Heat effects of ambient apparent temperature on all-cause mortality in Cape Town, Durban and Johannesburg, South Africa: 2006-2010

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Highlights
- This is the first study of its kind in South Africa.
- The study addressed some of the limitations of the few previous studies from Sub-Saharan Africa.
- Overall a significant increase in mortality above city-specific Tapp thresholds was observed.
- The elderly (≥65 year group) was more at risk.
- The observed risks are similar to those of other countries.

Graphical abstract
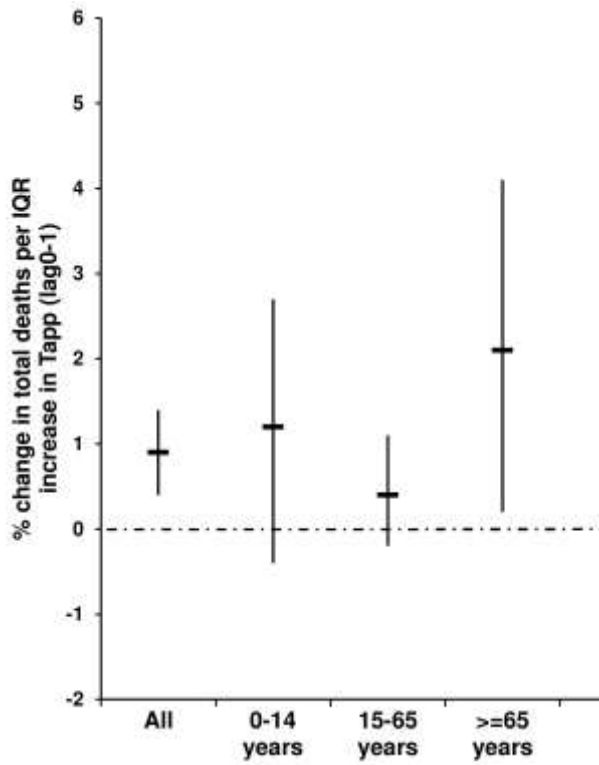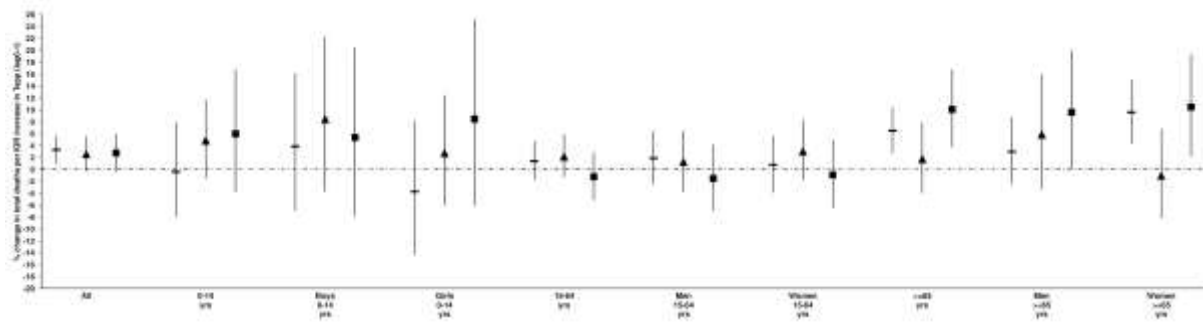
Abstract

Due to climate change, an increase of 3−4°C in ambient temperature is projected along the South African coast and 6−7°C inland during the next 80 years. The objective of this study was to investigate the association between daily ambient apparent temperature (Tapp) and daily all-cause non-accidental mortality (hereafter mortality) in Cape Town, Durban and Johannesburg during a 5-year study period (2006−2010). Susceptibility by sex and age groups (<15 years, 15−64 years and ≥65 years) was also investigated. The associations were investigated with the time-stratified case-crossover epidemiological design. Models were controlled for PM_{10}, public holidays and influenza epidemics. City-specific Tapp thresholds were determined using quasi-Poisson generalised additive models. The pooled estimates by sex and age groups were determined in meta-analyses. The city-specific Tapp thresholds were 18.6°C, 24.8°C and 18.7°C, respectively for Cape Town, Durban and Johannesburg. A 3.3%, 2.6% and 2.8% increase in mortality per IQR increase in Tapp (lag0-1) was observed in Cape Town, Durban and Johannesburg, respectively above the city-specific thresholds. The elderly were more at risk in Cape Town and Johannesburg. No difference in risk was observed for males and females in the three cities. In the meta-analysis an overall significant increase of 0.9% in mortality per 1°C increase in Tapp (lag0-1) was observed for all age groups combined in the three cities. For the ≥65 year group a significant increase of 2.1% in mortality was observed. In conclusion, the risks for all age groups combined and the elderly are similar to those reported in studies from developed and developing countries. The results can be used in present-day early warning systems and in risk assessments to estimate the impact of increased Tapp in the country due to climate change. Future research should investigate the association between Tapp and cause-specific mortality and also morbidity.

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1. Introduction

In 2009 Byass raised the question: Climate change and population health in Africa: where are the scientists? Eight years ago Byass only found 31 journal articles that covered this research topic − from almost 2 million published globally.

In the meantime South Africa launched its National Climate Change Response Plan White Paper (NCCRP) in 2011, prior to hosting the 17th session of the Conference of the Parties (COP17) to the United Nations Framework Convention on Climate Change in Durban, South Africa (Department of Environmental Affairs, 2011). The NCCRP calls for increased data collection and research on links between climate and health, and tracking of climate-related diseases as part of a national Monitoring and Evaluation system. The South African National Department of Health adds to the NCCRP by expanding further on the potential health impacts of climate change in its draft National Climate Change and Health Adaptation Plan (Department of Health, 2012).

Fourteen research and review articles, commentaries and editorials were published thus far on the *anticipated* health effects due to climate or climate change in South Africa and the need for local epidemiological studies to assist policy makers in formulating preventive actions − the first nearly 40 years ago (Sweijd et al, 2015; Wright and Norval; 2015; Kjellstrom et al 2014; Bowles and Butler, 2014; Garland, 2014; Abayomi and Cowan, 2014; Wright et al 2014a; Wright and Norval; 2014; Wright et al 2014b; Myers et al, 2011a; Myers et al, 2011a; Bateman, 2009; Jones, 1997; Wyndham et al, 1978).

One of the key climatic change indicators is rising temperature as it has direct and indirect effects on health (Wright and Norval; 2015; Wright et al 2014a; Wright et al 2014b). Hanna and Tait (2015) reported in detail on the physiological and external environmental factors that determine human thermoregulation and acclimatisation. The underlying mechanisms for increases in deaths after exposure to high temperatures may be due to blood flow shifts to subcutaneous areas and away from the vital organs, in an effort to cool the body. Increased blood viscosity due to dehydration, elevated cholesterol levels and a higher sweating threshold in the elderly may trigger heat-related mortality in susceptible individuals. Factors that hamper sweating, such as high ambient humidity, reduced air currents or anticholinergic drugs reduce resistance to high temperature.

South Africa includes several Köppen-Geiger climatic zones. [18] It is estimated that the eastern parts of South Africa will become wetter, with the western and interior parts becoming drier during the next 100 years (Peel et al, 2007) By 2100, warming is projected to reach around 3−4°C along the South African coast, and 6−7°C inland, thus higher than the global average warming (Department of Environmental Affairs, 2010).

It is this likelihood of higher temperatures under climate change in South Africa that highlights the need to elucidate how the population responds to ambient temperature. As mentioned above, the results can assist local policy makers in formulating preventive actions. Globally, epidemiological studies investigated the relationship between non-heat wave or heat wave ambient temperature and cause-specific or all-cause non-accidental mortality (Basu, 2009; Hajat and Kosatsky 2010; Åström et al, 2011; Yu et al, 2012; Guo et al, 2014; Benmarhnia et al, 2015; Bunker et al, 2016) and morbidity (Åström et al, 2011; Lian et al, 2015; Bunker et al, 2016; Phung et al, 2016). The vast majority of these studies were conducted in developed countries. Few studies were conducted in developing countries and even fewer in Africa (Amegah et al, 2016).

It is likely that the overall effect of elevated temperature strongly depends on the type of health outcome (i.e. death or hospital admission; communicable or non-communicable; injury or non-injury) and the factors that have the potential to influence vulnerability. Globally the greatest burden of all the climate change indicators combined will fall on low and middle income countries (such as South Africa) due to a high burden of existing vulnerabilities such as poverty, informal housing with poor protection against heat, inadequate public health services, pre-existing diseases such as TB, HIV/AIDS, dementia, diabetes, chronic respiratory and cardiovascular diseases (Basu, 2009; Hajat and Kosatsky 2010; Åström et al, 2011; Yu et al, 2012; Guo et al, 2014; Benmarhnia et al, 2015; Lian et al, 2015; Amegah et al, 2016; Bunker et al, 2016; Phung et al, 2016).

Amegah et al (2016) reported in a review on the association between daily temperature and all-cause mortality from *only* four time-series epidemiological studies conducted in Sub-Saharan Africa. Only one study, that was conducted in Cape Town, South Africa using data from the 1990s, controlled for air pollution as a possible confounder, specifically for particulate matter with a diameter small than $10\mu m$ (PM_{10}) (McMichael et al, 2008). Three of the four studies were not based on large national representative mortality data sets and generally had small sample sizes (Azongo et al, 2012; Diboulo et al, 2012; Egondi et al, 2012). The four studies investigated different age groups (even smaller sample sizes), but did not test whether the stratified and unstratified results differed significantly.

The present study is the very first epidemiological study using large national representative data from in three major cities in South Africa: Cape Town, Durban and Johannesburg. These three cities are located in different Köppen-Geiger climatic zones. Cape Town has a Mediterranean climate (Csb). Durban has a humid subtropical climate (Cfa), which closely borders a tropical wet and dry climate (Aw). Johannesburg has a subtropical highland climate (Cwb). The study also addressed some of the limitations of the previous studies from Sub-Saharan Africa: investigated confounding by PM_{10} and explored effect modification by age and sex by stratification and interaction models.

The objective was to investigate the association between daily ambient apparent temperature (Tapp) and daily all-cause non-accidental mortality (hereafter all-cause mortality) during the study period 2006–2010. Susceptibility by sex and age groups (<15 years, 15−64 years and ≥65 years) was also investigated.

