Global and Regional Burden of Aortic Dissection and Aneurysms

Mortality Trends in 21 World Regions, 1990 to 2010

Uchechukwu K. A. Sampson*, Paul E. Norman[†], F. Gerald R. Fowkes[‡], Victor Aboyans[§], Yanna Song^{||}, Frank E. Harrell, Jr.^{||}, Mohammad H. Forouzanfar[¶], Mohsen Naghavi[¶], Julie O. Denenberg[#], Mary M. McDermott**, Michael H. Criqui[#], George A. Mensah^{††}, Majid Ezzati^{¶,‡‡}, Christopher Murray[¶] *Nashville, TN, USA; Fremantle, Western Australia, Australia; Edinburgh and London, United Kingdom; Limoges, France; Seattle, WA, USA; San Diego, CA, USA; Chicago, IL, USA; and Bethesda, MD, USA*

ABSTRACT

A comprehensive and systematic assessment of the global burden of aortic aneurysms (AA) has been lacking. Therefore, we estimated AA regional deaths and years of life lost (YLL) in 21 regions worldwide for 1990 and 2010. We used the GBD (Global Burden of Disease) 2010 study causes of death database and the cause of death ensemble modeling approach to assess levels and trends of AA deaths by age, sex, and GBD region. The global AA death rate per 100,000 population was 2.49 (95% CI: 1.78 to 3.27) in 1990 and 2.78 (95% CI: 2.04 to 3.62) in 2010. In 1990 and 2010, the highest mean death rates were in Australasia and Western Europe: 8.82 (95% CI: 6.96 to 10.79) and 7.69 (95% CI: 6.11 to 9.57) in 1990 and 8.38 (95% CI: 6.48 to 10.86) and 7.68 (95% CI: 6.13 to 9.54) in 2010. YLL rates by GBD region mirrored the mortality rate pattern. Overall, men had higher AA death rates than women: 2.86 (95% CI: 1.90 to 4.22) versus 2.12 (95% CI: 1.33 to 3.00) in 1990 and 3.40 (95% CI: 2.26 to 5.01) versus 2.15 (95% CI: 1.44 to 2.89) in 2010. The relative change in median death rate was +0.22 (95% CI: 0.10 to 0.33) in developed nations versus +0.71 (95% CI: 0.28 to 1.40) in developing nations. The smallest relative changes in median death rate were noted in North America high income, Central Europe, Western Europe, and Australasia, with estimates of +0.07 (95% CI: -0.26 to 0.37), +0.08 (95% CI: -0.02 to 0.23), +0.09 (95% CI: -0.02 to 0.21), and +0.22 (95% CI: -0.08 to 0.46), respectively. The largest increases were in Asia Pacific high income, Southeast Asia, Latin America tropical, Oceania, South Asia, and Central Sub-Saharan Africa. Women rather than men drove the increase in the Asia Pacific highincome region: the relative change in median rates was +2.92 (95% CI: 0.6 to 4.35) versus +1.05 (95% CI: 0.61 to 2.42). In contrast to high-income regions, the observed pattern in developing regions suggests increasing AA burden, which portends future health system challenges in these regions.

Aortic aneurysms (AA) are significant causes of mortality in developed nations such as the United States [1-6]. Cases of AA are asymptomatic until dissection or rupture occurs, resulting in high fatality rates, particularly in the absence of surgery. The reality that patients may initially present with AA dissection and/or rupture led to screening recommendations to enable early detection, monitoring, and timely interventions aimed at decreasing the risk of adverse events in patients at high risk for AA. There has been a worldwide increase in the burden of hypertension, smoking, and atherosclerotic cardiovascular disease [7], which are prime modifiable risk factors for thoracic AA and abdominal AA [8]. Despite the awareness of increasing prevalence and burden of major AA risk factors, the worldwide distribution of AA and its global burden is uncertain.

Because worldwide epidemiology of AA has neither been reported in the literature nor past global burden of disease (GBD) projects, most of our knowledge of AA distribution and burden is largely limited to epidemiological surveys executed in developed countries. However, in the recent GBD 2010 study, AA was included in the cause of death database, thus providing an opportunity to shed light on the global burden of AA. Consequently, we have undertaken the first known comprehensive and systematic assessment of the global burden of AA in an effort to bridge the existing knowledge gap and to potentially inform health policy decisions and potentially mitigate the contribution of AA to the global cardiovascular disease burden. In this report, we present estimates of AA deaths and years of life lost (YLL) in 21 world regions for 1990 and 2010.

METHODS

Prior GBD publications provide details of the methods used in this analysis, some of which are briefly described next The authors report no relationships that could be construed as a conflict of interest.

The views expressed in this article are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute, National Institutes of Health. Department of Health and Human Services, or any other government entity From the *Department of Medicine, Vanderbilt University Medical Center (VUMC), Nashville, TN, USA; †School of Surgery, University of Western Australia. Fremantle, Western Australia, Australia; ‡Centre for Population Health Sciences. University of Edinburgh, Edinburgh, United Kingdom: SDepartment of Cardiology, Dupuytren University Hospital and INSERM U1094, Tropical Neuroepidemiology, Limoges, France; ||Department of Biostatistics, VUMC, Nashville, TN, USA: ¶Institute for Health Metrics and Evaluation, Seattle, WA, USA; #Department of Family and Preventive Medicine, University of California, San Diego, CA, USA: **Department of Medicine and Preventive Medicine. Northwestern University Feinberg School of Medicine, Chicago, IL, USA; ††Center for Translation Research and Implementation Science (CTRIS). National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, USA; and 11School of Public Health, Imperial College London, United Kingdom, Correspondence: Uchechukwu K. A. Sampson (u.sampson@vanderbilt. edu).

GLOBAL HEART © 2014 World Heart Federation (Geneva). Published by Elsevier Ltd. All rights reserved. VOL. 9, NO. 1, 2014 ISSN 2211-8160/\$36.00. http://dx.doi.org/10.1016/ j.gheart.2013.12.010 [7,9–13]. Table 1 delineates the International Classification of Diseases 10 codes and subgroups that embody the GBD AA cause code (G174). Because patients with AA are usually asymptomatic until rupture, resulting in a high fatality rate, we did not analyze the burden attributed to nonfatal health outcomes from AA cases; years lived with nonfatal disease disability was not applicable to the assessment of AA burden. Therefore, the assessment of AA disease included only quantification of mortality attributable to AA. Thus, the summary measurements of population health for AA in the GBD 2010 study were death and YLL rates in 1990 and 2010 [10]. For mortality and YLL estimates, the GBD 2010 study assembled a global cause of death database. The AA raw mortality data include vital registration (from Japan, New Zealand, the United States, Australia, the United Kingdom, and Hong Kong), verbal autopsy (a method for obtaining cause of death information in settings without vital registration and medical certification of causes of death) [14], and other survey data. A complete description of the cause of death data by source type (vital registration, verbal autopsy, surveillance, survey or census, cancer registry, sibling history, burial or mortuary, hospital records, and police records) has been published in the supplementary appendix to Lozano et al. [9].

