporal	2	1	138	138	-	0.8028	-13.41 [-118.60, 91.79]
Thyroid peroxidase antibody	U/mL	Temporal	2	1	138	138	-	0.2604	-145.08 [-397.73, 107.57]
Thyroid stimulating antibody	%	Temporal	2	1	207	207	-	0.3010	-33.68 [-97.50, 30.14]
Thyroid stimulating hormone	µIU/mL	Temporal	2	1	207	207	-	0.6377	-0.39 [-2.03, 1.24]
Thyrotropin receptor antibody	IU/L	Temporal	2	1	207	207	-	0.8392	-1.08 [-11.48, 9.32]
Total cholesterol	mg/dL	Temporal	3 to 79	5	4,743	5,147	21.9%	0.4537	0.83 [-1.35, 3.02]
Total protein	g/dL	Temporal	1	1	205	205	-	0.0360	0.10 [0.01, 0.19]
Triglycerides	mg/dL	Temporal	3 to 79	4	708	1,112	58.8%	0.9014	-0.77 [-12.98, 11.44]
Urea nitrogen	mg/dL	Temporal	2	1	25	25	-	0.8365	-0.90 [-9.45, 7.65]
Urea	mg/dL	Temporal	1	1	205	205	-	0.4329	1.10 [-1.65, 3.85]
Uric acid	mg/dL	Temporal	1 to 14	2	4,240	4,240	68.1%	0.7469	0.04 [-0.19, 0.27]
White blood cells	count/µL	Geographical	36	1	14	16	-	0.0145	3205.00 [634.42, 5775.58]



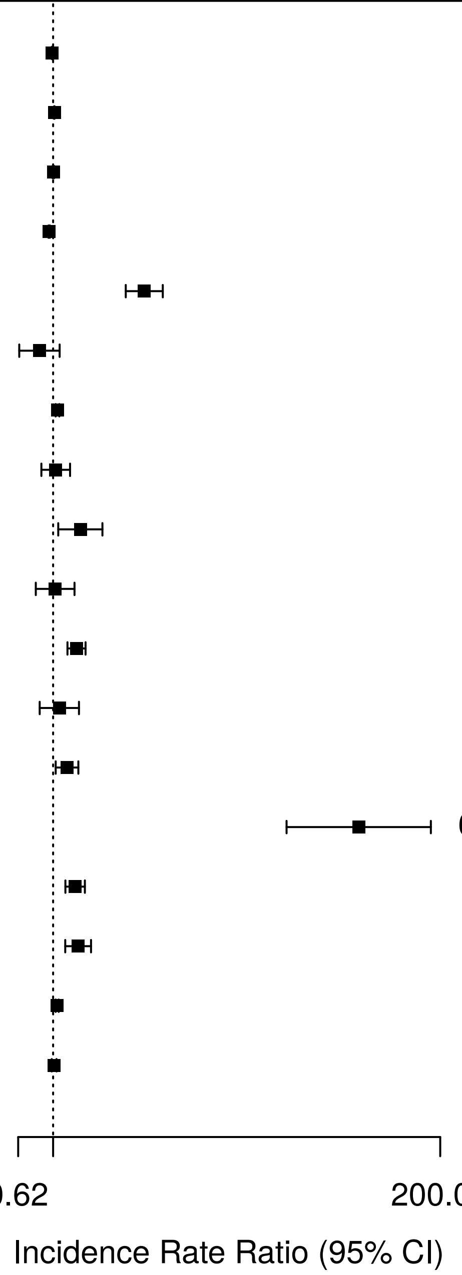
Lifestyle & prevention

	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I²	Effect p-value	Risk Ratio (95% CI)
Alcohol, abuse/dependence	Geographical	24	1	50/543	34/409	-	0.6302	1.11 [0.73, 1.68]
Alcohol, outside meals	Temporal	19	1	83/947	27/281	-	0.6628	0.91 [0.60, 1.38]
Alcohol, past-30-day drinking	Temporal	19	1	501/947	173/281	-	0.0070	0.86 [0.77, 0.96]
Alcohol, regular excessive consumption	Temporal	19	1	38/945	17/280	-	0.1465	0.66 [0.38, 1.16]
Daily fruit & vegetables consuption, 1-2 portions	Temporal	19	1	447/955	148/283	-	0.0950	0.90 [0.79, 1.02]
Daily fruit & vegetables consuption, 3-4 portions	Temporal	19	1	375/955	90/283	-	0.0279	1.23 [1.02, 1.49]
Daily fruit & vegetables consuption, 5+ portions	Temporal	19	1	114/955	35/283	-	0.8449	0.97 [0.68, 1.38]
Daily fruit & vegetables consuption, no portions	Temporal	19	1	19/955	10/283	-	0.1355	0.56 [0.26, 1.20]
Illicit drugs, abuse/dependence	Geographical	24	1	27/543	19/409	-	0.8160	1.07 [0.60, 1.90]
Physical activity, active	Temporal	19	1	301/943	113/271	-	0.0019	0.77 [0.65, 0.91]
Physical activity, partly active	Temporal	19	1	278/943	106/271	-	0.0019	0.75 [0.63, 0.90]
Physical activity, sedentaty behaviour	Temporal	19	1	364/943	52/271	-	1.0080e-07	2.01 [1.56, 2.60]
Smoking, abuse/dependence	Geographical	24	1	107/543	47/409	-	0.0009	1.71 [1.25, 2.36]
Smoking ban, compliance at workplace	Temporal	19	1	482/548	150/179	-	0.1843	1.05 [0.98, 1.13]
Smoking ban, compliance in public places	Temporal	19	1	782/889	239/283	-	0.1509	1.04 [0.99, 1.10]
Smoking, cessation attempt	Temporal	19	1	95/316	36/86	-	0.0309	0.72 [0.53, 0.97]
Smoking, current	Temporal	19	1	325/956	89/283	-	0.4299	1.08 [0.89, 1.31]
Smoking, former	Temporal	19	1	156/956	69/283	-	0.0017	0.67 [0.52, 0.86]
Smoking, physician cessation advice	Temporal	19	1	56/113	29/58	-	0.9562	0.99 [0.72, 1.36]
Traffic injury prevention, use of front seat belt	Temporal	19	1	750/951	213/281	-	0.2927	1.04 [0.97, 1.12]
Traffic injury prevention, use of motorbike helmet	Temporal	19	1	183/206	62/67	-	0.3377	0.96 [0.88, 1.04]
Traffic injury prevention, use of rear seat belt	Temporal	19	1	109/845	27/208	-	0.9750	0.99 [0.67, 1.47]



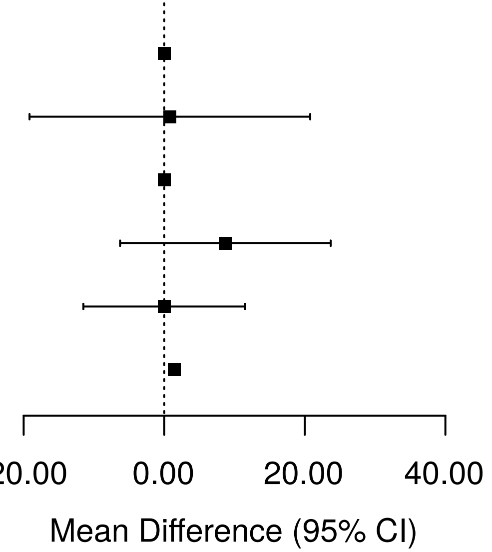
Pharmacology (Incidence Rate Ratio)

