

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Socioeconomic status in relation to cardiovascular disease and cause-specific mortality: a comparison of Asian and Australasian populations in a pooled analysis
AUTHORS	Woodward, Mark; Peters, Sanne; Batty, David; Ueshima, Hirotsugu; Woo, J; Giles, Graham; Barzi, Federica; Ho, Suzanne; Huxley, Rachel; Arima, Hisatomi; Fang, Xianghua; Dobson, Annette; Lam, Tai Hing; Vathesatogkit, Prin

VERSION 1 - REVIEW

REVIEWER	K. Srinath Reddy Public Health Foundation of India, India
REVIEW RETURNED	18-Nov-2014

GENERAL COMMENTS	This is an excellent paper with a clear message on the socioeconomic gradients for CVD in Asian and Australasian populations. The only limitation is the use of the term 'Asian' for cohort which do not include large populations in South Asia and South East Asia. Since 77% of the Asian data were from a Chinese occupational cohort and that data set had several missing values, generalization to all of 'Asia' would be difficult. However, this is understandable because many of the other Asian countries have not had long standing cohort which could have been included in these analyses. However, there are published cross-sectional survey data from India which also show an inverse association between educational level and several cardiovascular risk factors.
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REVIEWER	Norrina Allen Northwestern University United States
REVIEW RETURNED	02-Dec-2014

GENERAL COMMENTS	This study examined the association between educational attainment and CVD and mortality among a large group of prospective cohorts from Asia and Australia\New Zealand. They found that lower educational attainment was associated with increased risk for mortality. These findings expand our understanding of the benefits of education to Asian and Australasian populations. The manuscript is very well written and the analyses were appropriate to answer the study questions. There are a few additional suggestions listed below, which if addressed could strengthen the paper. 1) While I agree with the authors analytic choices, I still have
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	<p>concerns given the large amount of missing data, especially in the Asian cohorts where missingness is highly related to education level. I would suggest that the authors move some of the description of the MICE imputation model , i.e. why this method was chosen over others, from page 15 of the discussion and place it in the methods section regarding the imputation model.</p> <p>2) The authors make a very important point in the last sentence of the discussion (pg 15) before the conclusions regarding the proportion of individuals having no schooling at all in the lowest education group being higher in the Asian countries. I think it is very likely the reason why effect sizes were smaller in the Australasian countries. Because of this, I don't think you can necessarily state that educational level was stronger in Asian countries as compared to Australasian countries. If you have additional details on the years of education you could examine this possibility.</p> <p>3) There is no discussion of why there were differences in the findings between CHD and CVD. What do the authors hypothesize are the reasons for this?</p> <p>4) When you look at Figure 1 it appears that these associations are only seen among men. All analyses should be stratified by gender.</p> <p>5) In the supplemental figures of cancers by site are any of the differences between educational groups statistically significant?</p> <p>6) Additional information is needed on how each of the non-fatal outcomes were defined and collected for the cohorts.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

This is an excellent paper with a clear message on the socioeconomic gradients for CVD in Asian and Australasian populations. The only limitation is the use of the term 'Asian' for cohort which do not include large populations in South Asia and South East Asia. Since 77% of the Asian data were from a Chinese occupational cohort and that data set had several missing values, generalization to all of 'Asia' would be difficult. However, this is understandable because many of the other Asian countries have not had long standing cohort which could have been included in these analyses. However, there are published cross-sectional survey data from India which also show an inverse association between educational level and several cardiovascular risk factors.

WE AGREE THAT THE SINGLE CHINESE COHORT DOMINATES THE ASIAN RESULT AND HAVE ADDED A COMMENT IN DISCUSSION. IN OUR DISCUSSION OF CROSS-SECTIONAL ASSOCIATIONS WE ALREADY INCLUDE REFERENCES TO INTERNATIONAL STUDIES. WE DON'T FEEL THAT IT WOULD BE ADVANTAGEOUS TO SINGLE OUT ANY STUDIES THAT ARE SPECIFIC TO INDIA, ALTHOUGH WE WOULD BE PREPARED TO CONSIDER ANY SPECIFIC STUDIES THAT THE REVIEWER CAN SUGGEST.

