PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Trends in Sudden Cardiac Death and Its Risk Factors in Japan from 1981 to 2005: The Circulatory Risk in Communities Study (CIRCS)
AUTHORS	Minako Maruyama, Tetsuya Ohira, Hironori Imano, Akihiko Kitamura, Masahiko Kiyama, Takeo Okada, Kenji Maeda, Kazumasa Yamagishi, Hiroyuki Noda, Yoshinori Ishikawa, Takashi Shimamoto and Hiroyasu Iso

VERSION 1 - REVIEW

REVIEWER	Empana JP, MD, PhD INSERM U970, Paris Cardiovascular Research Center (PARCC), Cardiovascular Epidemiology& Sudden Death Unit (team #4), Paris Descartes University, France
REVIEW RETURNED	24/11/2011

THE STUDY	The design of the CIRC Study is not described adequately: in particular we do not know whether one single survey was used or if 5 repeated surveys by 5-year interval was used to estimate incidence rates. The participation rates are not reported so that we do not known about the representativeness of the data
GENERAL COMMENTS	In this paper, the authors examined trends in the incidence rates of sudden cardiac death (SCD) using data from the Circulatory Risk in Communities Study (CIRC), as well as trends in the prevalence of some risk factors using annual cross sectional national population based surveys. The periods covered ranged between 1981 and 2005 and the target population is the adult Japanese population aged 30-84 years. Data on incidence rates of SCD remain scarce especially in the Asian population, rendering this paper of potential interest. The strengths of the paper includes 1) the long term period examined over 25 years allowing to describe secular trends, 2) the use of accurate and stringent criteria to define outcomes including SCD, 3) the availability of trends for other outcomes including CHD and myocardial infarction allowing for comparisons, 4) the reporting of trends on the prevalence of some risk factors allowing to generate explanatory hypotheses on the observed trends on the outcomes However, several important clarifications need to be made: 1) CIRC Study: - it is not clear whether the incidence rate of SCD over 25 years was estimated in a single same study on the same individuals, or if it was calculated by 5-year intervals in 5 different cohorts ? In any case, the design of the (each) study should be briefly summarized including the sampling procedures

	- in the same vein, it is said in the manuscript that consent was obtained among the community representatives only. Does it mean that all inhabitants of a given community participate to the survey? Say differently, we need to know the participation rate of the studies. - we also need to know the number at risk at the beginning of each 5 year intervals - did the surveillance procedure for the events was specific to the CIRC study or did it correspond to the existing surveillance system of morbidity in Japan. In the first case, we need to have information on the rate of lost to follow-up for instance. In the second case, we need to have information about the reliability of the surveillance system 2) Annual risk factors surveys: as far as the reviewer understands, annual mean of a given risk factor was available in the annual risk factors surveys; does the 5-year mean of that risk factor corresponds to the mean of the mean ? 3) It would be of particular interest if the authors had data on the SCD or MI/CHD survival rate trends over the same period.

REVIEWER	Alawi Alsheikh-Ali, MD, MSc Consultant Heart and Vascular Institute Sheikh Khalifa Medican City Abu Dhabi, UAE
REVIEW RETURNED	04/12/2011

THE STUDY	Authors need to elaborate on how they labeled a death as SCD. They indicate that if death occured within one hour of symptom onset or 24 hours of being observed alive and symptom-free then it would be labeled as SCD. However, was timing of symptoms or last sighting available for all cases? How were such missing details handled? Please review the paper for several grammatical deficiencies For statitical methods, please report confidence intervals aroung the estimate of SCD.
RESULTS & CONCLUSIONS	The observation that the reduction in SCD rates coincided with a reduction in hypertension is not enough to infer that the two are related. I would suggest being more circumspect in discussing this observation.

VERSION 1 – AUTHOR RESPONSE

Reviewer: Dr Empana JP

Comment: The design of the CIRC Study is not described adequately: in particular we do not know whether one single survey was used or if 5 repeated surveys by 5-year interval was used to estimate incidence rates. The participation rates are not reported so that we do not known about the representativeness of the data
In this paper, the authors examined trends in the incidence rates of sudden cardiac death (SCD) using data from the Circulatory Risk in Communities Study (CIRC), as well as trends in the prevalence of some risk factors using annual cross sectional national population based surveys. The periods

covered ranged between 1981 and 2005 and the target population is the adult Japanese population aged 30-84 years.