	Comparison	Follow-up (months)	Studies	Exposed Events/Person-years	Unexposed Events/Person-years	I²	Effect p-value	Incidence Rate Ratio (95% CI)
Anti-depressants, other	Temporal	11	1	194,732/275,590	215,030/300,818	-	0.0002	0.99 [0.98, 0.99]
Anti-depressants, serotonin reuptake inhibitors	Temporal	11	1	518,236/275,590	556,427/300,818	-	1.3524e-17	1.02 [1.01, 1.02]
Anti-depressants	Temporal	11	1	75,890/275,590	82,615/300,819	-	0.5931	1.00 [0.99, 1.01]
Anti-depressants, tryciclics	Temporal	11	1	81,998/275,590	94,447/300,818	-	2.0293e-29	0.95 [0.94, 0.96]
Anti-psychotics, Amilsulpride	Temporal	1	1	268/25,054	77/25,068	-	4.9081e-22	3.48 [2.70, 4.49]
Anti-psychotics, Aripiprazole	Temporal	1	1	92/25,054	111/25,068	-	0.1844	0.83 [0.63, 1.09]
Anti-psychotics, atypical	Temporal	11	1	11,923/275,590	12,261/300,818	-	3.5421e-06	1.06 [1.04, 1.09]
Anti-psychotics, Chlorpromazine	Temporal	1	1	203/25,054	196/25,068	-	0.7217	1.04 [0.85, 1.26]
Anti-psychotics, Clotiapine	Temporal	1	1	103/25,054	71/25,068	-	0.0157	1.45 [1.07, 1.96]
Anti-psychotics, Clozapine	Temporal	1	1	111/25,054	108/25,068	-	0.8360	1.03 [0.79, 1.34]
Anti-psychotics, Haloperidol	Temporal	1	1	596/25,054	433/25,068	-	3.9997e-07	1.38 [1.22, 1.56]
Anti-psychotics, Levomeprazine	Temporal	1	1	111/25,054	102/25,068	-	0.5348	1.09 [0.83, 1.42]
Anti-psychotics, Olanzapine	Temporal	1	1	353/25,054	292/25,068	-	0.0161	1.21 [1.04, 1.41]
Anti-psychotics, Promazine	Temporal	1	1	262/25,054	4/25,068	-	1.0227e-16	65.54 [24.41, 175.93]
Anti-psychotics, Quetiapine	Temporal	1	1	508/25,054	376/25,068	-	9.3605e-06	1.35 [1.18, 1.54]
Anti-psychotics, Risperidone	Temporal	1	1	297/25,054	211/25,068	-	0.0001	1.41 [1.18, 1.68]
Anti-psychotics	Temporal	11	1	17,445/275,590	18,012/300,819	-	1.6512e-07	1.06 [1.04, 1.08]
Anti-psychotics, typical	Temporal	11	1	6,950/275,590	7,481/300,818	-	0.4019	1.01 [0.98, 1.05]



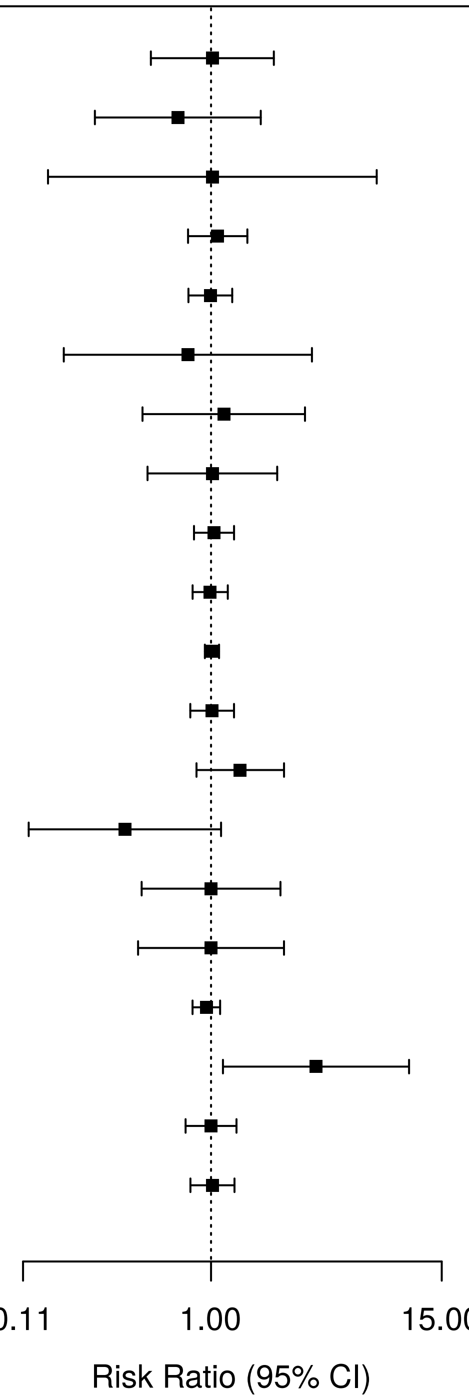
Pharmachology (Mean Difference)

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	Mean Difference (95% CI)
Anti-diabetic drugs, insulin	U/kg/day	Temporal	12	1	64	65	-	0.8393	0.01 [-0.09, 0.11]
Ccyclophosphamide, initial dose	mg/day	Geographical	36	1	14	16	-	0.9374	0.80 [-19.17, 20.77]
Haemodialisis adequacy (Kt/V)	-	Temporal	2	1	25	25	-	1.0000	0.00 [-0.14, 0.14]
Prednisolone, initial dose	mg/day	Geographical	36	1	14	16	-	0.2550	8.70 [-6.28, 23.68]
Propylthiouracil	mg/day	Temporal	2	1	76	76	-	1.0000	0.00 [-11.50, 11.50]
Pulse methylprednisolone, courses	-	Geographical	36	1	14	16	-	3.0812e-05	1.40 [0.74, 2.06]

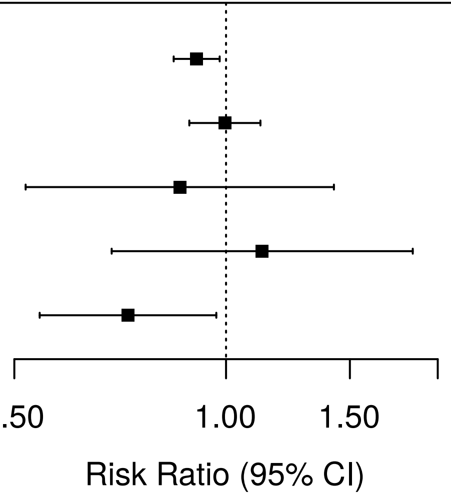


Pharmachology (Risk Ratio)