2. Methods
Ethical approval (reference 341/2014) was obtained from the Research Ethics Committee, Faculty of Health Sciences, University of Pretoria in 2014 (Supplementary text 1).

2.1 Study design
As in other studies, the associations were investigated with the case-crossover epidemiological design (Basu, 2009; Hajat and Kosatsky 2010; Åström et al, 2011; Wichmann et al, 2011; Yu et al, 2012; Guo et al, 2014; Benmarhnia et al, 2015; Lian et al, 2015; Amegah et al, 2016; Bunker et al, 2016; Phung et al, 2016).

The case-crossover epidemiological study design was developed as a variant of the case-control design to study the effects of transient exposures on emergency events, comparing each person's exposure in a time period just prior to a case-defining event with person's exposure at other times (Maclure, 1991). If the control days are chosen close to the event day,

personal characteristics that vary slowly over a short time period of 24 hours are controlled by matching. Such characteristics may include co-morbidities (e.g. HIV status, hypertension), smoking status and so forth). Nevertheless, such characteristics may be potential effect modifiers, i.e. indicate susceptibility. However, information on such characteristics is not provided by mortality registers.

The time-stratified approach was applied to select the control days, defining the day of death as the case day and same day of the week in the same month and year as control days (i.e. theoretically 3 to 4 control days per case day) (Carracedo-Martínez et al, 2010).

Although intra-individual factors cannot be examined due to the nature of the case-crossover design where each person is his/her own control, inter-individual variation using an interaction term between the susceptibility variable and an exposure variable in the model yields the possibility to detect a p-value for interaction and when significant the subgroup specific estimates are valid. Hence the case-crossover design was selected as the main analysis and not the time-series design (see Section 2.3). In the time-series design it is not possible to include interaction terms in the models as the unit of analysis is on the population level, i.e. number of deaths per day. Only stratified analyses can be run, but the significance of the difference between the ORs of the stratified analysis and the unstratified analysis cannot be determined.

2.2 Exposure and mortality data

City-level all-cause non-accidental mortality data (International Classification of Disease, 10th version [ICD-10] (A00–R99) were obtained from Statistics South Africa after a lengthy waiting period. Data were obtained for the study period 1 January 2006 – 31 December 2010. A strict data agreement was signed. Generally, all-cause mortality is often used to avoid the common misclassification of temperature-related mortality (Hajat and Kosatsky, 2010).

Hourly temperature (°C) and relative humidity (%) data for the three cities were obtained from the South African Weather Service (SAWS) for the study period, after signing a data agreement.

The main exposure of interest was apparent temperature (Tapp), which reflects the physiological experience of combined exposure to humidity and temperature and thereby better capture the response on health than temperature alone (Steadman 1984). According to Barnett et al (2010) there is no single temperature measure that is superior to others. More recently, Zhang et al (2014) concluded that Tapp appeared to be the most important predictor for heat-related mortality. Tapp has been applied in several studies (Basu, 2009; Hajat and Kosatsky 2010; Åström et al, 2011; Wichmann et al, 2011; Yu et al, 2012; Guo et al, 2014; Benmarhnia et al, 2015; Lian et al, 2015; Amegah et al, 2016; Bunker et al, 2016; Phung et al, 2016).

A network of air pollution monitors in the three cities continuously assess real-time concentrations of the criteria air pollutants using equivalent methods of the United States Environmental Protection Agency and in accordance with ISO 17025 guidelines (National Environmental Management: Air Quality Act, 2004). The National Environmental Management: Air Quality Act of 2004 requires the monitoring of criteria air pollutants. Hourly air pollution data were obtained from SAWS for the study period, after signing a data agreement. SAWS manages the data that are deposited in the South African Air Quality

Information System. In the end only PM_{10} was investigated as a possible confounder, due to large data gaps for the other pollutants (Supplementary table 1).

Daily 24-hour means (midnight-to-midnight) levels of Tapp and PM_{10} were calculated from the hourly data. A daily mean was based on at least 20 1-hour values in accordance with the ISO 17025 guidelines and was set as missing otherwise. The daily mean Tapp experienced throughout the whole day and night usually provides more easily interpreted results within a policy context (Anderson and Bell, 2009). An aggregated 24-hr mean for PM_{10} was calculated across the selected sites in each city, which as applied in the statistical analyses. Such an approach was applied in the large Air Pollution and Health: A European Approach (APHEA) study (Katsouyanni et al, 1996).

Influenza data were only available on provincial level and as weekly data. The method from the APHEA study was thus used to control for influenza: a dummy variable taking the value of one when the 7-day moving average of the respiratory disease mortality was greater than the 90th percentile of its city-specific distribution during the entire study period of 1 January 2006 to 31 December 2010 (Touloumi et al, 2004; Samoli et al., 2005).

2.3 Statistical analysis
Correlation between Tapp and PM_{10} were investigated using Pearson correlation analyses.

There is no standard method to select lags (Anderson et al., 2007; Basu, 2009; Hajat and Kosatsky 2010; Åström et al, 2011; Wichmann et al, 2011; Yu et al, 2012; Guo et al, 2014; Benmarhnia et al, 2015; Lian et al, 2015; Amegah et al, 2016; Bunker et al, 2016; Phung et al, 2016). Most studies on heat effects selected short lags, e.g. lag0 (same day of exposure as day of death), lag1 (day prior to day of death) or lag0-1 (mean of lag0 and lag1). Hence the results in the present study will focus on lag0-1. Other lags were nevertheless also investigated (Supplementary figures 1 to 9).

As in other studies, the shape (i.e. linear or non-linear) of the association between the lag0-1 of Tapp and all-cause non-accidental mortality in each city was first investigated in the time-series epidemiological study design lags (Basu, 2009; Hajat and Kosatsky 2010; Åström et al, 2011; Wichmann et al, 2011; Yu et al, 2012; Guo et al, 2014; Benmarhnia et al, 2015; Lian et al, 2015; Amegah et al, 2016; Bunker et al, 2016; Phung et al, 2016). The time-series and time-stratified case-crossover designs are equivalent to each other (Lu and Zeger, 2007). Quasi-Poisson generalised additive models (GAM) were applied as the distribution of daily counts of deaths typically has an overdispersed Poisson distribution. The gam procedure and mgcv package of the R statistical software was applied (R Development Core Team, 2016). The gam procedure in R produces graphs that can easily be used to visually inspect linearity.

For Cape Town and the 0–14 year age group the GAM equation is given below.

$$\log(E(Y_t) = \alpha + \ s_1 \ (Tapp_t,3) + \ s_2(time,5*year) + \beta_1 PM_{10t} + \ \eta I_{dow} + \beta_2 I_{flu} + \beta_3 I_{hol}$$

where t refers to the day of the observation, α refers to the intercept, $E(Y_t)$ refers to the expected mortality count on day t, s refers to smoothing splines, $Tapp_t$ refers to the daily mean Tapp on day t, $time$ refers to calendar time (seasonality) numbered from 1 (1 January 2006) to 1826 (31 December 2010), PM_{10t} as a linear term refers to the daily mean PM_{10} on day t, I_{dow}, I_{flu} and I_{hol} are indicators for day of the week, influenza epidemics and public holidays.

β and η are coefficients. 3 degrees of freedom (df) were applied to smooth the Tapp variable. Lag0-1 of Tapp and PM_{10} were used in the GAM analyses.

The optimal df for *time* was selected that minimised the sum of the absolute values of the partial autocorrelation function (PACF) of the model's residuals. See Supplementary table 2 for df used for *time* for the other cities and other age groups

Whether the non-linear term of lag0-1 of Tapp (i.e. $s(Tapp_t,3)$) improved the model was checked with log likelihood ratio tests, i.e. compared it to a model that included $Tapp_t$ and not $s(Tapp_t,3)$. It was observed that the non-linear terms of Tapp (lag0-1) were significant and added value to the model for some of the age groups (Supplementary figures 10 to 12).

The minimum Tapp of a city is the threshold if Tapp has a linear association with all-cause non-accidental mortality across its range. However, it was decided to use the same city-specific threshold for the three age groups, i.e. that of the ≥65 year old group, which was higher than the minimum Tapp of each city. The reason for this is that only one Tapp threshold for a city can be used in the case-crossover analyses when investigating interaction between Tapp and age groups.

Crude city-specific thresholds were first determined by visual inspection of the graphs produced after running the GAM in R – as done in previous studies (Yu et al, 2011). The crude city-specific thresholds were: Cape Town (15°C), Durban (20°C), Johannesburg (13°C) (Supplementary figures 10 to 12). Fine tuning was then applied to select the city-specific Tapp thresholds using R. Quasi Akaike Information Criteria (AIC) values were iteratively calculated using 0.1°C increments increase in Tapp from 10°C to 25°C, which was selected based on the visual inspection of the graphs (Yu et al, 2011). The temperature corresponding to the model with the lowest quasi AIC value was chosen as the threshold Tapp. The city-specific thresholds were 18.6°C, 24.8°C and 18.7°C, respectively for Cape Town, Durban and Johannesburg.

The association between Tapp and all-cause non-accidental mortality above the city-specific thresholds was then investigated with the case-crossover design using conditional logistic regression models (PROC PHREG in SAS 9.2, SAS Institute, Cary, NC). Models were adjusted for public holiday variable (binary variable), influenza (binary variable) and PM_{10} (Supplementary figures 1 to 9). The same lag (e.g. lag0-1) for Tapp and PM_{10} were used in a model. Previous studies reported a linear relationship between the PM_{10} and all-cause non-accidental mortality, as observed in this study (Supplementary figures 13–15). PM_{10} was therefore adjusted for as a linear term.

Odds ratios (OR) and the 95% confidence intervals (CI) were calculated per inter-quartile range (IQR) increase in Tapp. This approach is commonly applied in other studies. The results were presented as the per cent excess risk in mortality per IQR increase in Tapp.

Susceptibility by sex and age groups (<15 years, 15–64 years and ≥65 years) were investigated in stratified analyses (to get subgroup estimates, see Section 2.1) for each city separately, followed by the inclusion of interaction terms in the city-specific model (Basu, 2009).

In the meta-analysis, the heterogeneity of the Tapp associations with mortality in the three cities was assessed for all ages and the three age groups. As there was not significant effect

modification by sex within age groups, no meta-analysis was done for the sex within age groups. A fixed-effect model was applied to summarise the pooled estimates as the Q and I^2 test statistics for heterogeneity were insignificant, except for the ≥65 year group for which heterogeneity was significant and a random-effect model was applied. The meta package of the R statistical software was applied (R Development Core Team, 2016).