Our modeling strategy for AA mortality used more cause of death data than have been used in previous studies and employed the novel CODEm approach [15], which produces an ensemble model that is more accurate than any of its component models. The CODEm explores a large variety of possible models to estimate trends in causes of death. Possible models are identified using a covariate selection algorithm that yields many plausible combinations of covariates, which are then run through 4 model classes. The model classes include mixed effects linear models and spatiotemporal Gaussian process regression (GPR) models for cause fractions and death rates. All models for AA

TABLE 1. ICD-10 code and subgroups of GBD cause code G174 (aortic aneurysm)

•						
	171	Aortic aneurysm and dissection				
	171.0	Dissection of aorta [any part]				
	171.1	Thoracic aortic aneurysm, ruptured				
	171.2	Thoracic aortic aneurysm, without mention of rupture				
	171.3	Abdominal aortic aneurysm, ruptured				
	171.4	Abdominal aortic aneurysm, without mention of rupture				
	171.5	Thoracoabdominal aortic aneurysm, ruptured				
	171.6	Thoracoabdominal aortic aneurysm, without mention of rupture				
	171.8	Aortic aneurysm of unspecified site, ruptured				
	171.9	Aortic aneurysm of unspecified site, without				
		mention of rupture				
	GBD, global burden of disease; ICD-10, International Classification of Disease 10.					

mortality were assessed using out-of-sample predictive validity and combined into an ensemble with optimal outof-sample predictive performance. Because data coverage was not complete for all countries and years, covariates and random effects helped to improve model predictions in out-of-sample environments. Our model of AA mortality is a single-cause fraction model. This means that the sum of the estimated cause-specific mortality may not equal the all-cause mortality envelope. Therefore, to produce more accurate estimates of AA deaths, we used the cause of death correct algorithm to correct AA mortality and other causes of mortality, such that the sum of cause-specific mortality rates equaled the mortality rate from all causes [16].

In our analysis, we modeled age groups from 25 to \geq 80 years, separately by sex. The covariates included in the mortality models were based on the epidemiology, etiology, and resource accessibility to care for the disease post-onset. The most frequently chosen covariates in the ensemble model process were alcohol consumption (liters per capita), smoking prevalence, cumulative cigarettes (10 years), cholesterol (total, mean per capita), vegetable consumption (kcal per capita), and polyunsaturated fatty acid omega-6 consumption (kcal per capita). These covariates helped predict levels and trends of AA deaths over age, time, sex, and country.

We formally evaluated the ability of our models to make accurate predictions by creating 50 train-test-test splits. We randomly assigned 70% of the data to the train set, 15% to the first test data set, and the last 15% to the second test data set. For each train data set, we reestimated each of the proposed models including both the mixed effects and the spatiotemporal GPR model. We used the results of the models estimated on the training data alone to predict for the first test set. The test data were not included in the model estimation; the performance of each model is therefore evaluated out of sample. Thus, the out-of-sample predictions for the test set are a fair evaluation of how each model will perform in predicting mortality when the data are sparse or missing. We assessed predictive validity using root mean square error, accuracy of predicted trend, and how well the model covered the test data using 95% prediction intervals.

RESULTS

The global AA death rate per 100,000 population in 1990 was 2.49 (95% CI: 1.78 to 3.27) in 1990 and 2.78 (95% CI: 2.04 to 3.62) in 2010. Overall, men had higher AA death rates than women: 2.86 (95% CI: 1.90 to 4.22) versus 2.12 (95% CI: 1.33 to 3.00) in 1990 and 3.4 (95% CI: 2.26 to 5.01) versus 2.15 (95% CI: 1.44 to 2.89) in 2010. The death rates by GBD region for 1990 and 2010 are depicted in Figure 1. In descending order, the GBD regions with the highest mean AA mortality rates in 1990 were Australasia, Western Europe, North America high income, and Central Europe (Fig. 1), with estimates of 8.82 (95% CI: 6.96 to 10.79), 7.69 (95% CI: 6.11 to 9.57), 7.11

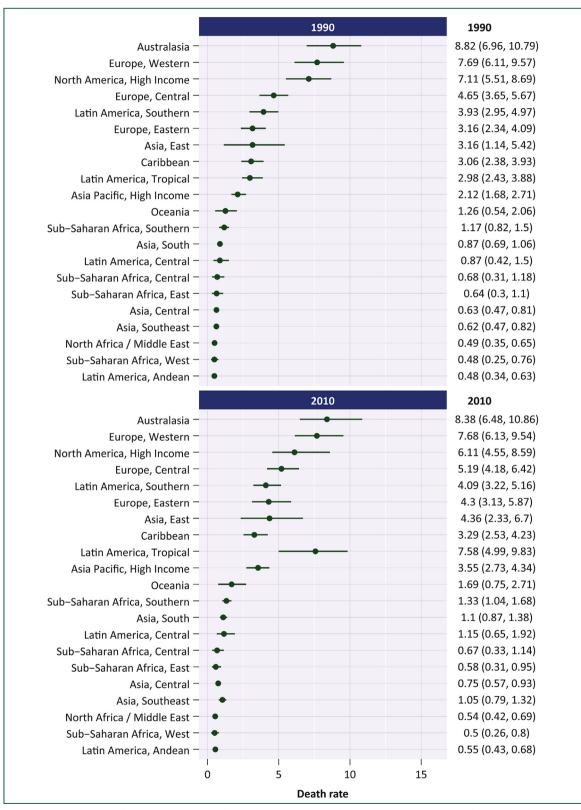


FIGURE 1. Death rates due to AA in 1990 and 2010 by GBD region. The dots denote estimates of mean death rates due to aortic aneurysms (AA) in all global burden of disease (GBD) regions. The bars around the estimates are the corresponding 95% uncertainty intervals. The rates are per 100,000 population.