	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I²	Effect p-value	
Anti-diabetic drugs, insulin, continuous subcutaneous rapid infusion	Temporal	12	1	12/64	12/65	-	0.9664	1.02 [0.49, 2.09]
Anti-diabetic drugs, insulin, multiple (four times) daily injections, rapid and intermediate	Temporal	12	1	6/64	9/65	-	0.4324	0.68 [0.26, 1.79]
Anti-diabetic drugs, insulin, multiple (four times) daily injections, short and/or intermediate	Temporal	12	1	2/64	2/65	-	0.9874	1.02 [0.15, 6.99]
Anti-diabetic drugs, insulin, multiple (four times) daily injectionss, rapid and long	Temporal	12	1	33/64	31/65	-	0.6605	1.08 [0.76, 1.53]
Anti-diabetic drugs, insulin, multiple (four times) daily injections	Temporal	12	1	41/64	42/65	-	0.9477	0.99 [0.77, 1.28]
Anti-diabetic drugs, insulin, twice daily injections, rapid and intermediate mixed	Temporal	12	1	3/64	4/65	-	0.7142	0.76 [0.18, 3.27]
Anti-diabetic drugs, insulin, twice daily injections, short and/or intermediate mixed	Temporal	12	1	8/64	7/65	-	0.7594	1.16 [0.45, 3.01]
Anti-diabetic drugs, insulin, twice daily injections	Temporal	12	1	11/64	11/65	-	0.9682	1.02 [0.47, 2.17]
Anti-diabetic drugs, oral and insulin	Temporal	6	1	87/222	84/222	-	0.7699	1.04 [0.82, 1.31]
Anti-diabetic drugs, oral	Temporal	6	1	99/222	100/222	-	0.9240	0.99 [0.81, 1.22]
Anti-diabetic drugs	Temporal	6	1	186/222	184/222	-	0.7990	1.01 [0.93, 1.10]
Anti-hypertensive drugs, alpha-blocker	Temporal	6	1	77/222	76/222	-	0.9205	1.01 [0.78, 1.31]
Anti-hypertensive drugs, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers, or calcium channel blockers with diuretics	Temporal	6	1	31/222	22/222	-	0.1907	1.41 [0.84, 2.36]
Anti-hypertensive drugs, angiotensin-converting enzyme inhibitors	Temporal	6	1	4/222	11/222	-	0.0791	0.36 [0.12, 1.12]
Anti-hypertensive drugs, angiotensin receptor blockers	Temporal	6	1	11/222	11/222	-	1.0000	1.00 [0.44, 2.26]
Anti-hypertensive drugs, calcium channel blockers	Temporal	6	1	10/222	10/222	-	1.0000	1.00 [0.42, 2.36]
Anti-hypertensive drugs	Temporal	6	1	123/222	130/222	-	0.5025	0.95 [0.80, 1.11]
Haemodialisis, emergency	Geographical	36	1	9/14	3/16	-	0.0270	3.43 [1.15, 10.22]
Iodine-131	Temporal	2	1	54/145	54/145	-	1.0000	1.00 [0.74, 1.35]
Thionamide	Temporal	2	1	61/128	60/128	-	0.9004	1.02 [0.78, 1.32]

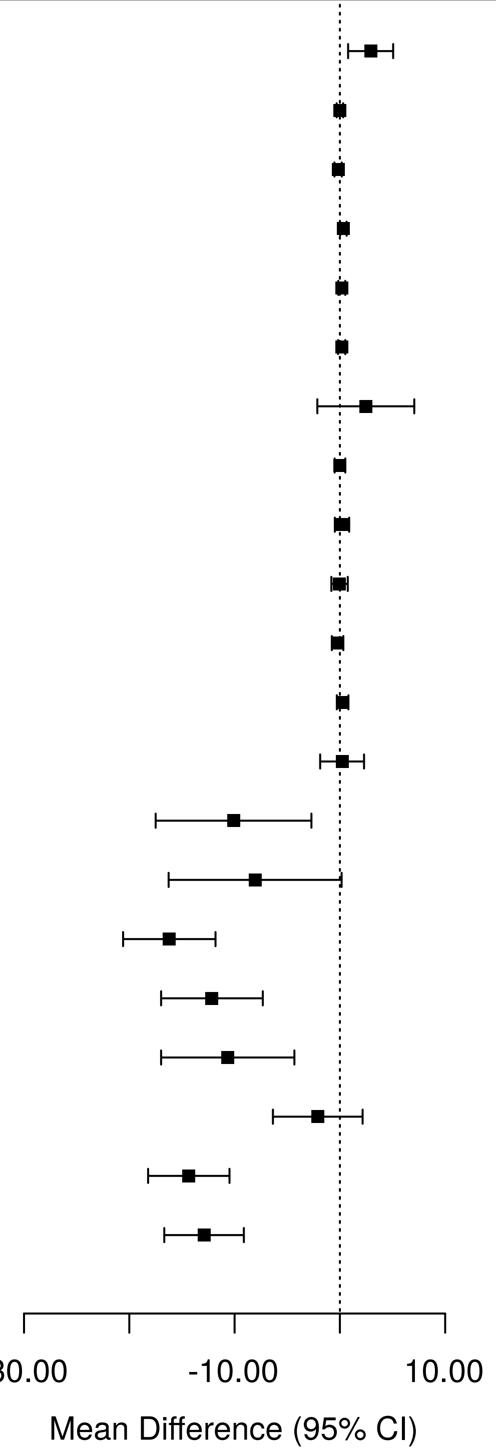


Screening

	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I^2	Effect p-value		
Blood pressure test	Temporal	19	1	672/956	219/283	-	0.0123		0.91 [0.84, 0.98]
Cholesterol test	Temporal	19	1	539/957	160/283	-	0.9488		1.00 [0.89, 1.12]
Colonoscopy	Temporal	19	1	51/370	17/106	-	0.5564		0.86 [0.52, 1.42]
Mammography	Temporal	19	1	58/184	14/50	-	0.6375		1.13 [0.69, 1.84]
Pap test	Temporal	19	1	113/405	40/104	-	0.0296		0.73 [0.54, 0.97]