Results

Over 460 000 all-cause non-accidental deaths occurred in Cape Town, Durban and Johannesburg during 2006–2010 (Table 1). The top five causes of death in the three cities were infectious and parasitic diseases (including HIV/AIDS) (A00–B99), diseases of the circulatory system (including cardiovascular and cerebrovascular system) (I00–I99), diseases of the respiratory system (J00–J99), neoplasms (cancer) (C00-D48) and endocrine, nutritional and metabolic diseases (E00–E90).

Table 1. Characteristics of all-cause non-accidental deaths in Cape Town, Durban and Johannesburg, South Africa during 2006–2010.

	Cape Town		Durban		Johannesburg	
	n	%	n	%	n	%
Population in 2011[a]	3 740 026	-	3 442 361	-	4 434 827	-
Total	123 951	100.0	177 298	100.0	163 022	100.0
Sex						
Male	62 538	50.5	84 910	47.9	80 884	49.6
Female	61 111	49.3	92 152	52.0	81 500	50.0
Missing	302	0.2	236	0.1	638	0.4
Age						
0-14 years	9 778	8	18 131	10	17 995	11
15-64 years	64 710	52	114 930	65	98 483	60
≥65 years	49 144	40	43 458	25	45 721	28
Missing	319	0	779	0	823	1

n: Number of deaths
[a]http://www.statssa.gov.za/?page_id=964

Table 1 summarises the characteristics of the deaths. The majority of deaths occurred in the 15–64 year group in all three cities (also see Table 3). Supplementary table 3 lists the causes of death for these three age groups in the three cities.

Table 2 summarises the descriptive statistics for daily meteorological and PM_{10} levels. The mean Tapp was 17, 23 and 15°C, respectively in Cape Town, Durban and Johannesburg. The highest mean PM_{10} was observed in Johannesburg (57.3 µg.m^{-3}). The daily PM_{10} levels exceeded the more conservative daily World Health Organization air quality guideline of 50 µg.m^{-3} on 200, 207 and 807 days, respectively in Cape Town, Durban and Johannesburg (World Health Organization, 2006). Tapp (lag0-1) had a weak correlation with PM10 (lag0-1) on days above the city-specific thresholds, namely 0.208 (587 days, p<0.0001), 0.085 (527 days, p=0.0517) and 0.128 (365 days, p=0.015), respectively in Cape Town, Durban and Johannesburg.

Figure 1 and Supplementary table 4 summarises the association between Tapp (lag0-1) and all-cause non-accidental mortality in the three cities, also by age groups and sex. The strongest association for all age groups combined was observed in Cape Town, namely 3.3% increase in mortality per IQR increase in Tapp (lag0-1) (3°C) above the city-specific threshold (18.6°C). A stronger association was observed in the ≥65 year group in Cape Town,

Table 2. Descriptive statistics for daily meteorological and PM$_{10}$ levels in Cape Town, Durban and Johannesburg, South Africa during 2006–2010.

	n missing	Mean	SD	Range	Percentiles 25th	50th	75th
Cape Town (1826 days)							
Tapp (°C)	2	16.6	4.6	6.0–31.0	13.0	16.0	20.0
Temperature (°C)	2	17.0	3.7	8.0–29.0	14.0	17.0	20.0
Relative humidity (%)	1	74.1	10.2	37.0–98.0	67.0	75.0	81.0
PM$_{10}$ (µg/m^3)	176	32.8	14.6	7.9–121.5	22.2	29.8	41.3
Durban (1826 days)							
Tapp (°C)	4	22.6	5.0	10.0–34.0	19.0	23.0	26.0
Temperature (°C)	4	21.0	3.1	12.0–28.0	19.0	21.0	23.0
Relative humidity (%)	4	75.6	8.8	36.0–97.0	71.0	77.0	81.0
PM$_{10}$ (µg/m^3)	300	32.2	19.2	5.8–146.4	19.5	27.1	38.4
Johannesburg (1826 days)							
Tapp (°C)	20	15.0	4.9	0.0–25.0	11.0	16.0	19.0
Temperature (°C)	20	16.4	4.3	2.0–26.0	13.0	17.0	20.0
Relative humidity (%)	20	56.1	19.2	10.0–98.0	41.0	57.0	71.0
PM$_{10}$ (µg/m^3)	269	57.3	27.5	7.7–273.3	37.4	51.0	72.5

SD: Standard deviation
IQR: Interquartile range
n: Number of days
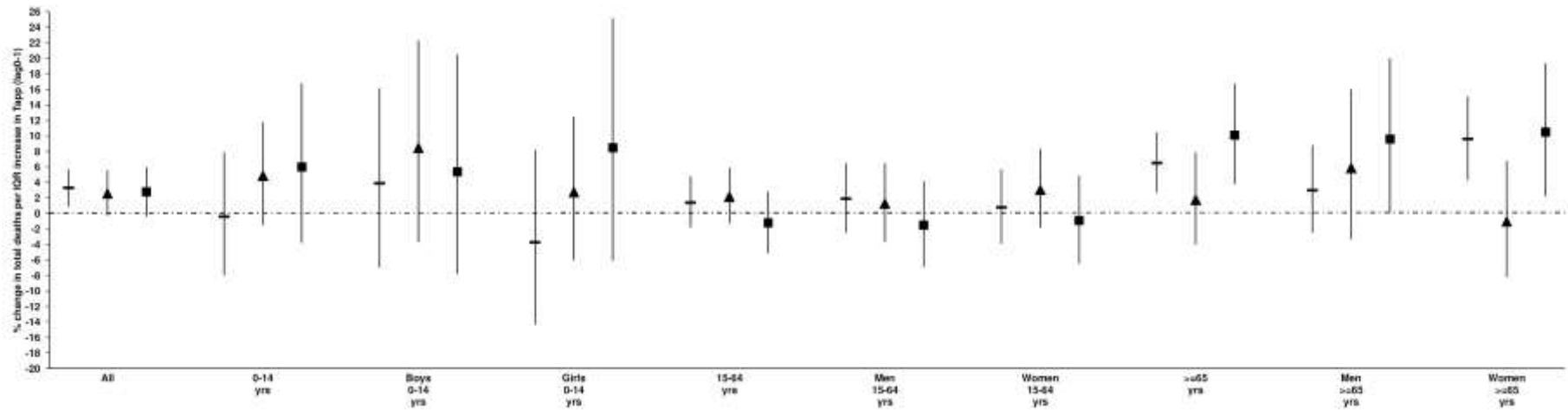
Figure 1. Association between Tapp (lag0-1) (in °C) and all-cause non-accidental mortality in Cape Town (–), Durban (▲) and Johannesburg (■) expressed as percentage increase in risk (%) and 95% confidence intervals per inter-quartile increase above the city-specific Tapp (lag0-1) threshold during 1 January 2006–31 December 2010 in South Africa.

Adjusted for public holidays. influenza and PM10.

City-specific thresholds: Cape Town (18.6°C), Durban (24.8°C), Johannesburg (18.7°C)

Cape Town: Interaction term p = 0.0139 for age groups. But interaction term p > 0.05 for sex within age groups

Durban: Interaction term p > 0.05

Johannesburg: Interaction term p > 0.05

More info in Supplementary table 4.

namely 6.5% increase in mortality, however not significantly different from all age groups combined (interaction p>0.05). Women in the ≥65 year group in Cape Town were significantly more vulnerable compared to men in this age group (interaction p < 0.05).

An increase in Tapp (lag0-1) above the city-specific thresholds was associated with 2.6% and 2.8% increase in all-cause non-accidental mortality in Durban and Johannesburg, albeit insignificantly. No vulnerable groups were identified in Durban. A stronger association was observed in the ≥65 year group in Johannesburg, namely 10.1% increase in mortality per IQR increase in Tapp (lag0-1) (2°C) above the city-specific threshold (18.7°C), however not significantly different from all age groups combined (interaction p>0.05). Women in the ≥65 year group in Johannesburg appeared to be more vulnerable compared to men in this age group, although significantly (interaction p > 0.05).

The meta-analysis indicated an overall significant increase of 0.9% in all-cause non-accidental mortality per 1°C increase in Tapp (lag0-1) for all age groups combined in the three cities. This translates to 2.7% (95% CI: 1.2–4.2) per IQR increase in Tapp (lag0-1) (3°C) (Figure 2 and Supplementary table 5). For the ≥65 year group a significant increase of 2.1% in mortality was observed, which translates to 6.5% (95% CI: 0.5–12.8) per IQR increase in Tapp (lag0-1) (3°C) (Table 4).
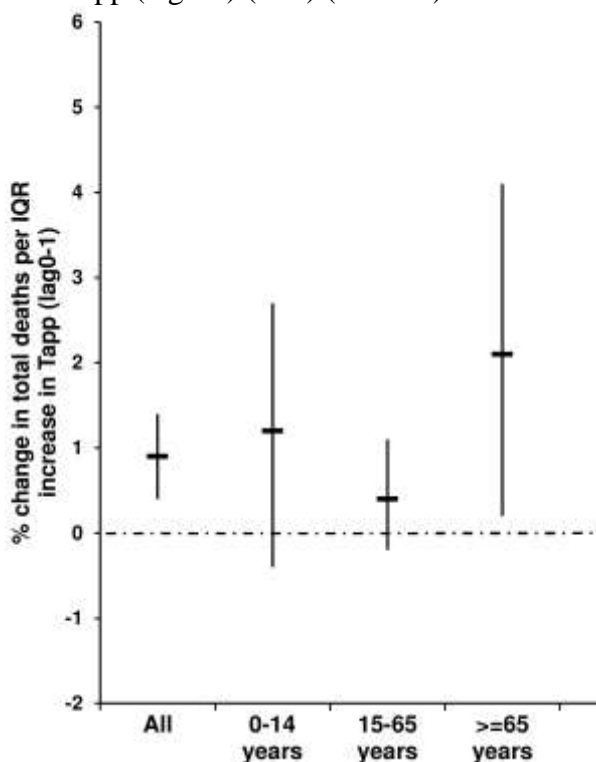
Figure 2. Overall pooled association between Tapp (lag0-1) (in °C) and all-cause non-accidental mortality expressed as percentage increase in risk (%) and 95% confidence intervals per unit increase above the city-specific threshold during 1 January 2006–31 December 2010 in Cape Town, Durban and Johannesburg, South Africa.
More info in Supplementary table 5.