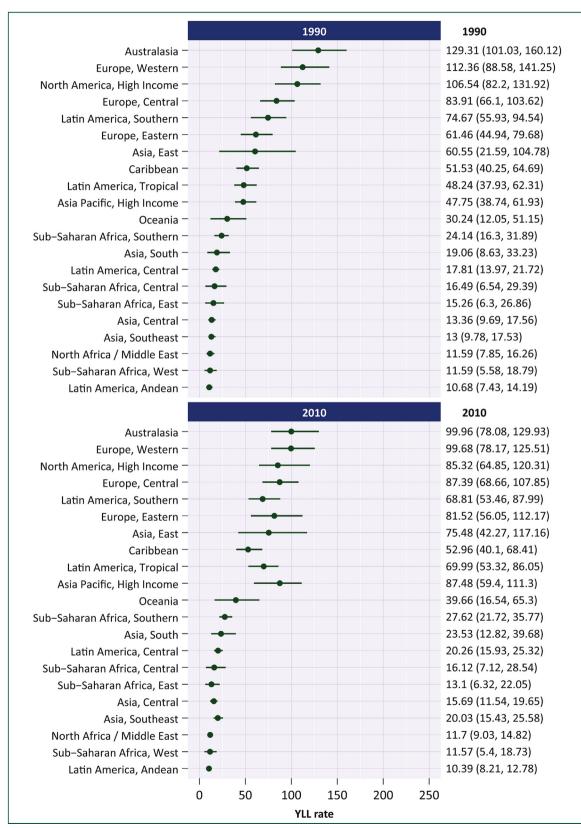


FIGURE 2. YLL rates due to AA in 1990 and 2010 by GBD region. The dots denote estimates of mean years of life lost (YLL) due to AA in all GBD regions. The bars around the estimates are the corresponding 95% uncertainty intervals. The rates are per 100,000 population. Other abbreviations as in Figure 1.

Age, yrs	Sex	Death rates in 1990	Death rates in 2010
25—29	Male	0.18 (0.1–0.32)	0.16 (0.1-0.27)
	Female	0.10 (0.04-0.17)	0.07 (0.04-0.11)
	Both	0.14 (0.08-0.21)	0.12 (0.08-0.17)
30—34	Male	0.29 (0.16-0.52)	0.25 (0.15-0.47)
	Female	0.18 (0.07-0.35)	0.11 (0.06-0.18)
	Both	0.24 (0.14-0.36)	0.18 (0.12-0.3)
35—39	Male	0.48 (0.28-0.89)	0.43 (0.25-0.74)
	Female	0.30 (0.12-0.65)	0.19 (0.1–0.35)
	Both	0.39 (0.24-0.66)	0.31 (0.21-0.48)
40—44	Male	0.84 (0.51-1.44)	0.78 (0.46-1.4)
	Female	0.53 (0.23-1.2)	0.35 (0.19-0.65)
	Both	0.69 (0.42-1.16)	0.57 (0.37–0.9)
45—49	Male	1.54 (0.91-2.65)	1.42 (0.88–2.37)
	Female	0.82 (0.37-1.75)	0.58 (0.32-1.15)
	Both	1.19 (0.72-2.02)	10 (0.66-1.52)
50—54	Male	2.86 (1.71-4.87)	2.64 (1.6-4.51)
	Female	1.44 (0.67-3.01)	1.02 (0.6-1.88)
	Both	2.15 (1.36-3.43)	1.82 (1.23–2.86)
55—59	Male	5.44 (3.16-9.13)	5.02 (3.05-8.43)
	Female	2.20 (1.21-3.83)	1.69 (1.05-2.7)
	Both	3.80 (2.46-5.8)	3.34 (2.25-5.02)
60—64	Male	10.37 (6.48–16.4)	9.41 (5.92—15.21)
	Female	4.35 (2.34-7.93)	3.31 (2.03-5.55)
	Both	7.26 (4.87–10.57)	6.27 (4.36-9.1)
65—69	Male	19.79 (12.62-31.32)	17.19 (10.9–28.76)
	Female	8.47 (4.63-14.91)	6.37 (3.97–10.25)
	Both	13.66 (9.19–20.1)	11.51 (7.89—17.25)
70—74	Male	33.52 (20.73-54.78)	29.11 (18.81–46.81)
	Female	17.09 (8.9–33.07)	12.33 (7.37–20.84)
	Both	24.38 (16.12-37.9)	19.98 (14.12–29.17)
75—79	Male	53.62 (34.66-80.46)	46.70 (29.85–73.76)
	Female	26.63 (16.46-44.07)	21.02 (13.4–33.43)
	Both	37.63 (26.3–52.55)	32.19 (22.64–46.78)
≥80	Male	88.93 (59.35-130.7)	86.82 (57.06-128.59)
	Female	59.65 (38.74-93.08)	52.46 (34.88-80.33)
	Both	69.83 (51.71-93.41)	65.29 (48.37-86.99)

TABLE 2. Global death rates in 1990 and 2010

(95% CI: 5.51 to 8.69), and 4.65 (95% CI: 3.65 to 5.67), respectively. In 2010, Australasia and Western Europe remained at the top of list with estimated rates of 8.38 (95% CI: 6.48 to 10.86) and 7.68 (95% CI: 6.13 to 9.54), respectively. However, the Asia Pacific high-income region had a remarkable increase in AA mortality rate from 2.98 (95% CI: 2.43 to 3.88) in 1990 to 7.58 (95% CI: 4.99 to 9.83) in 2010, thus ranking third among regions with the highest AA death rate. The pattern observed for YLL rate by GBD region for 1990 and 2010 (Fig. 2) mirrored the AA mortality rate pattern with the same regions at the top of the list. In all GBD regions, men had higher AA mortality rates and were the main drivers in regions with very high AA mortality (Online Figs. 1A and 1B); similar patterns

were noted for YLL rates by sex in 1990 and 2010 (Online Figs. 2A and 2B).