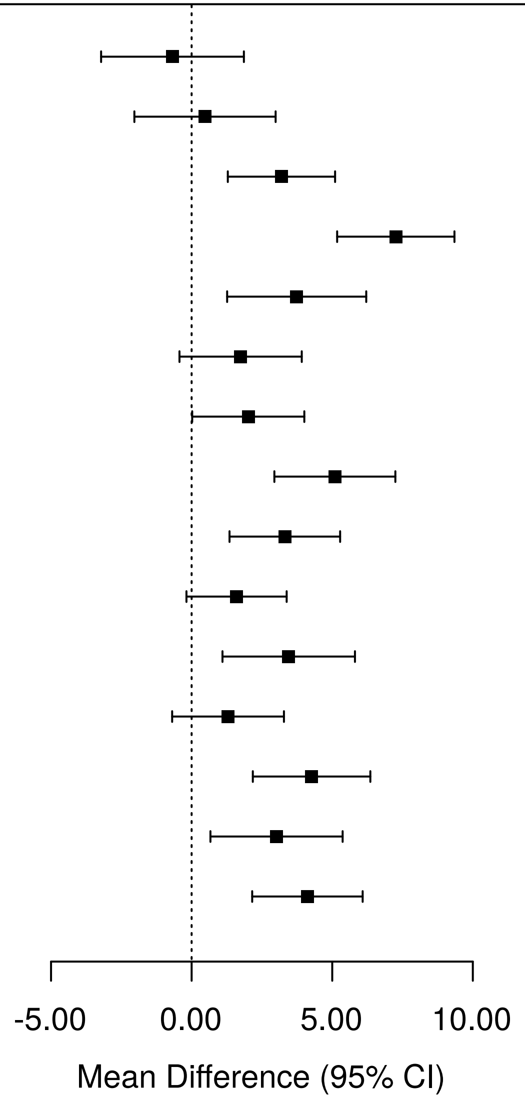
Psychometric scales, Children

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	Mean Difference (95% CI)
Children’s Depression Inventory	-	Geographical	6	1	115	48	-	0.0075	2.92 [0.78, 5.06]
Screen for Child Anxiety Related Emotional Disorders, Factor 1	-	Geographical	6	1	115	48	-	1.0000	0.00 [-0.31, 0.31]
Screen for Child Anxiety Related Emotional Disorders, Factor 2	-	Geographical	6	1	115	48	-	0.3368	-0.17 [-0.52, 0.18]
Screen for Child Anxiety Related Emotional Disorders, Factor 3	-	Geographical	6	1	115	48	-	0.0348	0.33 [0.02, 0.64]
Screen for Child Anxiety Related Emotional Disorders, Factor 4	-	Geographical	6	1	115	48	-	0.2895	0.18 [-0.15, 0.51]
Screen for Child Anxiety Related Emotional Disorders, Factor 5	-	Geographical	6	1	115	48	-	0.3334	0.17 [-0.17, 0.51]
Screen for Child Anxiety Related Emotional Disorders, Total score	-	Geographical	6	1	115	48	-	0.2949	2.46 [-2.14, 7.06]
Strengths and Difficulties Questionnaire, Conduct problems score	-	Geographical	6	1	115	36	-	0.9691	0.01 [-0.50, 0.52]
Strengths and Difficulties Questionnaire, Emotional symptoms score	-	Geographical	6	1	115	36	-	0.5654	0.20 [-0.48, 0.88]
Strengths and Difficulties Questionnaire, Hyperactivity score	-	Geographical	6	1	115	36	-	0.9398	-0.03 [-0.81, 0.75]
Strengths and Difficulties Questionnaire, Peer problems score	-	Geographical	6	1	115	36	-	0.4325	-0.22 [-0.77, 0.33]
Strengths and Difficulties Questionnaire, Prosocial score	-	Geographical	6	1	115	36	-	0.3558	0.26 [-0.29, 0.81]
Strengths and Difficulties Questionnaire, Total difficulties	-	Geographical	6	1	115	36	-	0.8434	0.21 [-1.87, 2.29]
Vineland Adaptive Behaviour Scales, Communication	-	Geographical	12	1	18	18	-	0.0074	-10.10 [-17.50, -2.70]
Vineland Adaptive Behaviour Scales, Communication	-	Temporal	12	1	18	18	-	0.0548	-8.05 [-16.27, 0.17]
Vineland Adaptive Behaviour Scales, Daily Living	-	Geographical	12	1	18	18	-	4.6349e-13	-16.20 [-20.59, -11.81]
Vineland Adaptive Behaviour Scales, Daily Living	-	Temporal	12	1	18	18	-	8.1598e-07	-12.15 [-16.98, -7.32]
Vineland Adaptive Behaviour Scales, Motor Skills	-	Geographical	12	1	18	18	-	0.0010	-10.65 [-16.98, -4.32]
Vineland Adaptive Behaviour Scales, Motor Skills	-	Temporal	12	1	18	18	-	0.3337	-2.10 [-6.36, 2.16]
Vineland Adaptive Behaviour Scales, Socialisation	-	Geographical	12	1	18	18	-	3.3819e-13	-14.35 [-18.21, -10.49]
Vineland Adaptive Behaviour Scales, Socialisation	-	Temporal	12	1	18	18	-	2.2391e-11	-12.90 [-16.68, -9.12]



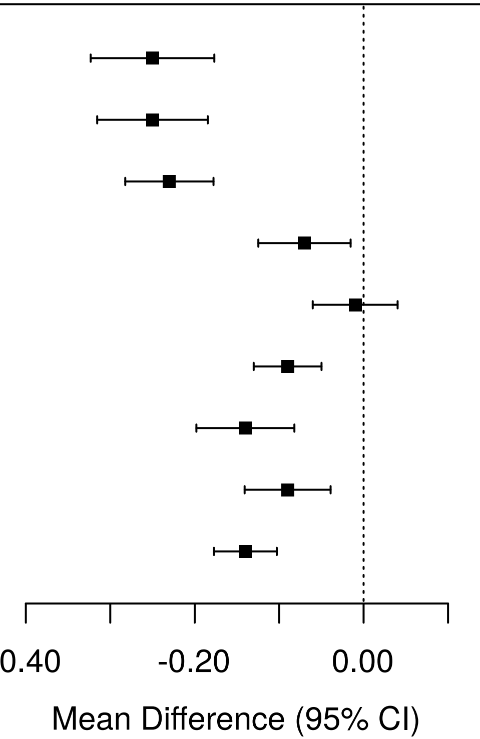
Psychometric scales, Minnesota Multiphasic Personality Inventory-Adolescent

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I^2	Effect p-value	Mean Difference (95% CI)
MMPI-A, Adolescent-Negative Treatment Indicators	-	Temporal	11	1	149	179	-	0.5994	-0.68 [-3.22, 1.86]
MMPI-A, Alienation	-	Temporal	11	1	149	179	-	0.7107	0.48 [-2.04, 2.99]
MMPI-A, Anger	-	Temporal	11	1	149	179	-	0.0010	3.19 [1.29, 5.10]
MMPI-A, Anxiety	-	Temporal	11	1	149	179	-	8.9411e-12	7.26 [5.17, 9.35]
MMPI-A, Bizarre Mentation	-	Temporal	11	1	149	179	-	0.0031	3.74 [1.26, 6.21]
MMPI-A, Conduct Problems	-	Temporal	11	1	149	179	-	0.1164	1.74 [-0.43, 3.92]
MMPI-A, Cynism	-	Temporal	11	1	149	179	-	0.0477	2.01 [0.02, 4.01]
MMPI-A, Depression	-	Temporal	11	1	149	179	-	3.4729e-06	5.09 [2.94, 7.24]
MMPI-A, Family Problems	-	Temporal	11	1	149	179	-	0.0010	3.31 [1.35, 5.28]
MMPI-A, Health Concerns	-	Temporal	11	1	149	179	-	0.0789	1.60 [-0.18, 3.38]
MMPI-A, Low Aspirations	-	Temporal	11	1	149	179	-	0.0041	3.45 [1.10, 5.81]
MMPI-A, Low Self-Esteem	-	Temporal	11	1	149	179	-	0.2017	1.30 [-0.69, 3.28]
MMPI-A, Obsessiveness	-	Temporal	11	1	149	179	-	6.3193e-05	4.27 [2.18, 6.36]
MMPI-A, School Problems	-	Temporal	11	1	149	179	-	0.0118	3.02 [0.67, 5.37]
MMPI-A, Social Discomfort	-	Temporal	11	1	149	179	-	3.9815e-05	4.12 [2.15, 6.08]



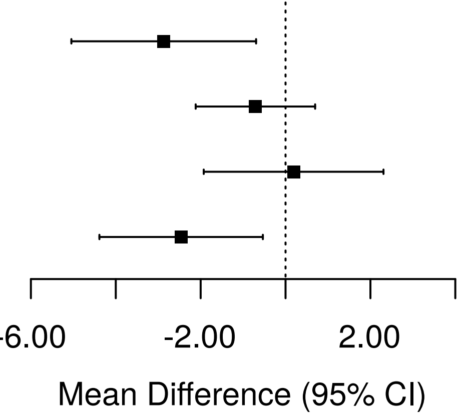
Psychometric scales, Community Assessment of Psychic Experiences

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	Mean Difference (95% CI)
CAPE, Distress, Depressive Dimension	SD change	Temporal	10	1	419	1,057	-	2.2102e-11	-0.25 [-0.32, -0.18]
CAPE, Distress, Negative Dimension	SD change	Temporal	10	1	419	1,057	-	7.2347e-14	-0.25 [-0.32, -0.18]
CAPE, Distress, Positive Dimension	SD change	Temporal	10	1	419	1,057	-	6.1871e-18	-0.23 [-0.28, -0.18]
CAPE, Frequency, Depressive Dimension	SD change	Temporal	10	1	419	1,057	-	0.0120	-0.07 [-0.12, -0.02]
CAPE, Frequency, Negative Dimension	SD change	Temporal	10	1	419	1,057	-	0.6967	-0.01 [-0.06, 0.04]
CAPE, Frequency, Positive Dimension	SD change	Temporal	10	1	419	1,057	-	1.1199e-05	-0.09 [-0.13, -0.05]
CAPE, Overall scores, Depressive Dimension	SD change	Temporal	10	1	419	1,057	-	2.2608e-06	-0.14 [-0.20, -0.08]
CAPE, Overall scores, Negative Dimension	SD change	Temporal	10	1	419	1,057	-	0.0005	-0.09 [-0.14, -0.04]
CAPE, Overall scores, Positive Dimension	SD change	Temporal	10	1	419	1,057	-	1.6345e-13	-0.14 [-0.18, -0.10]