Response;
We appreciate your comments on our manuscript.
Concerning the survey of SCD and its risk factors, we conducted annual surveys to estimate incidence rates of SCD among all residents aged 30 to 84 years in the surveyed communities and prevalence of risk factors among those who participated in the risk factor surveys. We added sentences to explain in more detail for the survey. Further, we added the participation rates during the survey periods according to your advice. (page 4, 3rd paragraph and page 6, 2nd paragraph)
However, since the participation rate among the subjects who aged 30 to 84 years was less than 50%, we analysed the data when the subjects were restricted to ages 40 to 74 years which yielded the higher rates. Furthermore, the participation rate for ages 40 to 74 years was particularly higher in Ikawa and Kyowa which yielded the more higher rate of 74 to 54%. Thus, we also examined the risk factor for ages 40 to 74 years (Supplemental Table 2), and also stratified by community (Ikawa and Kyowa / Yao and Noichi). (page 6, 2nd paragraph, page 9, 2nd paragraph, and Supplemental Tables 3 and 4)

Comment: Data on incidence rates of SCD remain scarce especially in the Asian population, rendering this paper of potential interest.
The strengths of the paper includes 1) the long term period examined over 25 years allowing to describe secular trends, 2) the use of accurate and stringent criteria to define outcomes including SCD, 3) the availability of trends for other outcomes including CHD and myocardial infarction allowing for comparisons, 4) the reporting of trends on the prevalence of some risk factors allowing to generate explanatory hypotheses on the observed trends on the outcomes
However, several important clarifications need to be made:
1) CIRC Study:
- it is not clear whether the incidence rate of SCD over 25 years was estimated in a single same study on the same individuals, or if it was calculated by 5-year intervals in 5 different cohorts ? In any case, the design of the (each) study should be briefly summarized including the sampling procedures.

Response;
As shown in the methods section, we surveyed the incidence of SCD in all residents aged 30 to 84 years in the four Japanese communities. Therefore, we calculated the incidence rate by 5-year intervals in the communities.
We changed the sentences concerning the explanation of SCD incidence. (page 4, 3rd paragraph and page 5, 3rd paragraph)

- in the same vein, it is said in the manuscript that consent was obtained among the community representatives only. Does it mean that all inhabitants of a given community participate to the survey? Say differently, we need to know the participation rate of the studies.

Response;
As we mentioned above, we added the participation rates for risk factor surveys in the five survey periods. (page 6, 2nd paragraph)

- we also need to know the number at risk at the beginning of each 5 year intervals.

Response;

We added the number at risk at the beginning of each 5 years. (Table 1)

- did the surveillance procedure for the events was specific to the CIRC study or did it correspond to the existing surveillance system of morbidity in Japan. In the first case, we need to have information on the rate of lost to follow-up for instance. In the second case, we need to have information about the reliability of the surveillance system

Response;
The surveillance procedure for the events is specific to the CIRCS study. We added the sentences to explain in more detail about the lost to the follow-up according to the reviewer's advice. We added the rate of moving out from the community during the survey periods. (page 4, 3rd paragraph and page 5, 3rd paragraph)

2) Annual risk factors surveys: as far as the reviewer understands, annual mean of a given risk factor was available in the annual risk factors surveys; does the 5-year mean of that risk factor corresponds to the mean of the mean ?

Response;
The 5-year means of these risk factor did not correspond to the mean of the mean. If the subjects participated in the risk factor survey more than once during each survey period, we used the data from the earliest year in each survey period.We added the sentences to explain in more detail about the way to select the data in each survey period. (page 6, 2nd paragraph)

3) It would be of particular interest if the authors had data on the SCD or MI/CHD survival rate trends over the same period.

Response;
Although trends of MI/CHD survival rate are of interest, it may be beyond the scope of the present study. Therefore, we did not include the survival data.

Reviewer: Dr Alawi Alsheikh-Ali

Comment: Authors need to elaborate on how they labeled a death as SCD. They indicate that if death occurred within one hour of symptom onset or 24 hours of being observed alive and symptom-free then it would be labeled as SCD. However, was timing of symptoms or last sighting available for all cases? How were such missing details handled?

Response;
If they survived for 24 hours after symptom onset, these cases were not regarded as SCD.
For all of 471 individuals with SCD, symptoms or last sighting were available, they were confirmed to be dead within 24 hours. Cases without sufficient information to confirm deaths within 24 hours were not regarded as SCD.

Please review the paper for several grammatical deficiencies

Response;

We had the native speaker check the manuscript.

For statistical methods, please report confidence intervals aroung the estimate of SCD.

Response;
We added confidence intervals for the estimate of SCD in the result section. (page 6, 4th paragraph, Result, page 8, and Table 1)

The observation that the reduction in SCD rates coincided with a reduction in hypertension is not enough to infer that the two are related. I would suggest being more circumspect in discussing this observation.