Global death rates in 1990 and 2010 demonstrated a consistent decrease in AA mortality rates between the two time points within each sex and across all age groups (Table 2). For instance, among men aged 50 to 54 years, the age-specific death rate per 100,000 dropped from 2.86 (95% CI: 1.71 to 4.87) in 1990 to 2.64 (95% CI: 1.6 to 4.51) in 2010; among women, the rates dropped from 1.44 (95% CI: 0.67 to 3.01) in 1990 to 1.02 (95% CI: 0.6 to 1.88) in 2010. Similarly, among men aged 75 to 79 years, the age-specific death rate per 100,000 dropped from 53.62 (95% CI: 34.66 to 80.46) to 46.7 (95% CI: 29.85 to 73.76); among women, the rates dropped from 26.63

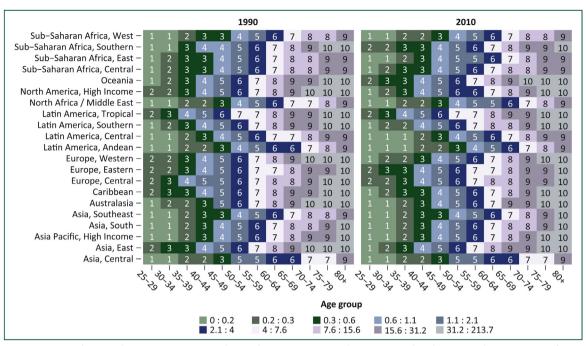


FIGURE 3. Death rates due to AA in 1990 and 2010 by GBD region and age group. The chart provides estimates of agespecific death rates due to AA for all GBD regions. Each color-coded box represents a range of age-specific death rates for a GBD region. Color gradations (also delineated by numbers within the color-coded boxes) represent different tiers of death rates. The color gradient from green to blue to purple to gray (or increasing numbers) observed with increasing age indicates increases in death rates by age in all regions in 1990 and 2010, as well as a general decrease in death rates in 2010 compared with 1990. Age groups are in years, and the rates are per 100,000 population. Abbreviations as in Figure 1.

(95% CI: 16.46 to 44.07) to 21.02 (95% CI: 13.4 to 33.43). At the regional level, the mortality rates increased consistently with advancing age in 1990 across all 21 GBD regions, and the same pattern was noted in 2010 (Fig. 3). A similar pattern was observed between YLL rate and age in 1990 and 2010, as well as a trend toward decreased YLL rates between the two time points (Fig. 4). Online Figures 3A, 3B, 4A, and 4B capture the striking sex differences in death and YLL rates, respectively, which were consistent across GBD regions.

Regionally, the smallest relative change in median death rates per 100,000 between 1990 and 2010 was noted in North America high income, Central Europe, Western Europe, and Australasia, with estimates of +0.07 (95% CI: -0.26 to 0.37), +0.08 (95% CI: -0.02 to 0.23), +0.09 (95% CI: -0.02 to 0.21), and +0.22 (95% CI: -0.08 to 0.46), respectively (Fig. 5). The negative lower bound of the CI of these estimates suggest the possibility of decreasing trends in AA death rates in some countries within these regions. By contrast, this pattern was not observed in other regions; instead, Asia Pacific high income, Southeast Asia, and Latin America tropical had the highest relative changes in median death rates between 1990 and 2010, followed closely by Oceania, South Asia, and Central Sub-Saharan Africa, respectively (Fig. 5).

When compared by country development status, the relative change in median death rate was 0.22 (95% CI: 0.10 to 0.33) in developed nations versus 0.71 (95% CI: 0.28 to 1.40) in developing nations. The same pattern was observed for the relative change in median YLL rates, which involved similar GBD regions at the bottom and the top of the ranking (Fig. 6). Of note, in the Asia Pacific high-income region, the relative change in median death rates between 1990 and 2010 was higher among women than men: 2.92 (95% CI: 0.60 to 4.35) versus 1.05 (95% CI: 0.61 to 2.42). Complete details of relative changes in median death and YLL rates by sex and region are depicted in Online Figures 5A, 5B, 6A, and 6B.

DISCUSSION

In this comprehensive and systematic comparative assessment of the global burden of AA, we observed an increase in overall global death rate from 2.49 per 100,000 (95% CI: 1.78 to 3.27) in 1990 to 2.78 (95% CI: 2.04 to 3.62) in 2010. The increase was noted for both men and women, but men had higher AA global death rates than women. However, the age-specific death rates, overall and within sex, decreased between 1990 and 2010. The discrepancy between age- and sex-specific changes versus the overall

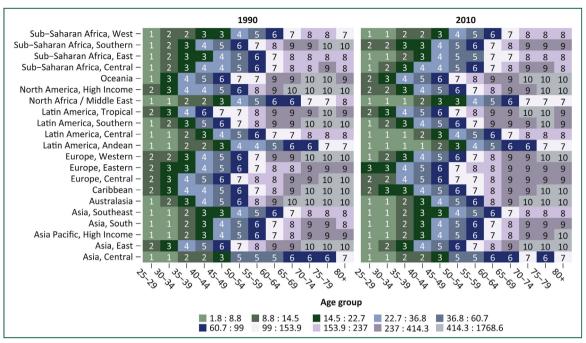


FIGURE 4. YLL rates due to AA in 1990 and 2010 by GBD region and age group. The charts delineate estimates of agespecific YLL rates due to AA for all GBD regions. Each color-coded box represents a range of age-specific YLL rates for a GBD region. Color gradations (also delineated by numbers within the color-coded boxes) represent different tiers of YLL rates. The color gradient from green to blue to purple to gray (or increasing numbers) observed with increasing age indicates increases in YLL rates by age in all regions in 1990 and 2010, as well as a general decrease in YLL rates in 2010 compared with 1990. Age groups are in years, and the rates are per 100,000 population. Abbreviations as in Figures 1 and 2.

changes probably reflects the increasing mean age of countries over the 20-year period, which needs to be verified.

Comparisons by country development status revealed that developing nations had a relative change in median death rate per 100,000 of 0.71 (95% CI: 0.28 to 1.40), which is more than 3 times the estimated 0.22 (95% CI: 0.10 to 0.33) observed in developed nations. The smallest relative changes in median death rates were noted in North America high-income, Central Europe, Western Europe, and Australasia regions. In fact, some countries in these regions experienced a decrease in AA death rate, as indicated by the negative lower bound of the uncertainty intervals for the estimated death rates. On the contrary, the largest relative increases in regional death rates in descending order were observed in Asia Pacific high income, Southeast Asia, and tropical Latin America followed closely by Oceania, South Asia, and Central Sub-Saharan Africa. Of note, within the Asia Pacific high-income region, although men had higher death rates than women, women experienced a greater relative increase in death rate from 1990 to 2010. The observations associated with YLL rates were generally congruent with those observed for death rates.