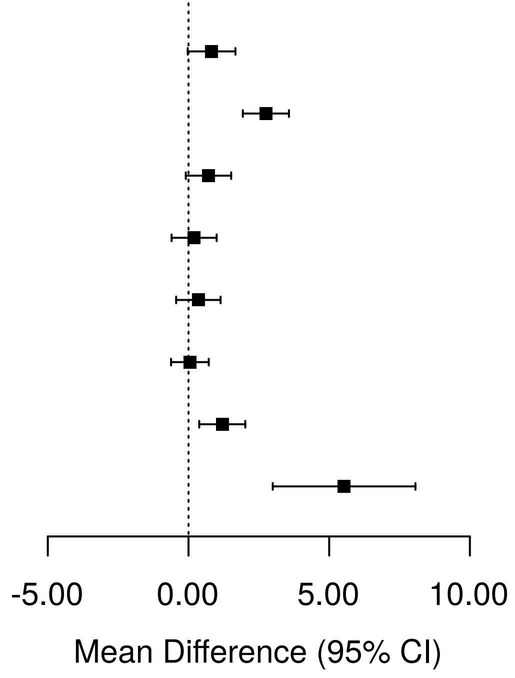
Psychometric scales, Coping Style Questionnaire

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	
CSQ, Avoidance	-	Geographical	3	1	52	29	-	0.0097	-2.87 [-5.05, -0.69]
CSQ, Detached	-	Geographical	3	1	52	29	-	0.3227	-0.71 [-2.12, 0.70]
CSQ, Emotional	-	Geographical	3	1	52	29	-	0.8604	0.19 [-1.93, 2.31]
CSQ, Rational	-	Geographical	3	1	52	29	-	0.0123	-2.46 [-4.39, -0.53]



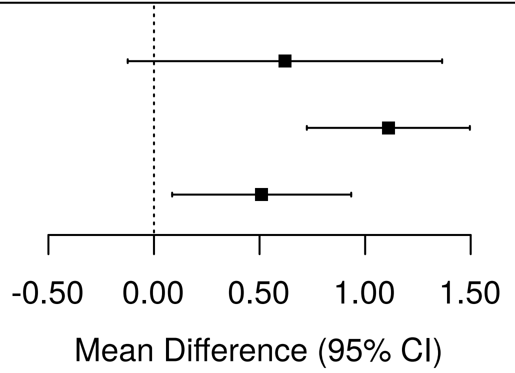
Psychometric scales, Crisis Support Scale

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I^2	Effect p-value	Mean Difference (95% CI)
CSS, Ability to express oneself	-	Geographical	3	1	52	29	-	0.0579	0.82 [-0.03, 1.67]
CSS, Contact with others in similar situation	-	Geographical	3	1	52	29	-	4.6594e-11	2.75 [1.93, 3.57]
CSS, Feeling let down	-	Geographical	3	1	52	29	-	0.0845	0.71 [-0.10, 1.52]
CSS, Practical support	-	Geographical	3	1	52	29	-	0.6245	0.20 [-0.60, 1.00]
CSS, Receiving sympathy	-	Geographical	3	1	52	29	-	0.3849	0.35 [-0.44, 1.14]
CSS, Satisfaction with support	-	Geographical	3	1	52	29	-	0.8835	0.05 [-0.62, 0.72]
CSS, Someone willing to listen	-	Geographical	3	1	52	29	-	0.0041	1.20 [0.38, 2.02]
CSS, Sum of social support	-	Geographical	3	1	52	29	-	1.9069e-05	5.53 [2.99, 8.07]



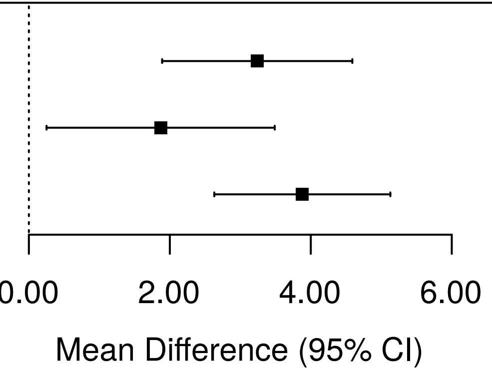
Psychometric scales, General Health Questionnaire

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	Mean Difference (95% CI)
GHQ, Sleep Disturbance or Anxiety	-	Geographical	2	2	314	554	88.4%	0.1026	0.62 [-0.12, 1.36]
GHQ, Social Dysfunction	-	Geographical	2	1	157	277	-	1.7488e-08	1.11 [0.72, 1.50]
GHQ, Somatic Symptoms	-	Geographical	2	1	157	277	-	0.0184	0.51 [0.09, 0.93]



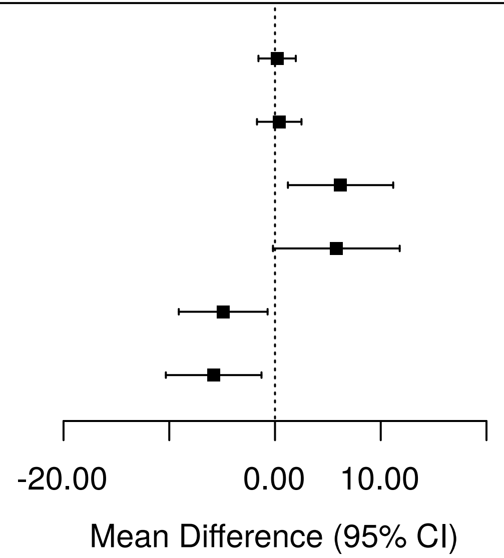
Psychometric scales, Harvard Trauma Questionnaire

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	Mean Difference (95% CI)
HTQ, Arousal	-	Geographical	3	1	52	29	-	2.5243e-06	3.24 [1.89, 4.59]
HTQ, Avoidance	-	Geographical	3	1	52	29	-	0.0236	1.87 [0.25, 3.49]
HTQ, Reexperiencing	-	Geographical	3	1	52	29	-	1.1336e-09	3.88 [2.63, 5.13]

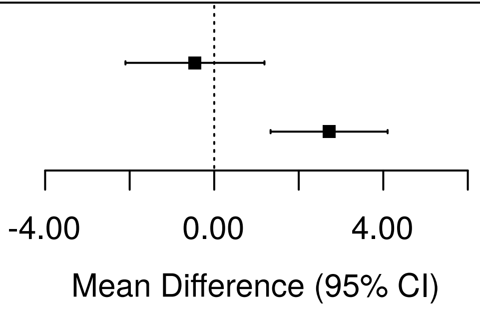


Psychometric scales, Human Services Survey - Maslach Burnout Inventory

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I^2	Effect p-value	Mean Difference (95% CI)
HSS-MBI, Depersonalization	-	Geographical	24	1	11	53	-	0.8244	0.20 [-1.57, 1.97]
HSS-MBI, Depersonalization	-	Temporal	24	1	11	11	-	0.7095	0.40 [-1.70, 2.50]
HSS-MBI, Emotional Exhaustion	-	Geographical	24	1	11	53	-	0.0146	6.20 [1.22, 11.18]
HSS-MBI, Emotional Exhaustion	-	Temporal	24	1	11	11	-	0.0579	5.80 [-0.19, 11.79]
HSS-MBI, Personal Accomplishment	-	Geographical	24	1	11	53	-	0.0222	-4.90 [-9.10, -0.70]
HSS-MBI, Personal Accomplishment	-	Temporal	24	1	11	11	-	0.0120	-5.80 [-10.32, -1.28]

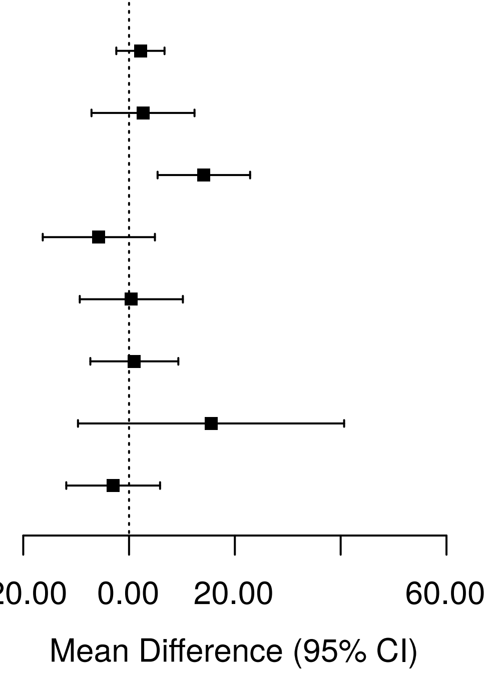


Psychometric scales, Positive and Negative Syndrome Scale

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I^2	Effect p-value		Mean Difference (95% CI)
PNSS, Negative symptoms	-	Temporal	3	1	101	117	-	0.5872		-0.46 [-2.10, 1.19]
PNSS, Positive symptoms	-	Temporal	3	1	101	117	-	0.0001		2.72 [1.33, 4.10]