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3. Discussion

This is the first study that investigated the association between the daily ambient Tapp and all-cause non-accidental mortality in three major cities in South Africa. The results of the study suggest that the general population has an increased risk of death with increasing Tapp above the city-specific thresholds.

The city-specific Tapp thresholds in this study were close to the city-specific 75th percentiles. A recent review also observed this across for 306 communities located in various climatic zones, which included only one study from Kenya (Egondi et al, 2012; Guo et al., 2014). The 75th percentile temperature thresholds of four studies conducted in Africa varied from 17.0° to 30.6 °C (Amegah et al, 2016). This is consistent with minimum-mortality temperatures in communities with cooler climatic zones being lower than in communities in warmer climatic zones. It is plausible that people adapt to their local climates by physiological, behavioural and technological adjustments (Basu, 2009; Hajat and Kosatsky 2010; Åström et al, 2011; Wichmann et al, 2011; Yu et al, 2012; Guo et al, 2014; Benmarhnia et al, 2015; Lian et al, 2015; Amegah et al, 2016; Bunker et al, 2016; Phung et al, 2016). Hence, globally the minimum-mortality temperatures are much lower than the body's core temperature of 38°C (Hanna and Tait, 2015). The present study's city-specific Tapp thresholds are also lower than those from the USA National Weather Service symptom chart that was applied by local researchers recently (Garland et al, 2015; National Weather Service Weather Forecast Office, 2016).

Amegah et al (2016) reported in a review on the association between daily temperature (not Tapp) and all-cause mortality (mostly including accidental deaths) from four time-series studies conducted in Sub-Saharan Africa (McMichael et al., 2008; Azongo et al, 2012; Diboulo et al., 2012; Egondi et al, 2012). Three studies observed non-linear associations (McMichael et al., 2008; Azongo et al, 2012; Egondi et al, 2012) and all four observed that the highest risk occurred at short lags (e.g. lag0-1).

McMichael et al (2008) reported on the association between daily temperature (not Tapp) and all-cause non-accidental mortality among all age groups in Cape Town during 1996–1999, namely a 0.5% (95% CI: −0.3–1.2) increase per 1 °C increase above the threshold (17.0°C). This is close to the present study's finding in Cape Town during 2006–2010 of a 1.1% (95% CI: 0.3–1.9) increase per 1 °C increase in Tapp above the threshold (18.6°C). As in most other studies, accidental deaths were excluded in the present study when investigating all-cause mortality (McMichael et al., 2008; Basu, 2009; Hajat and Kosatsky 2010; Åström et al, 2011; Wichmann et al, 2011; Yu et al, 2012; Guo et al, 2014; Benmarhnia et al, 2015; Lian et al, 2015; Bunker et al, 2016; Phung et al, 2016).

The pooled risk for all age groups combined in this study is similar to that of a study from Ghana: 1.1% significant increase in all-cause mortality risk per 1°C increase in daily temperature above 30.6 °C (Azongo et al, 2012). A review also reported similar risks for all age groups combined: 1–3% increase in all-cause mortality risk per 1°C increase above city-specific thresholds (Hajat and Kosatsky, 2010). The review included mostly studies from developed countries, but also two studies from China and Lebanon. Two other studies from Sub-Saharan Africa reported 0.0% (95% CI: 0.0–1.0) and 2.6% (95% CI: 0.1–5.2) increased risk in Kenya (above 20.0 °C) and Burkina Faso (above minimum of 20.0°C), respectively (Diboulo et al., 2012; Egondi et al, 2012).

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The present study's findings suggest that the population in South Africa may not necessarily be more vulnerable to heat-related mortality than those in developed countries. A recent meta-regression analysis by Guo et al (2014) also concluded this when developing to developed countries were compared. However, Guo et al (2014) stressed that it is premature to consider this as strong evidence, hence more research is needed in developing countries.

The present study along with reviews and meta-analyses are strengthening evidence that the elderly are more vulnerable to heat exposure (Basu, 2009; Hajat and Kosatsky 2010; Åström et al, 2011; Wichmann et al, 2011; Yu et al, 2012; Guo et al, 2014; Benmarhnia et al, 2015; Lian et al, 2015; Bunker et al, 2016; Phung et al, 2016). The pooled risk for the ≥65 year group in this study is similar to that of a meta-analysis that included 15 studies and nearly 13 million all-cause deaths in developed and developing countries, but none from Africa (Yu et al, 2012). The four studies reviewed by Amegah et al investigated different age groups (small sample sizes), but did not test whether the stratified and unstratified results differed significantly (McMichael et al., 2008; Azongo et al, 2012; Diboulo et al., 2012; Egondi et al, 2012).

Benmarhnia et al (2015) investigated vulnerability to heat-related mortality in a meta-analysis of 41 studies that were conducted developed and developing countries (but none from Africa). They reported a 2% increase in all-cause mortality among the ≥65 year group compared to the 15-64 year group per 1°C increase in temperature indicator. This is exactly what the present study also observed in the pooled effects from the meta-analysis.

Hanna and Tait (2015) discussed in-depth the current evidence of the physiological and behavioural processes involved in coping with increasing and decreasing ambient temperatures, the operational thermal range of thermoregulation and protection afforded by acclimatisation. Numerous biological mechanisms have been suggested for susceptible groups to heat-related mortality, mostly the elderly (Basu, 2009; Hajat and Kosatsky 2010; Åström et al, 2011; Wichmann et al, 2011; Yu et al, 2012; Guo et al, 2014; Benmarhnia et al, 2015; Hanna and Tait, 2015; Lian et al, 2015; Bunker et al, 2016; Phung et al, 2016). Physiological responses to variable ambient temperatures decline with ageing, such as reduced ability to maintain core temperature, reduced sweat gland output, reduced skin blood flow, smaller increase in cardiac output and less redistribution of blood flow from renal and splanchnic circulations. The elderly are also more likely to take medication that may interfere with an already weak thermoregulation. In healthy people, when body temperatures rise, blood flow generally shifts from the vital organs to underneath the skin's surface in an effort to cool down. This may not be optimal in the elderly. Furthermore, thermoregulation may be impeded when too much blood is diverted, putting increased stress on the heart and lungs. Additionally mental disorders, such as dementia, also alter risk perception and protective behaviours. Social factors, such as living alone, living in nursing homes or being confined to bed also adds to the increased risk.

Elderly women have been reported to be more vulnerable than elderly men to heat exposure in some studies, as in the present study's findings for Cape Town (Basu, 2009; Hajat and Kosatsky 2010; Åström et al, 2011; Yu et al, 2012; Guo et al, 2014; Benmarhnia et al, 2015; Lian et al, 2015; Bunker et al, 2016; Phung et al, 2016). However, it is not certain whether the gender effect may be due to social factors described above.

A report by Bradshaw et al (2010) concluded that South Africa fits into the category of countries with medium rather than poor quality. Many European countries are in the medium quality category. Another advantage of the present study is that the days with missing exposure data and the actual number of deaths included in the regression models were reported, unlike most studies.

A limitation of all case-crossover and time-series epidemiological studies is the assumption that the ambient air pollution and meteorological variables measured at a few sites are the same across the entire city, which might have resulted in a measurement error. This exposure misclassification is non-differential and bias the effect estimates towards the null (Hatch and Thomas, 1993).

As with other studies that used temperature data of the past one to two decade, the estimates of temperature-mortality relationships are limited to the range of observable temperature data under current climate conditions. While this may be adequate for near-term predictions of climate-attributable health impacts, scenarios indicate that temperatures in South Africa will exceed currently observed ranges with consequent health impacts that are difficult to predict (Department of Environmental Affairs, 2010).

4. Conclusions

This study is very relevant in stressing the importance of increasing Tapp on all-cause non-accidental mortality risk in South Africa, especially among the elderly. The observed risk is similar to that of developed and developing countries. In line with other studies, the city-specific Tapp thresholds are much lower than the body's core temperature of 38°C. The results can be used by local policy makers in formulating preventive actions, e.g. early warning systems. The observed exposure-responses can be applied in risk assessments to estimate the impact of increased Tapp in the country due to projected climate change. Future research should investigate the association between Tapp and cause-specific mortality and also morbidity.

Conflicts of Interest

The author declares no conflict of interest.

References

Abayomi, A., Cowan, M.N., 2014. The HIV/AIDS epidemic in South Africa: Convergence with tuberculosis, socioecological vulnerability, and climate change patterns. S. Afr. Med. J. 104(8), 583.

Amegah, A.F., Rezza, G., Jaakkola, J.J.K., 2016. Temperature-related morbidity and mortality in Sub-Saharan Africa: A systematic review of the empirical evidence. Environ. Int. 91, 133–149. doi: 10.1016/j.envint.2016.02.027.

Anderson, B.G., Bell, M.L., 2009. Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. Epidemiology. 20, 205–213. doi: 10.1097/EDE.0b013e318190ee08.

Anderson, H.R., Atkinson, R.W., Bremner, S.A., et al., 2007. Quantitative systematic review of short term associations between ambient air pollution (particulate matter, ozone, nitrogen dioxide, sulphur dioxide and carbon monoxide), and mortality and morbidity. Report to Department of Health revised following first review. Available: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_121200. Last accessed 16 September 2016.

Åström, D.O., Forsberg, B., Rocklöv, J., 2011. Heat wave impact on morbidity and mortality in the elderly population: a review of recent studies. Maturitas. 69(2), 99–105. doi: 10.1016/j.maturitas.2011.03.008.

Azongo, D.K., Awine, T., Wak, G., et al., 2012. A time series analysis of weather variability and all-cause mortality in the Kasena-Nankana Districts of Northern Ghana, 1995–2010. Glob. Health Action. 5, 14–22. doi: 10.3402/gha.v5i0.19073.

Barnett, A.G., Tong, S., Clements, A.C.A., 2010. What measure of temperature is the best predictor of mortality? Environ. Res. 110, 604–611. doi: 10.1016/j.envres.2010.05.006.

Basu, R., 2009. High ambient temperature and mortality: a review of epidemiologic studies from 2001 to 2008. Environ. Health. (40). doi:10.1186/1476-069X-8-40.