The findings of this study have important implications. The favorable pattern of small relative increase (or decrease in some countries) in median death rates in developed regions likely reflects the benefits of robust health systems that are stemming the tide of AA disease burden via risk factor modulation and treatment. On the contrary, larger increases noted in developing nations support the notion that AA is another component of the recognized epidemiological transition in these regions. This signals potential challenges ahead because the health systems in these regions are not robust enough to handle the associated future challenges. Furthermore, it is very likely that we underestimated the magnitude of AA burden in low-income regions due to paucity of surveillance data from these regions, thus the very low rates for these regions in general. Yet, despite this potential underestimation, the changes in rates between 1990 and 2010 were more outstanding for developing versus developed countries. In this context, due to poor surveillance data, we cannot fully appreciate the impending strain on the health systems in these regions caused by increasing AA burden. The greater increase in death rate among women in the Asia Pacific high-income region may be a wake-up call to the fact that AA, like lower-extremity peripheral arterial disease, may increasingly affect women in some parts of the world, as recently reported by Fowkes et al. [17].

Studies of this nature have several limitations. The greatest limitation is the availability of cause of death data.

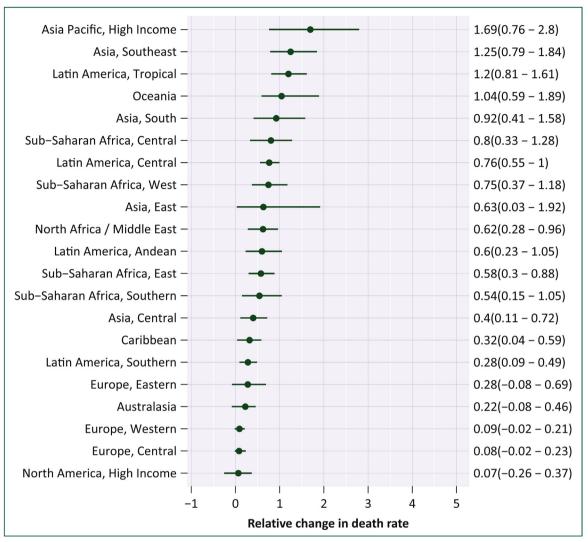


FIGURE 5. Relative change in median death rates between 1990 and 2010 by GBD region. The dots denote the relative change in median death rates due to AA in all GBD regions. The bars around the estimates are the corresponding 95% uncertainty intervals. The rates are per 100,000 population. Abbreviations as in Figure 1.

The lack of good-quality vital registration and disease surveillance data leads to unreliable disease burden estimates in some regions [18]. Consequently, much could be learned about causes of death in countries where death certification is poor through more widespread testing and application of recent advances in verbal autopsy methods, which greatly reduce heterogeneity in diagnostic practices across populations in which they are currently used. The ambition to estimate mortality from AA across 21 world regions in 1990 and 2010 means that many choices and assumptions about data sources and modeling strategies had to be made. In this context, the GBD made estimates for a region by "borrowing strength" from cause of death and epidemiology study data within that region and, in a geographically nested fashion, from other world regions. The wide range of uncertainty surrounding our estimates imply that CODEm can be improved in the future by including a broader set of model families and the use of more robust disease surveillance data.

SUMMARY

The tide of AA disease burden appears to have been mitigated in developed nations or high-income regions. There are challenges ahead for developing nations where larger relative increases in death rates suggest an evolving epidemiological transition and a future increase in AA burden that health systems in these regions are inadequately resourced to address. This may be an early indication of the need for more aggressive prevention policy

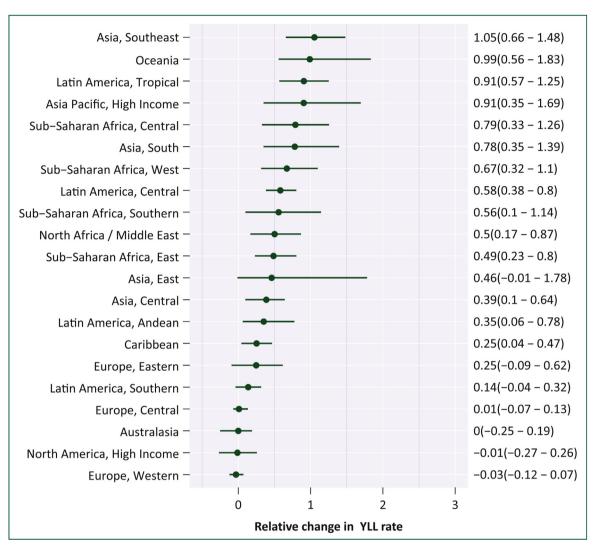


FIGURE 6. Relative change in median YLL rates between 1990 and 2010 by GBD region. The dots denote the relative change in median YLL rates due to AA in all GBD regions. The bars around the estimates are the corresponding 95% uncertainty intervals. The rates are per 100,000 population. Abbreviations as in Figures 1 and 2.

intervention, especially regarding smoking prevention or cessation and blood pressure control in these areas. Conceivably, the implementation and evaluation of any health policy will be facilitated by disease surveillance improvements in these areas, which perhaps represents a reasonable starting point.

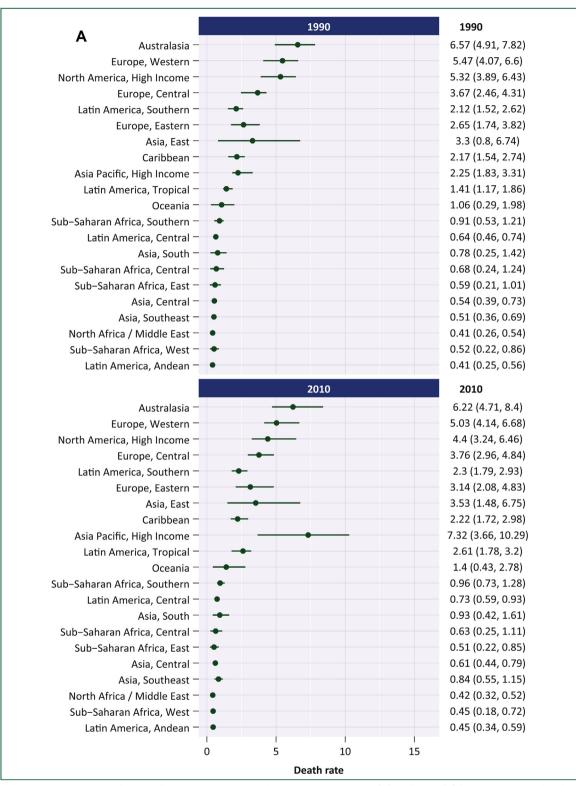
REFERENCES

- Kniemeyer HW, Kessler T, Reber PU, Ris HB, Hakki H, Widmer MK. Treatment of ruptured abdominal aortic aneurysm, a permanent challenge or a waste of resources? Prediction of outcome using a multi-organ-dysfunction score. Eur J Vasc Endovasc Surg 2000;19: 190–6.
- 2. Gillum RF. Epidemiology of aortic aneurysm in the United States. J Clin Epidemiol 1995;48:1289–98.
- van der Vliet JA, Boll AP. Abdominal aortic aneurysm. Lancet 1997; 349:863–6.