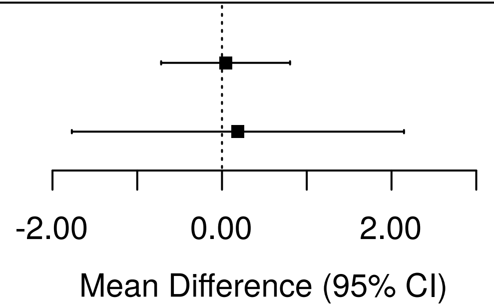
Psychometric scales, Profile of Mood States

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	Mean Difference (95% CI)
General Health Questionnaire score	-	Temporal	3	1	14	15	-	0.3552	2.15 [-2.41, 6.71]
POMS, Anger-Hostility score	-	Temporal	3	1	14	15	-	0.5951	2.64 [-7.10, 12.38]
POMS, Confusion score	-	Temporal	3	1	14	15	-	0.0015	14.14 [5.39, 22.89]
POMS, Depression-Dejection score	-	Temporal	3	1	14	15	-	0.2912	-5.71 [-16.31, 4.89]
POMS, Fatigue-Inertia score	-	Temporal	3	1	14	15	-	0.9311	0.43 [-9.32, 10.18]
POMS, Tension-Anxiety score	-	Temporal	3	1	14	15	-	0.8137	1.00 [-7.32, 9.32]
POMS, Total Mood Disturbance score	-	Temporal	3	1	14	15	-	0.2271	15.50 [-9.65, 40.65]
POMS, Vigour-Activity score	-	Temporal	3	1	14	15	-	0.5071	-3.00 [-11.86, 5.86]



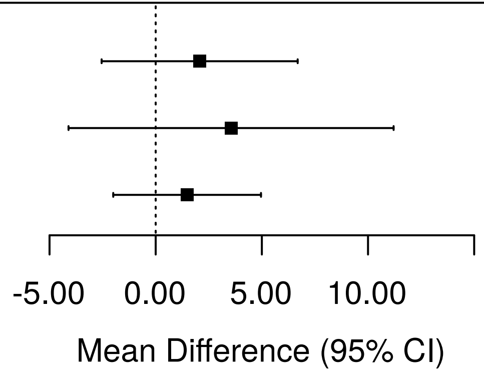
Psychometric scales, Rey Complex Figure Test

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	Mean Difference (95% CI)
RCFT, Copy	-	Temporal	3	1	101	117	-	0.9128	0.04 [-0.72, 0.80]
RCFT, Recall	-	Temporal	3	1	101	117	-	0.8510	0.19 [-1.77, 2.15]



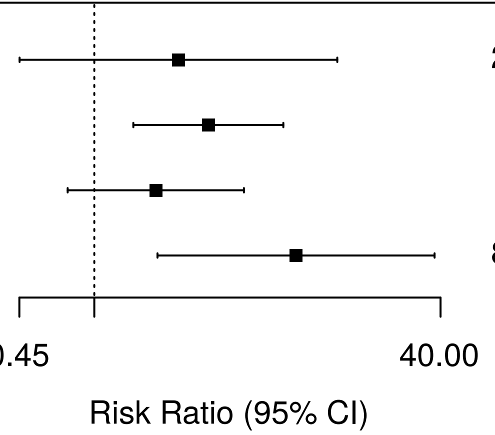
Psychometric scales, State and Trait Anxiety Inventory

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	Mean Difference (95% CI)
STAI, State	-	Geographical	6	1	115	36	-	0.3795	2.07 [-2.55, 6.69]
STAI, Total	-	Geographical	6	1	115	36	-	0.3634	3.55 [-4.11, 11.21]
STAI, Trait	-	Geographical	6	1	115	36	-	0.4045	1.48 [-2.00, 4.96]



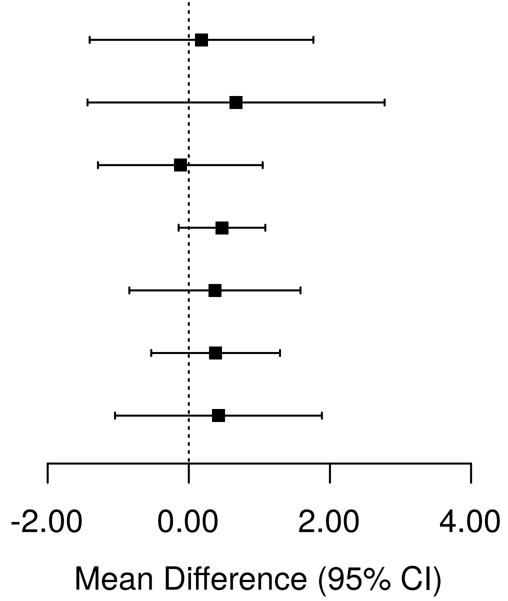
Psychometric scales, Trauma and Loss Spectrum-Self Report

	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I²	Effect p-value	Risk Ratio (95% CI)
TALS-SR, Attempt suicide	Geographical	12	1	4/426	2/522	-	0.2993	2.45 [0.45, 13.32]
TALS-SR, Endorsed any suicidal screening items	Geographical	12	1	22/426	8/522	-	0.0029	3.37 [1.52, 7.49]
TALS-SR, Intentionally scratch, cut, burn or hurt 11 yoursel	Geographical	12	1	11/426	7/522	-	0.1714	1.93 [0.75, 4.92]
TALS-SR, Think about ending your life	Geographical	12	1	14/426	2/522	-	0.0043	8.58 [1.96, 37.53]



Psychometric scales, Trauma Symptom Checklist

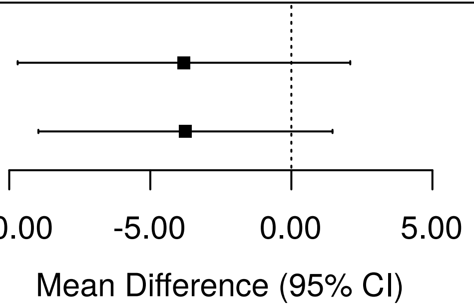
	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I^2	Effect p-value	Mean Difference (95% CI)
TSC, Anxiety	-	Geographical	3	1	52	29	-	0.8239	0.18 [-1.41, 1.77]
TSC, Depression	-	Geographical	3	1	52	29	-	0.5327	0.67 [-1.44, 2.78]
TSC, Dissociation	-	Geographical	3	1	52	29	-	0.8403	-0.12 [-1.29, 1.05]
TSC, Hostility	-	Geographical	3	1	52	29	-	0.1337	0.47 [-0.14, 1.08]
TSC, Interp. Prob.	-	Geographical	3	1	52	29	-	0.5499	0.37 [-0.84, 1.58]
TSC, Sleep problems	-	Geographical	3	1	52	29	-	0.4143	0.38 [-0.53, 1.29]
TSC, Somatization	-	Geographical	3	1	52	29	-	0.5744	0.42 [-1.05, 1.89]