Bateman, C., 2009. Climate change kills at least 300 000 every year. S. Afr. Med. J. 99(1), 20–24.

Benmarhnia, T., Deguen, S., Kaufman, J.S., et al. 2015. Vulnerability to Heat-related Mortality: A Systematic Review, Meta-analysis, and Meta-regression Analysis. Epidemiology. 26(6), 781–793. doi: 10.1097/EDE.0000000000000375.

Bowles, D.C., Butler, C.D., 2014. Socially, politically and economically mediated health effects of climate change: Possible consequences for Africa. S. Afr. Med. J. 104(8), 585.

Bradshaw, D., Pillay-Van Wyk, V., Laubscher, R. et al., 2010. Cause of Death Statistics for South Africa: Challenges and Possibilities for Improvement. Available: http://www.mrc.ac.za/bod/cause_death_statsSA.pdf. Last accessed 19 September 2016.

Bunker, A., Wildenhain, J., Vandenbergh, A., et al., 2016. Effects of Air Temperature on Climate-Sensitive Mortality and Morbidity Outcomes in the Elderly; a Systematic Review and Meta-analysis of Epidemiological Evidence. EBioMedicine. 6, 258–268. doi: 10.1016/j.ebiom.2016.02.034.

Byass, P., 2009. Climate change and population health in Africa: where are the scientists? Glob. Health. Action. 2. doi: 10.3402/gha.v2i0.2065.

Carracedo-Martínez, E., Taracido, M., Tobias, A. et al., 2010. Case-crossover analysis of air pollution health effects: a systematic review of methodology and application. Environ. Health Perspect. 118(8), 1173–1182. doi: 10.1289/ehp.0901485.

Department of Environmental Affairs. National Climate Change Response Plan White Paper, 2011. Pretoria.

Department of Environmental Affairs. South Africa's Second National Communication Under the United Nations Framework Convention on Climate Change. 2010. Pretoria.

Department of Health. National Climate Change and Health Adaptation Plan, 2012. Pretoria.

Diboulo, E,. Sié, A., Rocklöv, J., et al., 2012. Weather and mortality: a 10 year retrospective analysis of the Nouna Health and Demographic Surveillance System, Burkina Faso. Glob. Health Action. 5, 6–13. doi: 10.3402/gha.v5i0.19078.

Egondi ,T., Kyobutungi, C., Kovats, S., et al., 2012. Time-series analysis of weather and mortality patterns in Nairobi's informal settlements. Glob. Health Action. 5, 23–32. doi: 10.3402/gha.v5i0.19065.

Garland, R.M., 2014. National policy response to climate change in South Africa. S. Afr. Med. J. 104(8), 584.

Garland, R.M., Matooane, M., Engelbrecht, F.A., et al. 2015. Regional projections of extreme apparent temperature days in Africa and the related potential risk to human health. Int. J. Environ. Res. Public Health. 12(10), 12577–12604. doi: 10.3390/ijerph121012577.

Guo, Y., Gasparrini, A., Armstrong, B., et al., 2014. Global variation in the effects of ambient temperature on mortality: a systematic evaluation. Epidemiology. 25(6), 781-9. doi: 10.1097/EDE.0000000000000165.

Hajat, S., Kosatsky, T., 2010. Heat-related mortality: a review and exploration of heterogeneity. J. Epidemiol. Community. Health. 64(9), 753–760. doi: 10.1136/jech.2009.087999.

Hanna, E.G., Tait, P.W., 2015. Limitations to Thermoregulation and Acclimatization Challenge Human Adaptation to Global Warming. Int. J. Environ. Res. Public Health. 12, 8034–8074. doi: 10.3390/ijerph120708034.

Hatch, M., Thomas, D. 1993. Measurement issues in environmental epidemiology. Environ. Health Perspect. 101, 49–57.

Jones, J.S., 1997. Climate change and human health. S. Afr. Med. J. 87(1), 13-4.

Katsouyanni, K., Schwartz, J., Spix, C., et al., 1996. Short term effects of air pollution on health: a European approach using epidemiologic time series data: the APHEA protocol. J. Epidemiol. Community. Health. 50, S12–S18.

Kjellstrom, T., Lemke, B., Hyatt, O., Otto, M., 2014. Climate change and occupational health: A South African perspective. S. Afr. Med. J. 104(8), 586.

Lian, H., Ruan, Y., Liang, R., et al. 2015. Short-term effect of ambient temperature and the risk of stroke: A systematic review and meta-analysis. Int. J. Environ. Res. Public Health. 12(8), 9068–9088. doi: 10.3390/ijerph120809068.

Lu, Y., Zeger, S.L., 2007. On the equivalence of case-crossover and time series methods in environmental epidemiology. Biostatistics. 8(2), 337–344.

Maclure, M. The case-crossover design: A method for studying transient effects on the risk of acute events. Am J Epidemiol 1991;133:144–153.

McMichael, A.J,. Wilkinson, P., Kovats, R.S., et al., 2008. International study of temperature, heat and urban mortality: the "ISOTHURM" project. Int. J. Epidemiol. 37(5), 1121–1131. doi: 10.1093/ije/dyn086.

Myers, J., Young, T., Galloway, M., Manyike, P., Tucker, T., 2011a. Responding to climate change in southern Africa - the role of research. S. Afr. Med. J. 101(11), 820–822.

Myers, J., Young, T., Galloway, M., Manyike, P., Tucker, T., 2011b. A public health approach to the impact of climate change on health in southern Africa – identifying priority modifiable risks. S. Afr. Med. J. 101(11), 817–820.

National Environmental Management: Air Quality Act. 2004. Available: http://www.saaqis.org.za/filedownload.aspx?fileid=22. Last accessed 19 September 2016.

National Weather Service Weather Forecast Office: Amarillo, T.X. What Is the Heat Index? 2016. Available: http://www.srh.noaa.gov/ama/?n=heatindex. Last accessed 16 September 2016.

Peel, M.C., Finlayson, B.L., McMahon, T.A., 2007. Updated world map of the Köppen-Geiger climate classification. Hydrol. Earth Syst. Sci. 11, 1633–1644.

Phung, D., Thai, P.K., Guo, Y., et al., 2016. Ambient temperature and risk of cardiovascular hospitalization: An updated systematic review and meta-analysis. Sci. Total. Environ. 550, 1084–1102. doi: 10.1016/j.scitotenv.2016.01.154.

Samoli, E., Analitis, A., Touloumi, G., Schwartz, J., Anderson, H.R., Sunyer, J., et al., 2005. Estimating the exposure–response relationships between particulate matter and mortality within the APHEA Multicity Project. Environ. Health Perspect. 113, 88–95. doi:10.1289/ehp.7387

Steadman, R., 1984. A Universal Scale of Apparent Temperature. J. Climate Appl. Meteor. 23, 1674–1687, doi: 10.1175/1520-0450

Sweijd, N.A., Wright, C.Y., Westwood, A., Rouault, M., Landman, W.A., MacKenzie, M.L., et al., 2015. Climate change is catchy--but when will it really hurt? S. Afr. Med. J. 105(12), 1018–1023. doi: 10.7196/SAMJ.2015.v105i12.10332.

Touloumi, G., Atkinson, R., Le Tertre, A., et al., 2004. Analysis of health outcome time series data in epidemiological studies. Environmetrics. 15, 101–117. doi: 10.1002/env.623.

Wichmann, J., Andersen, Z.J., Ketzel, M. et al., 2011. Apparent temperature and cause-specific mortality in Copenhagen, Denmark: a case-crossover analysis. Int. J. Environ. Res. Public Health. 8(9), 3712–3727. doi: 10.3390/ijerph8093712.

World Health Organization: Air Quality Guideline Global Update 2005. Copenhagen, Denmark. 2006. Available: http://www.who.int/phe/health_topics/outdoorair_aqg/en. Last accessed 20 September 2016.

Wright, C.Y., Garland, R.M., Norval,, M., Vogel, C., 2014a. Human health impacts in a changing South African climate. S. Afr. Med. J. 104(8), 579–582.

Wright, C.Y., Mathee, A., Garland, R.M., 2014b. Climate change, human health and the role of environmental health practitioners. S. Afr. Med. J. 104(8), 518–519. doi: 10.7196/samj.7994.

Wright, C.Y., Norval, M., 2014. Climate change: One of the greatest threats to public health in the 21st century. S. Afr. Med. J. 104(8): 578.

Wright, C.Y., Norval, M., Albers, P.N., 2015. Climate change, public health and COP21—a South African perspective. S. Afr. Med. J. 105(12), 997–998. doi:10.7196/SAMJ.2015.v105i12.10232.

Wyndham, C.H., Fellingham, S.A., 1978. Climate and disease. S. Afr. Med. J. 53(26), 1051–1061.

Yu, W., Hu, W,. Mengersen, K., et al., 2011. Time course of temperature effects on cardiovascular mortality in Brisbane, Australia. Heart. 97(13), 1089–1093. doi: 10.1136/hrt.2010.217166.

Yu, W., Mengersen, K., Wang, X,. et al., 2012. Daily average temperature and mortality among the elderly: a meta-analysis and systematic review of epidemiological evidence. Int J. Biometeorol. 56(4), 569–581.

Zhang, K., Li, Y., Schwartz, J.D. et al., 2014. What weather variables are important in predicting heat-related mortality? A new application of statistical learning methods. Environ. Res. 132, 350–359. doi: 10.1016/j.envres.2014.04.004.

Supplementary text 1

UNIVERSITEIT VAN PRETORIA
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Faculty of Health Sciences Research Ethics Committee

2/10/2014

Approval Certificate
New Application

Ethics Reference No.: 341/2014

Title: Increase in apparent temperature (Tapp) and risk to non-communicable disease deaths in South Africa during 2006-2010

Dear Dr Janine Wichmann

The **New Application** as supported by documents specified in your cover letter for your research received on the 25/09/2014, was approved by the Faculty of Health Sciences Research Ethics Committee on the 1/10/2014.

Please note the following about your ethics approval:
- Ethics Approval is valid for 3 years.
- Please remember to use your protocol number (**341/2014**) on any documents or correspondence with the Research Ethics Committee regarding your research.
- Please note that the Research Ethics Committee may ask further questions, seek additional information, require further modification, or monitor the conduct of your research.