- Blanchard JF. Epidemiology of abdominal aortic aneurysms. Epidemiol Rev 1999;21:207–21.
- Minino AM, Murphy SL, Xu J, Kochanek KD. Deaths: final data for 2008. Natl Vital Stat Rep 2011;59:1–126.
- Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. Circulation 2013;127:e6–245.
- Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2224–60.
- Ramanath VS, Oh JK, Sundt TM 3rd, Eagle KA. Acute aortic syndromes and thoracic aortic aneurysm. Mayo Clinic Proc 2009;84:465–81.
- Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2095–128.
- Murray CJ, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic

analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380:2197–223.

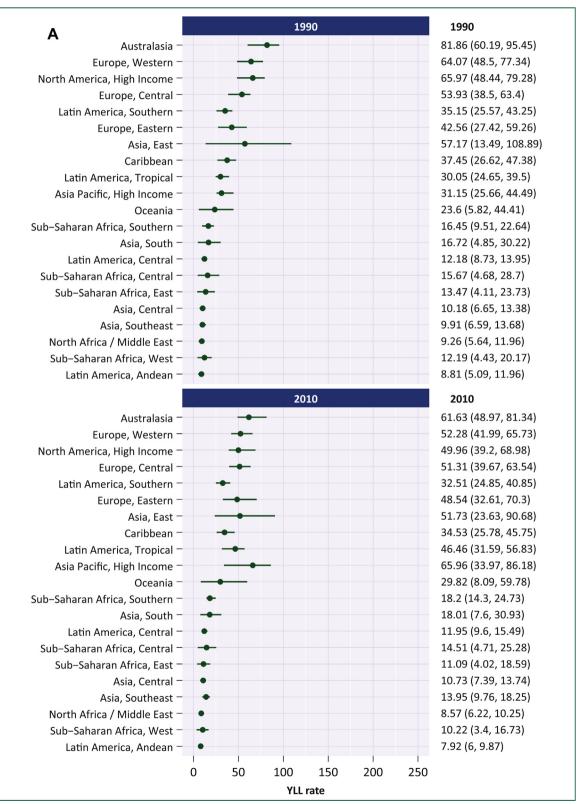
- Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2163–96.
- Naghavi M, Makela S, Foreman K, O'Brien J, Pourmalek F, Lozano R. Algorithms for enhancing public health utility of national causes-ofdeath data. Popul Health Metr 2010;8:9.
- **13.** Murray CJ, Ezzati M, Flaxman AD, et al. GBD 2010: design, definitions, and metrics. Lancet 2012;380:2063–6.
- Murray CJ, Lozano R, Flaxman AD, Vahdatpour A, Lopez AD. Robust metrics for assessing the performance of different verbal autopsy cause assignment methods in validation studies. Popul Health Metr 2011;9:28.
- Foreman KJ, Lozano R, Lopez AD, Murray CJ. Modeling causes of death: an integrated approach using CODEm. Popul Health Metr 2012;10:1.
- Wang H, Dwyer-Lindgren L, Lofgren KT, et al. Age-specific and sexspecific mortality in 187 countries, 1970–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380: 2071–94.
- **17.** Fowkes FG, Rudan D, Rudan I, et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. Lancet 2013;382: 1329–40.
- Cooper RS, Osotimehin B, Kaufman JS, Forrester T. Disease burden in sub-Saharan Africa: what should we conclude in the absence of data? Lancet 1998;351:208–10.



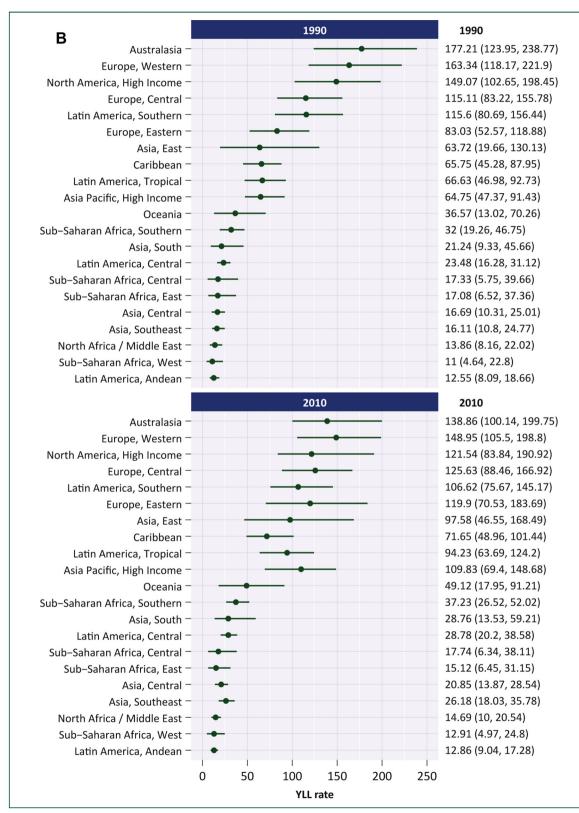
ONLINE FIGURE 1. Death rates due to AA in 1990 and 2010 among women (A) and men (B) by GBD region. The dots denote estimates of mean death rates among women (A) and men (B) in all 21 GBD regions. The bars around the estimates are the corresponding 95% uncertainty intervals. The rates are per 100,000 population. GBD, global burden of disease; AA, aortic dissection and aneurysm per GBD study code.