Response;
We made more comprehensive discussion or this issue, as follows;
Hypertension, current smoking, and diabetes mellitus were found the potential risk factors for SCD among Japanese [20,29]. In the present study, the SCD incidence decreased from 1981 to 1995, which correspond to a reduction in the prevalence of hypertension and current smoking. The plateaued trend for SCD incidence from 1996 to 2005 is explained partly by the unchanged prevalence of hypertension, the decreased prevalence of current smoking and the increased prevalence of diabetes mellitus. (Abstract, Page 11, 3rd paragraph and page 12, 3rd paragraph)

VERSION 2 – REVIEW

REVIEWER	Dr Empana JP INSERM U970, Paris Cardiovascular Research Center, Paris, France Competing of interest: none
REVIEW RETURNED	23/01/2012

RESULTS & CONCLUSIONS	the way the authors correlate trends of risk factors with trends in SCD is too causal although the design of their study does not allow to do this. Please temperate
GENERAL COMMENTS	The authors rightly addressed most of the issues raised by the present reviewer. Some minor points summarized below remain to be discussed : 1. in some aspects, the interpretation of the authors regarding trends in risk factors and trends in SCD is too causal. The best they can do is to put them in parallel; please temperate the conclusion of the abstract and of the discussion section (L 45 to 48) 2. Trends in MI: the decline of MI incidence was observed only for the last period; please rephrase 3. SCD definition: it is unclear whether resuscitated SCD were also included? Inclusion of only "fatal" SCD might underestimate the true incidence of SCD 4. Some editing mistakes remain so please revise: for instance in L 21, please correct as "further" instead of "Farther"

REVIEWER	Alawi Alsheikh-Ali, MD Consultant Sheikh Khalifa Medical City UAE
REVIEW RETURNED	31/01/2012

GENERAL COMMENTS	The concerns and questions raised in the initial review are adequately addressed in the revised version of the paper.

VERSION 2 – AUTHOR RESPONSE

Reviewer: Dr Empana JP

Comment:
1. in some aspects, the interpretation of the authors regarding trends in risk factors and trends in SCD is too causal. The best they can do is to put them in parallel; please temperate the conclusion of the abstract and of the discussion section (L 45 to 48)

Response;
As the reviewer suggested, we described the incidence of SCD and risk factors in a parallel way, as follows;
In the present study, the SCD incidence decreased from 1981 to 1995 when a reduction in the prevalence of hypertension and current smoking was observed. The SCD incidence remained unchanged from 1996 to 2005 when there were the unchanged prevalence of hypertension, the decreased prevalence of current smoking and the increased prevalence of diabetes mellitus. (Abstract, Page 11, 3rd paragraph and page 12, 3rd paragraph)

Comment:
2. Trends in MI: the decline of MI incidence was observed only for the last period; please rephrase

Response;
We changed the sentence concerning MI incidence, according to the reviewer's advice, as follows;
A similar trend was observed for age- and sex-adjusted incidence of CHD; the annual incidence (95%CI) of CHD per 100,000 person-year was 98.2(62.7 to 133.7), 87.0(56.0 to 118.0), 78.0(50.9 to 105.1), 50.0(29.8 to 70.2) and 57.5(36.5 to 78.5), respectively, while a slightly different trend was observed for MI; the annual incidence (95%CI) of MI per 100,000 person-year was 55.2(28.6 to 81.8), 58.9(33.4 to 84.4), 57.5(34.4 to 80.6), 34.6(17.9 to 51.3) and 45.6(26.9 to 64.3) (not shown in Table).(Page 8, 2nd paragraph)

Comment:
3. SCD definition: it is unclear whether resuscitated SCD were also included? Inclusion of only "fatal" SCD might underestimate the true incidence of SCD

Response;
We did not include the resuscitated SCD for over 24 hours after symptom onset, which might underestimate the true incidence of SCD, as the reviewer suggested. We added sentence about this issue in the discussion section, as follows;
Third, since we did not include the resuscitated SCD for over 24 hours after symptom onset, the true incidence of SCD might be underestimated. However, the magnitude of underestimation should be small because the annual number of resuscitated cardiac arrest cases in our surveyed population was estimated only around 0.7, based on the 2005 statistics of Fire and Disaster Management Agency [30]. (Page12, 2nd paragraph)

Comment:
4. Some editing mistakes remain so please revise: for instance in L 21, please correct as "further" instead of "Farther"

Response;
We checked typos throughout the text, and corrected them thoroughly.