Ethics approval is subject to the following:
- The ethics approval is conditional on the receipt of 6 monthly written Progress Reports, and
- The ethics approval is conditional on the research being conducted as stipulated by the details of all documents submitted to the Committee. In the event that a further need arises to change who the investigators are, the methods or any other aspect, such changes must be submitted as an Amendment for approval by the Committee.

We wish you the best with your research.

Yours sincerely

_____

Dr R Sommers; MBChB; MMed (Int); MPharMed.
Deputy Chairperson of the Faculty of Health Sciences Research Ethics Committee, University of Pretoria

The Faculty of Health Sciences Research Ethics Committee complies with the SA National Act 61 of 2003 as it pertains to health research and the United States Code of Federal Regulations Title 45 and 46. This committee abides by the ethical norms and principles for research, established by the Declaration of Helsinki, the South African Medical Research Council Guidelines as well as the Guidelines for Ethical Research: Principles Structures and Processes 2004 (Department of Health).

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** Kindly collect your original signed approval certificate from our offices, Faculty of Health Sciences, Research Ethics Committee, H W Snyman South Building, Room 2.33 / 2.34.

Supplementary table 1. Descriptive statistics for daily NO$_2$ and SO$_2$ levels (lag0) in Cape Town, Durban and Johannesburg, South Africa during 2006-2010.

	No. days missing data	Mean	SD	Range	Percentiles			IQR
					25th	50th	75th	
Cape Town (1826 days)								
NO$_2$ (µg/m^3)	535	17.5	8.7	3.4–59.8	11.2	15.6	22.2	11.0
SO$_2$ (µg/m^3)	277	10.4	6.4	0.8–53.5	6.0	8.8	13.2	7.2
Durban (1826 days)								
NO$_2$ (µg/m^3)	86	33.2	14.8	9.9–131.1	23.1	30.1	39.6	16.5
SO$_2$ (µg/m^3)	82	20.3	10.3	3.1–76.9	12.8	18.1	25.7	12.9
Johannesburg (1826 days)								
NO$_2$ (µg/m^3)	1137	51.9	20.9	0.9–123.1	37.3	50.8	64.4	27.1
SO$_2$ (µg/m^3)	957	16.9	13.5	1.2–90.7	6.9	13.0	23.3	16.3

SD: Standard deviation

IQR: Interquartile range

Supplementary table 2. Optimal df for *time* for Cape Town, Durban and Johannesburg and the age groups.

	Cape Town	**Durban**	**Johannesburg**
0-14 years	4.0 df/year	2.4 df/year	5.6 df/year
15-64 years	2.4 df/year	4.0 df/year	8.0 df/year
≥65 years	3.2 df/year	4.8 df/year	4.0 df/year

Optimal df for *time* was selected that minimised the sum of the absolute values of the partial autocorrelation function of the model's residuals.

Study period 5 years: 1 January 2006 to 31 December 2010

Supplementary table 3. Major groups of all-cause non-accidental deaths in Cape Town, Durban and Johannesburg, South Africa during 2006-2010.

ICD10	Description	Cape Town		Durban		Johannesburg	
		No.	%	No.	%	No.	%
A00-B99	Certain infectious and parasitic diseases	26215	21.15	54852	30.94	36858	22.61
C00-D48	Neoplasms	21956	17.71	11657	6.57	16303	10.00
D50-D89	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	1565	1.26	2970	1.68	4680	2.87
E00-E90	Endocrine, nutritional and metabolic diseases	10776	8.69	11366	6.41	7684	4.71
F00-F99	Mental and behavioural disorders	1067	0.86	446	0.25	745	0.46
G00-G99	Diseases of the nervous system	3335	2.69	5767	3.25	4437	2.72
H00-H59	Diseases of the eye and adnexa	11	0.01	7	0.00	5	0.00
H60-H95	Diseases of the ear and mastoid process	18	0.01	23	0.01	20	0.01
I00-I99	Diseases of the circulatory system	26773	21.60	28743	16.21	24871	15.26
J00-J99	Diseases of the respiratory system	10936	8.82	17893	10.09	18847	11.56
K00-K93	Diseases of the digestive system	3210	2.59	4924	2.78	4518	2.77
L00-L99	Diseases of the skin and subcutaneous tissue	271	0.22	374	0.21	365	0.22
M00-M99	Diseases of the musculoskeletal system and connective tissue	590	0.48	417	0.24	664	0.41
N00-N99	Diseases of the genitourinary system	2332	1.88	3770	2.13	3696	2.27
O00-O99	Pregnancy, childbirth and the puerperium	282	0.23	610	0.34	557	0.34

P00-P96	Certain conditions originating in the perinatal period	2810	2.27	4074	2.30	4593	2.82
Q00-Q99	Congenital malformations, deformations and chromosomal abnormalities	925	0.75	719	0.41	1056	0.65
R00-R99	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	10879	8.78	28686	16.18	33123	20.32
		123951	**100**	**177298**	**100**	**163022**	**100**

Supplementary table 4. Association between Tapp (lag0-1) (in °C) and all-cause non-accidental mortality expressed as percentage increase in risk (%) and 95% confidence intervals per inter-quartile increase above the city-specific threshold during 1 January 2006–31 December 2010 in South Africa.

	Cape Town[a]					Durban[b]					Johannesburg[c]				
	n	IQR	%	95% CI		n	IQR	%	95% CI		n	IQR	%	95% CI	
All	36402	3	**3.3**	**0.9**	**5.7**	48828	4	2.6	-0.3	5.6	29668	2	2.8	-0.4	6.0
Age and/or sex															
0-14 years	2957	3	-0.4	-8.0	7.9	5457	3	4.9	-1.5	11.8	3210	2	6.0	-3.8	16.8
Men	1527	3	3.9	-7.0	16.2	2807	4	8.5	-3.7	22.3	1711	2	5.4	-7.8	20.5
Women	1382	3	-3.7	-14.3	8.2	2619	3	2.8	-6.0	12.5	1457	2	8.5	-6.1	25.2
15-64 years	18889	3	1.4	-1.8	4.8	31548	4	2.2	-1.3	5.9	18150	2	-1.2	-5.1	2.8
Men	10263	3	1.9	-2.5	6.5	15466	4	1.3	-3.7	6.5	9380	2	-1.5	-6.9	4.2
Women	8581	3	0.8	-3.9	5.7	16063	4	3.1	-1.8	8.3	8726	2	-0.9	-6.5	4.9
≥65 years	14455	3	**6.5**	**2.7**	**10.5**	11596	4	1.8	-4.0	7.9	8155	2	**10.1**	**3.8**	**16.8**
Men	6514	3	3.0	-2.5	8.8	4723	4	5.9	-3.3	16.0	3482	2	**9.6**	**0.1**	**20.0**
Women	7929	3	**9.6**	**4.3**	**15.1**	6869	4	-1.0	-8.2	6.8	4667	2	**10.5**	**2.2**	**19.4**

Adjusted for public holidays. influenza and PM_{10}.

City-specific thresholds: Cape Town (18.6°C), Durban (24.8°C), Johannesburg (18.7°C)

IQR: Interquartile range

n: Number of deaths used in model

[a]Interaction term p = 0.0139 for age groups. But interaction term p > 0.05 for sex within age groups

[b]Interaction term p > 0.05

[c]Interaction term p > 0.05

Supplementary table 5. Overall pooled association between Tapp (lag0-1) (in °C) and all-cause non-accidental mortality expressed as percentage increase in risk (%) and 95% confidence intervals per unit increase above the city-specific threshold during 1 January 2006–31 December 2010 in Cape Town, Durban and Johannesburg, South Africa.

	n	%	95% CI	
All ages	114 898	**0.9**	**0.4**	**1.4**
0-14 years	11 624	1.2	-0.4	2.7
15-64 years	68 587	0.4	-0.2	1.1
≥65 years	34 206	**2.1**	**0.2**	**4.1**

n: Number of deaths used in model

(a)

(b)

(c)
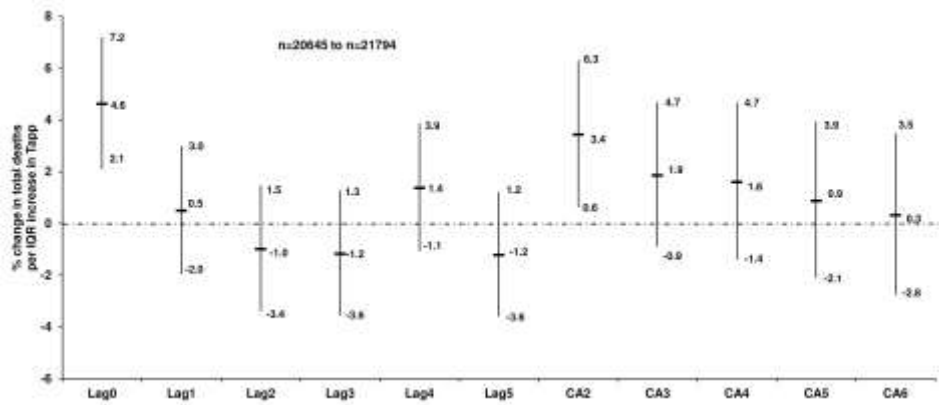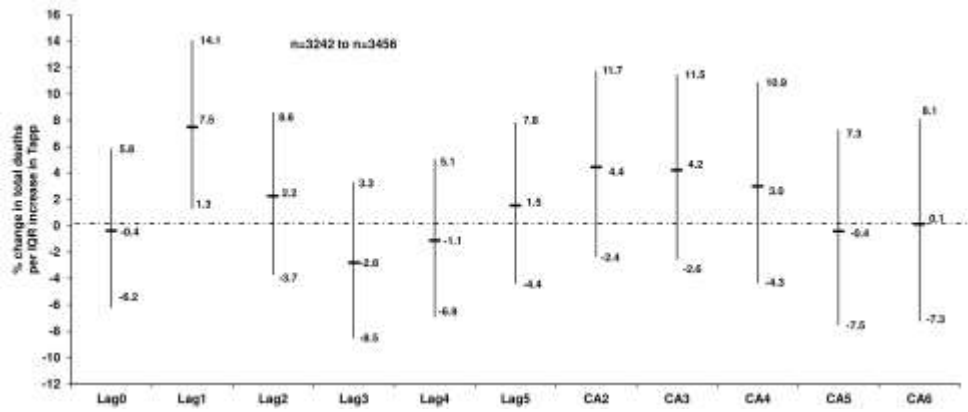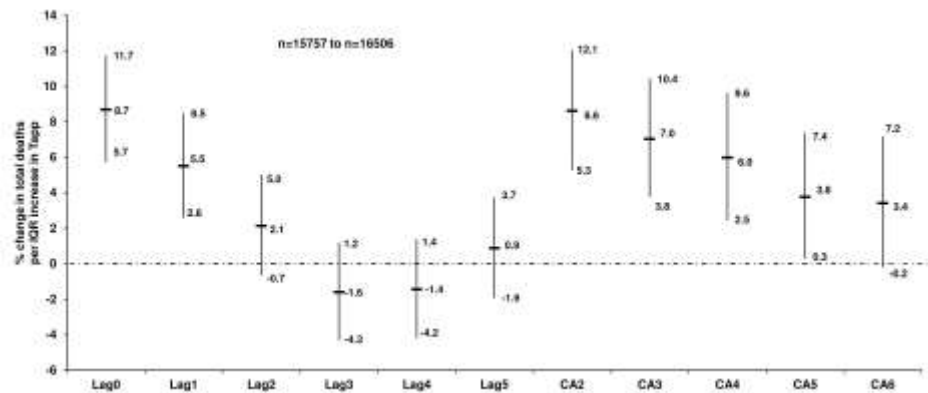
Supplementary figure 1. Percentage change (95% CI) in all-cause mortality in Cape Town per inter-quartile range increase in Tapp (≥18.6°C) during 2001 -2006, adjusted for public holidays and influenza (but not for PM_{10}): (a) 0-14 years, (b) 15-64 years, (c) ≥65 years