В	1990 1990
Australasia –	11.09 (7.72, 14.
Europe, Western –	—— 10.04 (7.23, 13.
North America, High Income –	
Europe, Central –	— 5.67 (4.09, 7.61
Latin America, Southern –	— — 5.81 (4.07, 7.81
Europe, Eastern –	3.75 (2.42, 5.32
Asia, East – 🚽 🗕	3.03 (0.94, 6.36
Caribbean – –	— 3.96 (2.68, 5.39
Asia Pacific, High Income –	• 3.72 (2.71, 5.3)
Latin America, Tropical – 🛛 🗕	2.83 (2.01, 3.99
Oceania – 🔶 🗕	1.44 (0.55, 2.74
Sub–Saharan Africa, Southern – 🗕 🗕	1.43 (0.89, 2.04
Latin America, Central –	1.1 (0.76, 1.47)
Asia, South – 🗕 –	0.95 (0.43, 2.04
Sub-Saharan Africa, Central – 🗕 🗕	0.68 (0.26, 1.57
Sub-Saharan Africa, East – 🗕 🗕	0.69 (0.29, 1.48
Asia, Central 🗕 🔶	0.72 (0.46, 1.03
Asia, Southeast – 🔶 🗕	0.74 (0.5, 1.14)
North Africa / Middle East – •	0.57 (0.35, 0.88
Sub–Saharan Africa, West – 🔶	0.45 (0.2, 0.91)
Latin America, Andean –	0.55 (0.35, 0.82
	2010 2010
Australasia –	• 10.58 (7.5, 15.2
Europe, Western –	10.43 (7.4, 14.1
North America, High Income	7.85 (5.21, 12.4
Europe, Central	6.71 (4.77, 8.97
Latin America, Southern –	
Europe, Eastern	—•—5.64 (3.64, 8.58
Asia, East -	5 .13 (2.3, 9)
Caribbean -	
Asia Pacific, High Income	
Latin America, Tropical –	4.52 (3.03, 5.96
Oceania -	- 1.98 (0.77, 3.61
Sub–Saharan Africa, Southern –	1.71 (1.21, 2.36
Latin America, Central –	1.48 (1.05, 1.99
Asia, South –	1.37 (0.66, 2.81
Sub–Saharan Africa, Central –	0.71 (0.29, 1.49
Sub–Saharan Africa, East – +	0.65 (0.31, 1.29
Asia, Central	0.9 (0.61, 1.22)
Asia, Southeast –	1.26 (0.86, 1.72
North Africa / Middle East –	0.65 (0.45, 0.93
Sub–Saharan Africa, West – •	0.55 (0.23, 1.03
Latin America, Andean	0.66 (0.46, 0.89
0	5 10 15

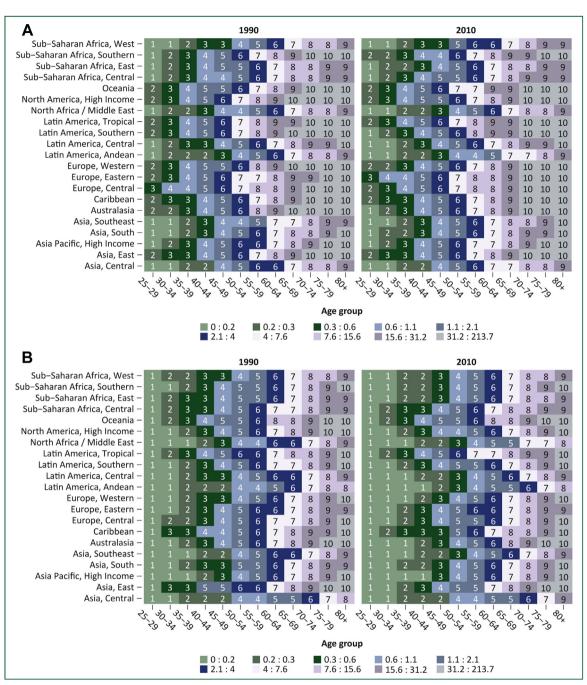
ONLINE FIGURE 1. (CONTINUED).



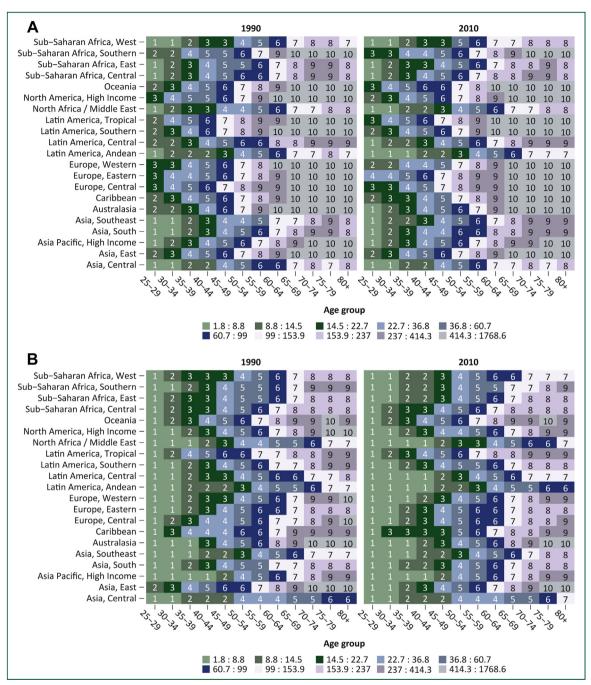
ONLINE FIGURE 2. YLL rates due to AA in 1990 and 2010 among women (A) and men (B) by GBD region. The dots denote estimates of mean YLL rates among women (A) and men (B) in all 21 GBD regions. The bars around the estimates are the corresponding 95% uncertainty intervals. The rates are per 100,000 population. YLL, years of life lost; GBD, global burden of disease; AA, aortic dissection and aneurysm per GBD study code.



ONLINE FIGURE 2. (CONTINUED).