Supplementary Materials 4. Full results of all earthquake effects

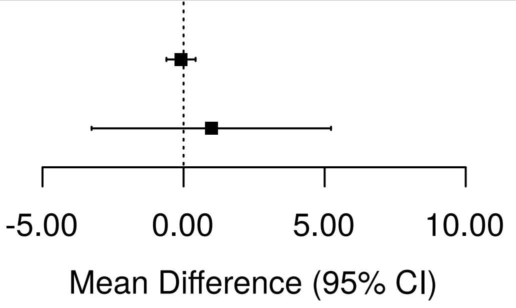
Psychometric scales, Wechsler Memory Scale-Revised

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	Mean Difference (95% CI)
IWMS-R, Immediate	-	Temporal	3	1	101	117	-	0.2055	-3.81 [-9.70, 2.09]
WMS-R, Delayed	-	Temporal	3	1	101	117	-	0.1581	-3.75 [-8.97, 1.46]



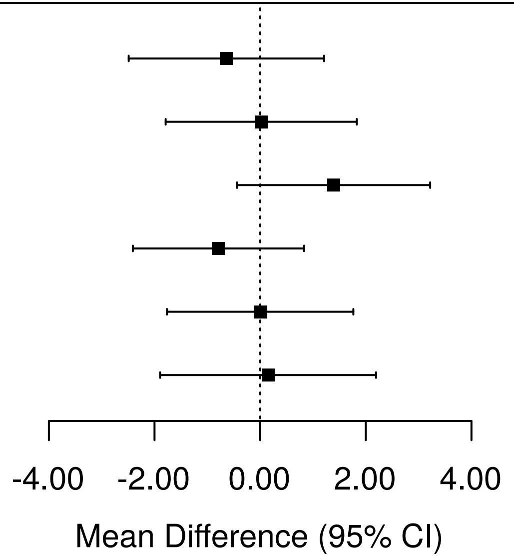
Psychometric scales, Wisconsin Card Sorting Test

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	Mean Difference (95% CI)
WCST, Categories	-	Temporal	3	1	101	117	-	0.7295	-0.09 [-0.61, 0.43]
WCST, Perseverative Errors	-	Temporal	3	1	101	117	-	0.6498	0.98 [-3.26, 5.23]



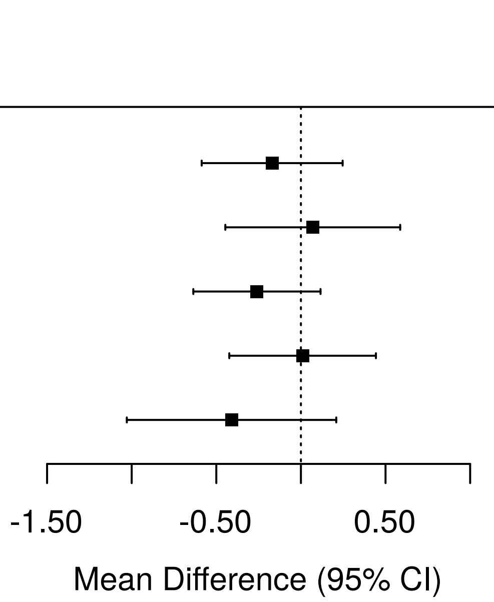
Psychometric scales, World Assumption Scale

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	Mean Difference (95% CI)
WAS, Benevolence of World	-	Geographical	3	1	52	29	-	0.4975	-0.64 [-2.49, 1.21]
WAS, Control	-	Geographical	3	1	52	29	-	0.9827	0.02 [-1.79, 1.83]
WAS, Luck	-	Geographical	3	1	52	29	-	0.1362	1.39 [-0.44, 3.22]
WAS, Randomness	-	Geographical	3	1	52	29	-	0.3394	-0.79 [-2.41, 0.83]
WAS, Self-control	-	Geographical	3	1	52	29	-	1.0000	0.00 [-1.76, 1.76]
WAS, Self-worth	-	Geographical	3	1	52	29	-	0.8856	0.15 [-1.89, 2.19]



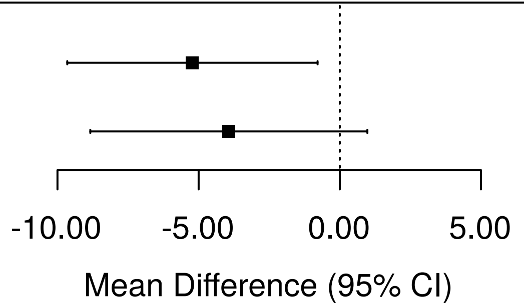
Psychometric scales, World Health Organization Quality of Life 26

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I^2	Effect p-value	Mean Difference (95% CI)
WHO-QOL26, Environmental functioning	-	Temporal	3	1	14	15	-	0.4237	-0.17 [-0.59, 0.25]
WHO-QOL26, Global functioning	-	Temporal	3	1	14	15	-	0.7906	0.07 [-0.45, 0.59]
WHO-QOL26, Physical functioning	-	Temporal	3	1	14	15	-	0.1752	-0.26 [-0.64, 0.12]
WHO-QOL26, Psychological functioning	-	Temporal	3	1	14	15	-	0.9639	0.01 [-0.42, 0.44]
WHO-QOL26, Social relationship	-	Temporal	3	1	14	15	-	0.1940	-0.41 [-1.03, 0.21]



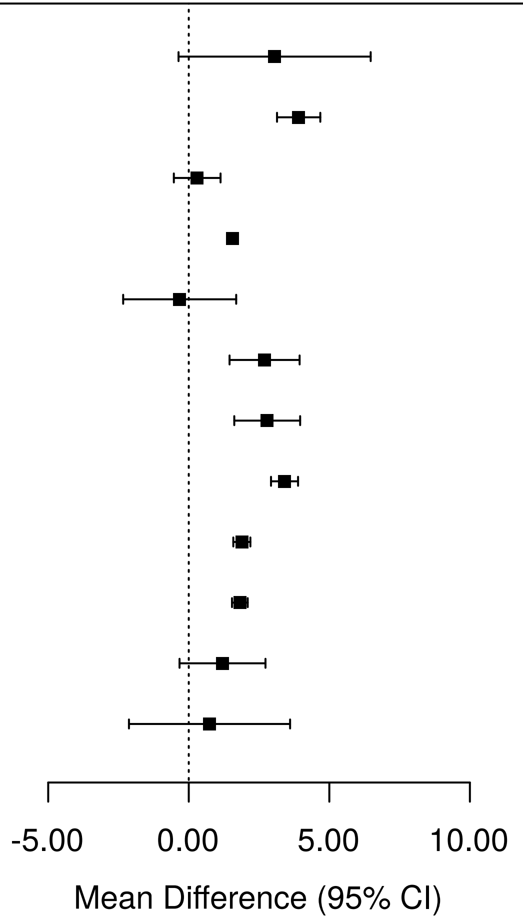
Psychometric scales, World Health Organization Subjective Well-being Inventory

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	Mean Difference (95% CI)
WHO-SUBI, Negative score	-	Temporal	3	1	14	15	-	0.0210	-5.22 [-9.65, -0.79]
WHO-SUBI, Positive score	-	Temporal	3	1	14	15	-	0.1165	-3.93 [-8.84, 0.98]



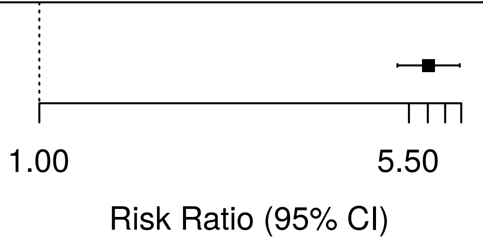
Psychometric scales, Others (Mean Difference)