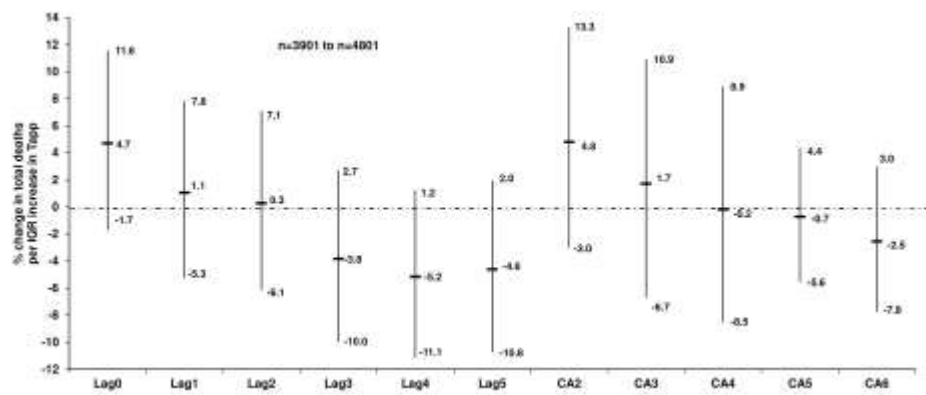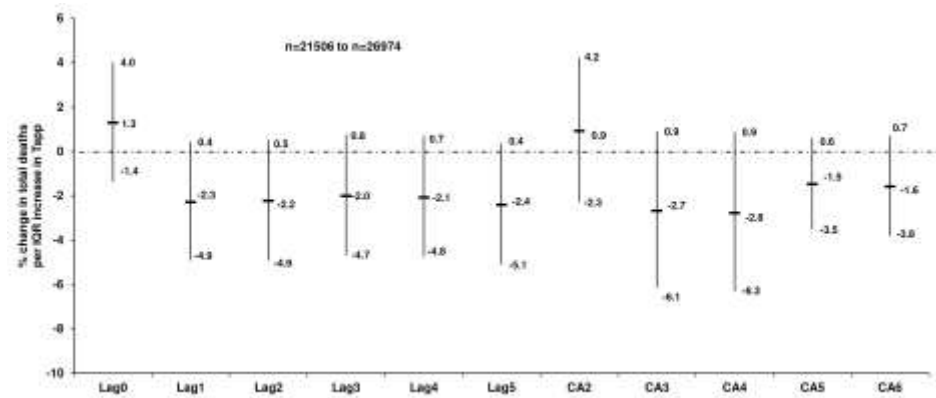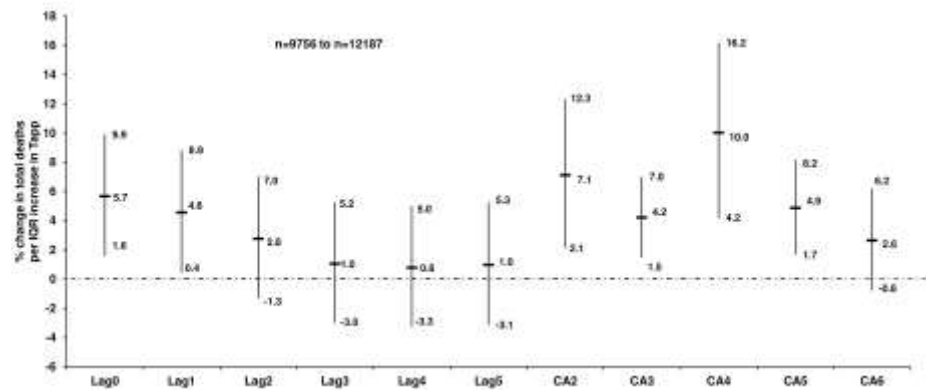CA=Cumulative average. CA2=lag0-1, CA3=lag0-2, CA4=lag0-3, CA5=lag0-4, CA6=lag0-5

(a)

(b)

(c)
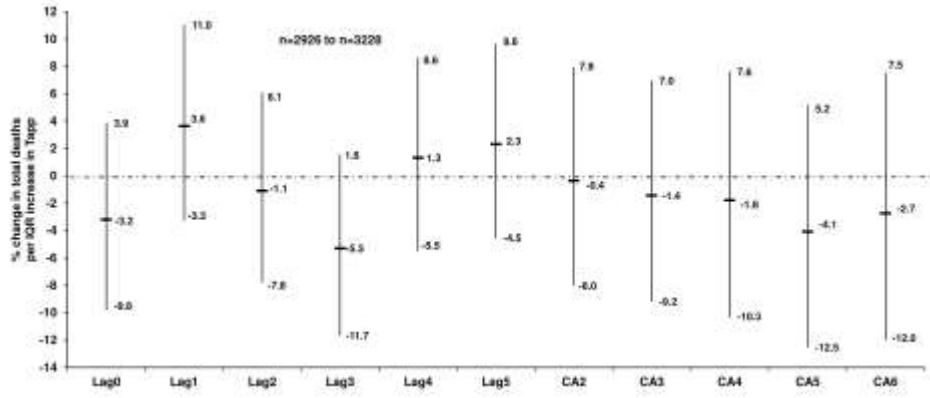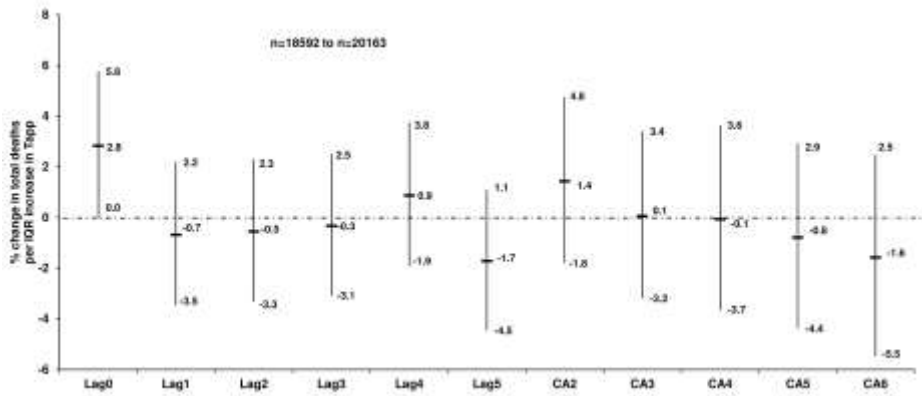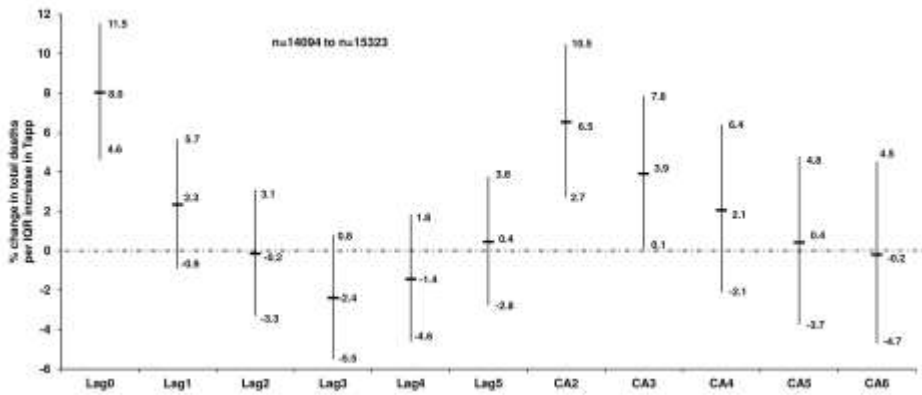
Supplementary figure 2. Percentage change (95% CI) in all-cause mortality in Cape Town per inter-quartile range increase in Tapp (≥18.6°C) during 2001 -2006, adjusted for PM$_{10}$, public holidays and influenza: (a) 0-14 years, (b) 15-64 years, (c) ≥65 years

CA=Cumulative average. CA2=lag0-1, CA3=lag0-2, CA4=lag0-3, CA5=lag0-4, CA6=lag0-5