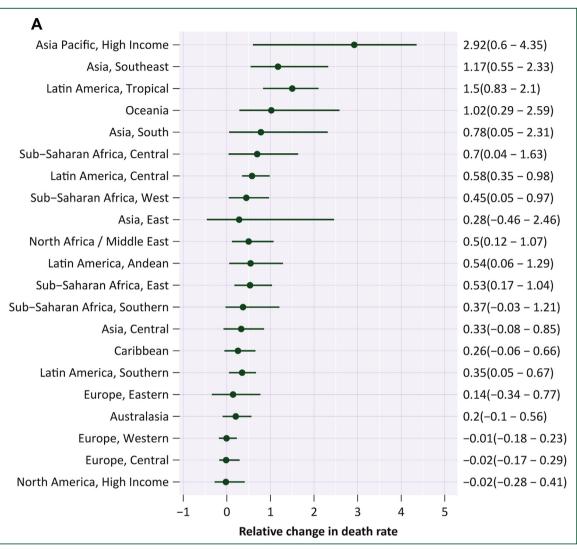


ONLINE FIGURE 3. Death rates due to AA in 1990 and 2010 among men (A) and women (B) by GBD region and age group. The chart provides estimates of age-specific death rates among men (A) and women (B) in all GBD regions. Each color-coded box represents a range of age-specific death rates for a GBD region. Color gradations (also delineated by numbers within the color-coded boxes) represent different tiers of death rates. The color gradient from green to blue to purple to gray (or increasing numbers) observed with increasing age indicates increases in death rates by age in all regions in 1990 and 2010, as well as a general decrease in death rates in 2010 compared with 1990. Age groups are in years, and the rates are per 100,000 population. GBD, global burden of disease; AA, aortic dissection and aneurysm per GBD study code.



ONLINE FIGURE 4. YLL rates due to AA in 1990 and 2010 among men (A) and women (B) by GBD region and age group. The chart provides estimates of age-specific YLL rates among men (A) and women (B) in all GBD regions. Each color-coded box represents a range of age-specific YLL rates for a GBD region. Color gradations (also delineated by numbers within the color-coded boxes) represent different tiers of YLL rates. The color gradations (also delineated by purple to gray (or increasing numbers) observed with increasing age indicates increases in YLL rates by age in all regions in 1990 and 2010, as well as a general decrease in YLL rates in 2010 compared with 1990. Age groups are in years, and the rates are per 100,000 population. YLL, years of life lost; GBD, global burden of disease; AA, aortic dissection and aneurysm per GBD study code.

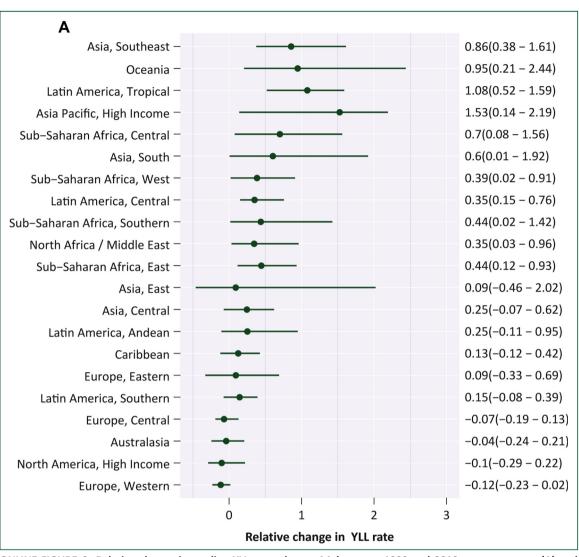
gREVIEW



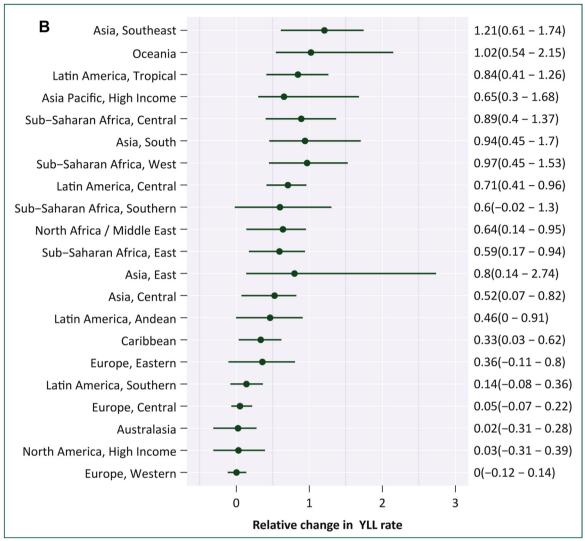
ONLINE FIGURE 5. Relative change in median death rates due to AA between 1990 and 2010 among women (A) and men (B) by GBD region. The dots denote relative changes in median death rates among women (A) and men (B) in all GBD regions. The bars are the corresponding 95% uncertainty intervals. The rates are per 100,000 population. YLL, years of life lost; GBD, global burden of disease; AA, aortic dissection and aneurysm per GBD study code.

В									
Asia Pacific, High Income –		-				1.05(0.6	1 – 2.42)		
Asia, Southeast –						1.3(0.67	– 2.07)		
Latin America, Tropical –						1.08(0.6	- 1.57)		
Oceania –		•				1.06(0.5	7 – 2.36)		
Asia, South –		•				1.06(0.5	5 – 1.92)		
Sub–Saharan Africa, Central –						0.91(0.4	5 – 1.35)		
Latin America, Central –						0.87(0.5	7 – 1.15)		
Sub-Saharan Africa, West -		•	_			1.08(0.5	2 – 1.69)		
Asia, East –		•				1(0.25 -	3.13)		
North Africa / Middle East –		•				0.76(0.2	4 – 1.07)		
Latin America, Andean –		•				0.71(0.1	7 – 1.16)		
Sub–Saharan Africa, East –		•				0.68(0.2	4 – 1.06)		
Sub–Saharan Africa, Southern –		•				0.63(0.0	7 – 1.28)		
Asia, Central –	-•	_				0.51(0.0	7 – 0.83)		
Caribbean –	-	-				0.35(-0.	02 – 0.7)		
Latin America, Southern –						0.27(0.0	3 – 0.52)		
Europe, Eastern –		_				0.41(-0.	03 – 0.89)		
Australasia –						0.25(-0.	18 – 0.58)		
Europe, Western –	•					0.14(0.0	1 – 0.27)		
Europe, Central –	•					0.14(0.0	2 – 0.28)		
North America, High Income –						0.12(-0.	33 – 0.53)		
-1	0	1	1	 3	1 4	۱ 5			
Relative change in death rate									

ONLINE FIGURE 5. (CONTINUED).



ONLINE FIGURE 6. Relative change in median YLL rates due to AA between 1990 and 2010 among women (A) and men (B) by GBD region. The dots denote relative changes in median YLL rates among women (A) and men (B) in all GBD regions. The bars are the corresponding 95% uncertainty intervals. The rates are per 100,000 population. YLL, years of life lost; GBD, global burden of disease; AA, aortic dissection and aneurysm per GBD study code.



ONLINE FIGURE 6. (CONTINUED).