	Unit	Comparison	Follow-up (months)	Studies	Exposed Participants	Unexposed Participants	I²	Effect p-value	
Acute Stress Disorder Scale	-	Geographical	2	1	168	177	-	0.0799	3.05 [-0.36, 6.47]
Beck Depression Inventory	-	Geographical	24	1	665	486	-	2.4729e-23	3.91 [3.14, 4.68]
Depression Self-Rating Scale	-	Geographical	3	1	1,685	252	-	0.4790	0.30 [-0.53, 1.13]
Difficulty falling or remaining asleep, continuous	-	Temporal	4	1	2,520	2,520	-	9.1795e-186	1.55 [1.45, 1.66]
Early information processing (digit span)	-	Temporal	3	1	101	117	-	0.7528	-0.32 [-2.33, 1.69]
Generalized Anxiety Disorder-7	-	Geographical	2	1	168	177	-	2.2145e-05	2.70 [1.45, 3.94]
Patient Health Questionnaire-9	-	Geographical	2	1	168	177	-	3.0571e-06	2.79 [1.62, 3.96]
Pittsburgh Sleep Quality Index-Addendum	-	Geographical	24	1	665	486	-	7.6300e-44	3.41 [2.93, 3.89]
Pittsburgh Sleep Quality Index	-	Geographical	24	1	665	486	-	3.9782e-34	1.89 [1.58, 2.19]
Pittsburgh Sleep Quality Index	-	Temporal	24	1	665	754	-	3.1284e-37	1.82 [1.54, 2.10]
Posttraumatic Stress Disorder Reaction Index	-	Geographical	3	1	1,685	252	-	0.1239	1.20 [-0.33, 2.73]
Visual attention (Continuous Performance Test)	-	Temporal	3	1	101	117	-	0.6136	0.74 [-2.13, 3.60]



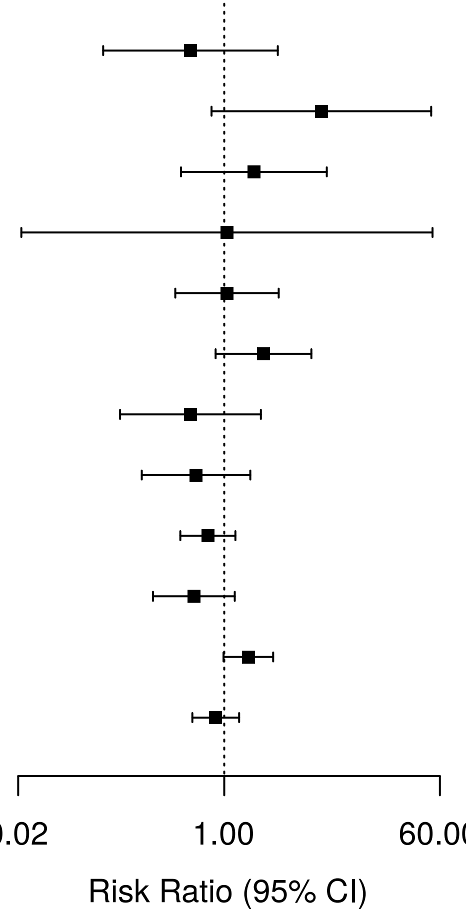
Psychometric scales, Others (Risk Ratio)

	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I²	Effect p-value	Risk Ratio (95% CI)
Difficulty falling or remaining asleep, binary	Temporal	4	1	1,138/2,520	189/2,520	-	2.1372e-132	6.02 [5.22, 6.95]



Cognitions and Superordinate Themes

	Comparison	Follow-up (months)	Studies	Exposed Events/Participants	Unexposed Events/Participants	I²	Effect p-value	Risk Ratio (95% CI)
Cognitions, Appeal to external forces	Geographical	2	1	2/56	4/59	-	0.4485	0.53 [0.10, 2.76]
Cognitions, Confusion and shock or overwhelmed	Geographical	2	1	6/56	1/59	-	0.0831	6.32 [0.79, 50.86]
Cognitions, Current threat	Geographical	2	1	5/56	3/59	-	0.4252	1.76 [0.44, 7.01]
Cognitions, Excitement	Geographical	2	1	0/56	0/59	-	0.9795	1.05 [0.02, 52.17]
Cognitions, More information	Geographical	2	1	7/56	7/59	-	0.9170	1.05 [0.39, 2.81]
Cognitions, Observing and explaining	Geographical	2	1	12/56	6/59	-	0.1081	2.11 [0.85, 5.23]
Cognitions, Safety-seeking	Geographical	2	1	3/56	6/59	-	0.3473	0.53 [0.14, 2.01]
Cognitions, Self-soothing	Geographical	2	1	5/56	9/59	-	0.3082	0.59 [0.21, 1.64]
Cognitions, Worry and concern	Geographical	2	1	16/56	23/59	-	0.2441	0.73 [0.43, 1.24]
Superordinate Theme, Action-orientedt	Geographical	2	1	8/56	15/59	-	0.1456	0.56 [0.26, 1.22]
Superordinate Theme, Passive-engagement	Geographical	2	1	27/56	18/59	-	0.0569	1.58 [0.99, 2.53]
Superordinate Theme, Threat	Geographical	2	1	21/56	26/59	-	0.4760	0.85 [0.55, 1.33]



Supplementary Materials 5. Description of the 39 earthquakes with magnitude ≥ 6.0 that occurred in high-income countries from 1990 to 2012 and were not investigated by the studies included in this review

Date	Country	Region	Magnitude[a]	N deaths[a]
25 March 2012	Chile	Maule	7.1	1
17 April 2012	Chile	Valparaiso	6.7	2
20 May 2012	Italy	Emilia, Northern Italy	6.0	7
7 April 2011	Japan	Near East coast of Honshu	7.1	3
11 April 2011	Japan	Eastern Honshu	6.6	7
10 July 2009	Japan	Near the south coast of Honshu	6.2	1
8 June 2008	Greece	Patras	6.4	2
13 June 2008	Japan	Eastern Honshu	6.9	13
15 July 2008	Greece	Dodecanese Islands	6.4	1
23 July 2008	Japan	Eastern Honshu	6.8	1
21 April 2007	Chile	Aisen	6.2	10
16 July 2007	Japan	Near the west coast of Honshu	6.6	9
2 August 2007	Russia	Tatar Strait	6.2	2
14 November 2007	Chile	Antofagasta	7.7	2
12 December 2007	New Zealand	Off east coast of the North Islan	6.6	1
20 March 2005	Japan	Kyushu	6.6	1
27 September 2003	Russia	Southwestern Siberia	7.3	3
22 December 2003	USA	San Simeon	6.6	2
22 January 2002	Greece	Crete	6.2	1
6 September 2002	Italy	Sicily	6.0	2
24 March 2001	Japan	Western Honshu	6.8	2
24 July 2001	Chile	Arica and Iquique	6.4	1
1 July 2000	Japan	Near the South Coast of Honshu	6.1	1
30 January 1998	Chile	Near coast of northern Chile	7.1	1
29 July 1998	Chile	Near the coast of central Chile	6.4	2
26 September 1997	Italy	Umbria e Marche, Central Italy	6.0	11
15 October 1997	Chile	Near Coast of Central Chile	7.1	8
9 October 1996	Cyprus	Cyprus Region	6.8	1
15 June 1995	Greece	Kozani-Grevena	6.5	26
30 July 1995	Chile	Near Coast of Northern Chile	8.0	3
28 December 1994	Japan	Off East Coast of Honshu	7.8	3
15 January 1993	Japan	Hokkaido	7.6	2
12 July 1993	Japan	Hokkaido	7.7	243
21 September 1993	USA	Oregon	6.0	2
11 October 1993	Japan	South of Honshu	6.9	1
28 June 1992	USA	Southern California	7.3	3
29 April 1991	Georgia	Georgia	7.0	114
15 June 1991	Georgia	Georgia	6.3	8
21 December 1990	Greece	Athens	6.1	1

[a] Magnitude and number of deaths obtained from the United States Geological Survey 1990-2012 archive [1]

1. U.S. Geological Survey. Earthquake Information by Year [Internet]. 2015 [cited 2015 Dec 18]. Available from: http://earthquake.usgs.gov/earthquakes/eqarchives/year/