Reviewer: 2

This study examined the association between educational attainment and CVD and mortality among a large group of prospective cohorts from Asia and Australia\New Zealand. They found that lower educational attainment was associated with increased risk for morality. These findings expand our understanding of the benefits of education to Asian and Australasian populations. The manuscript is very well written and the analyses were appropriate to answer the study questions. There are a few

additional suggestions listed below, which if addressed could strengthen the paper.

1) While I agree with the authors analytic choices, I still have concerns given the large amount of missing data, especially in the Asian cohorts where missingness is highly related to education level. I would suggest that the authors move some of the description of the MICE imputation model, i.e. why this method was chosen over others, from page 15 of the discussion and place it in the methods section regarding the imputation model.

DONE

2) The authors make a very important point in the last sentence of the discussion (pg 15) before the conclusions regarding the proportion of individuals having no schooling at all in the lowest education group being higher in the Asian countries. I think it is very likely the reason why effect sizes were smaller in the Australasian countries. Because of this, I don't think you can necessarily state that educational level was stronger in Asian countries as compared to Australasian countries. If you have additional details on the years of education you could examine this possibility.

WE FEEL THAT WE HAVE ALREADY MADE THE CAVEAT ABOUT HETEROGENEITY IN EDUCATIONAL CLASSIFICATIONS. UNFORTUNATELY WE ARE UNABLE TO ANALYSE YEARS OF EDUCATION AS SUCH DATA WERE NOT COLLECTED.

3) There is no discussion of why there were differences in the findings between CHD and CVD. What do the authors hypothesize are the reasons for this?

THE DIFFERENCES BETWEEN CHD AND CVD WERE ONLY SEEN IN ASIA. IN ASIA, STROKE HAS BEEN THE MOST COMMON TYPE OF CARDIOVASCULAR CONDITION FOR MANY YEARS AND HENCE STROKE AND CVD CAN BE EXPECTED TO SHOW SIMILAR RESULTS IN ASIA, AS THEY DO IN THIS STUDY (TABLE 4). IN CONTRAST, IN WESTERN POPULATIONS ONE DOES, AS THE REVIEWER SUGGESTS, EXPECT TO SEE CHD AND CVD RESULTS BEING SIMILAR – AS THEY ARE IN THIS PAPER FOR AUSTRALASIA (SEE TABLE 4). THIS IS NOW NOTED IN RESULTS.

4) When you look at Figure 1 it appears that these associations are only seen among men. All analyses should be stratified by gender.

WE DISAGREE. WE STATE THAT THERE ARE NO SEX INTERACTIONS (PAGE 8) AND HENCE IT WOULD BE MISLEADING TO PRESENT SEX-SPECIFIC RESULTS IN ANY DETAIL.

5) In the supplemental figures of cancers by site are any of the differences between educational groups statistically significant?

THIS IS AN INTERESTING COMMENT. PREVIOUSLY WE AVOIDED DOING ANY FORMAL ANALYSES OF CANCER SITES BECAUSE OUR DATA ARE MUCH TOO FEW TO PRODUCE RELIABLE RESULTS. HOWEVER, ON REFLECTION, IT IS BETTER THAT WE GIVE AT LEAST AGE/SEX-ADJUSTED HAZARD RATIOS THAN SIMPLE GRAPHS OF CRUDE DEATH RATES. HENCE WE HAVE NOW REPLACED APPENDIX FIGURES 1 AND 2 WITH APPENDIX TABLE 6, WHICH ANSWERS THE REFEREE'S QUESTION (YES, SOME ARE SIGNIFICANT). WE ARE RELUCTANT TO GO FURTHER SO AS TO AVOID GIVING MISLEADING INFERENCES.

6) Additional information is needed on how each of the non-fatal outcomes were defined and collected for the cohorts.

SINCE SUCH INFORMATION WAS NOT COLLECTED FROM THE INDIVIDUAL STUDY CENTRES WE ARE UNABLE TO GIVE ANY USEFUL DETAILS. WE HAVE ADDED THIS AS A LIMITATION TO THE STUDY (IN DISCUSSION).