28

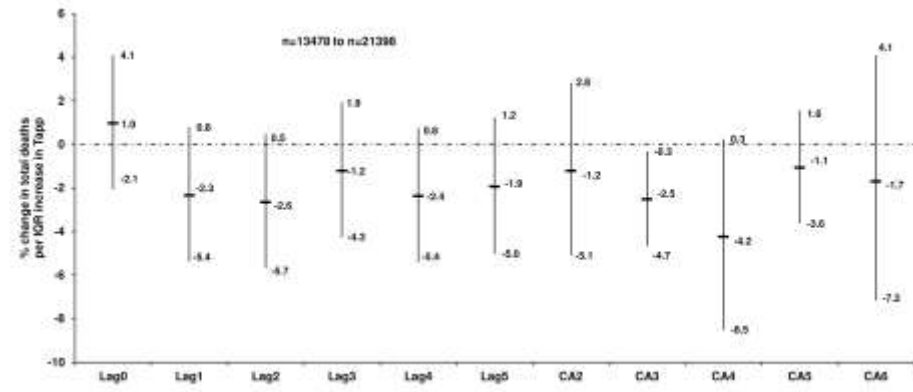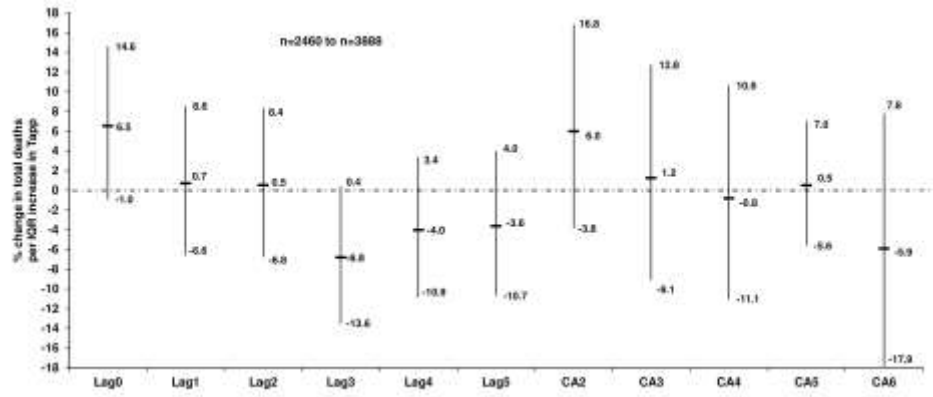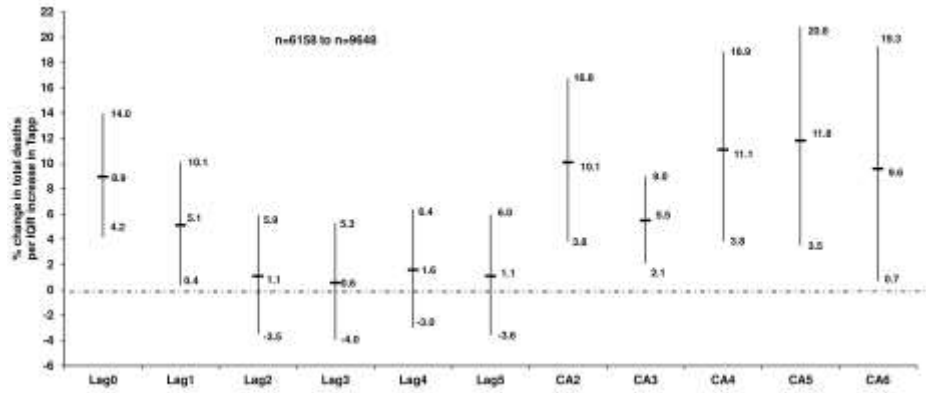(a)   (b)

(c)
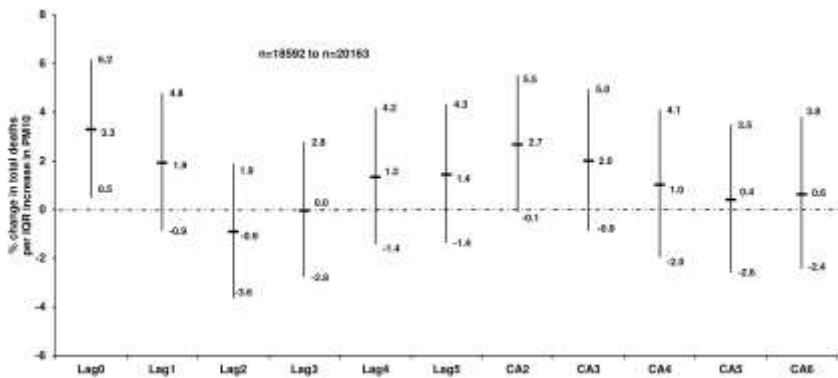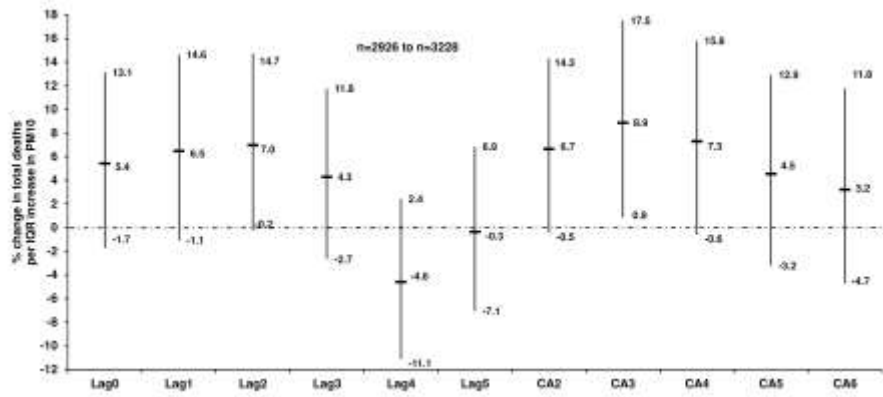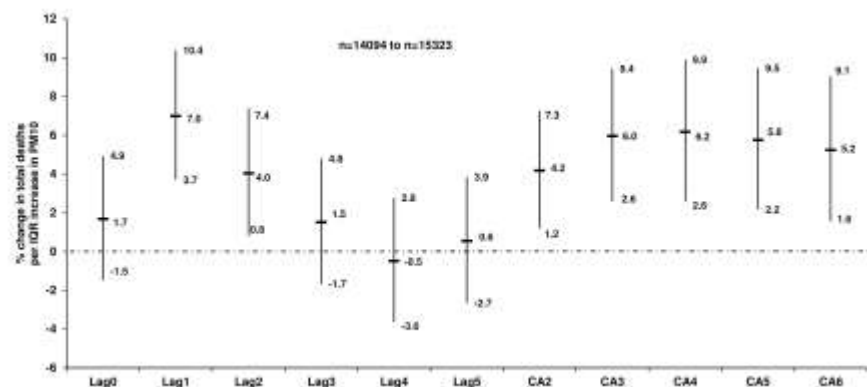
Supplementary figure 3. Percentage change (95% CI) in all-cause mortality in Cape Town per inter-quartile range increase in PM$_{10}$ during 2001 -2006, adjusted for Tapp (≥18.6°C), public holidays and influenza: (a) 0-14 years, (b) 15-64 years, (c) ≥65 years

CA=Cumulative average. CA2=lag0-1, CA3=lag0-2, CA4=lag0-3, CA5=lag0-4, CA6=lag0-5

29

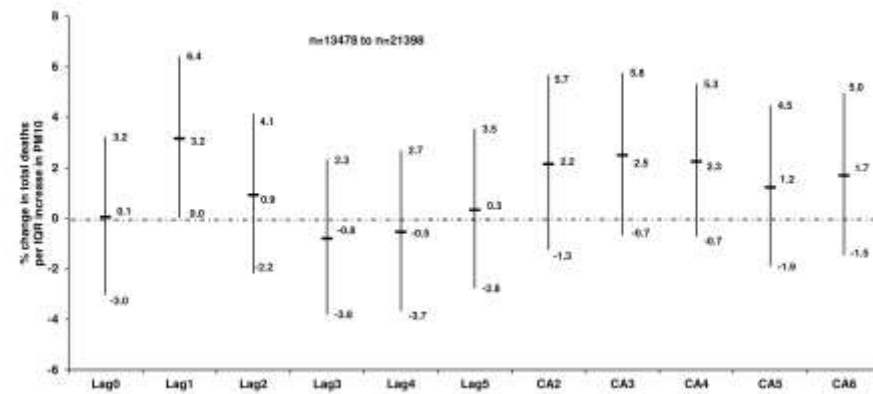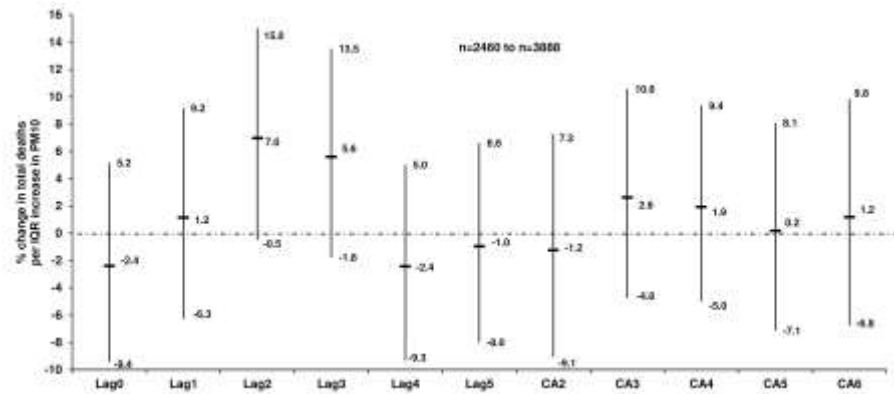(a)   (b)

(c)
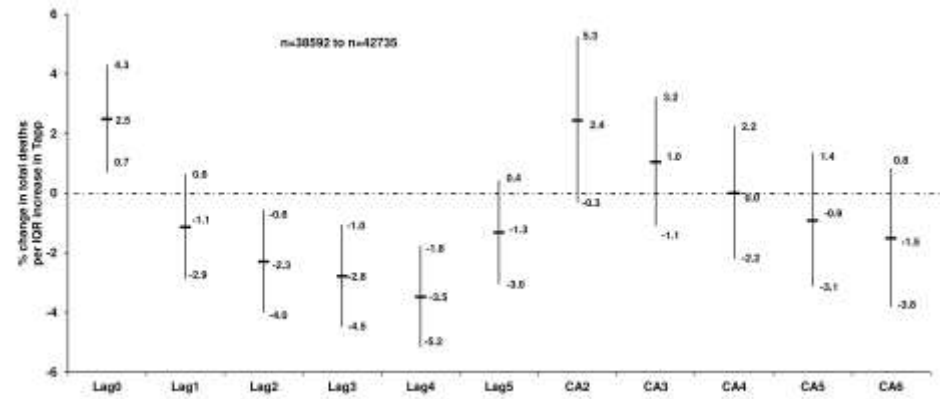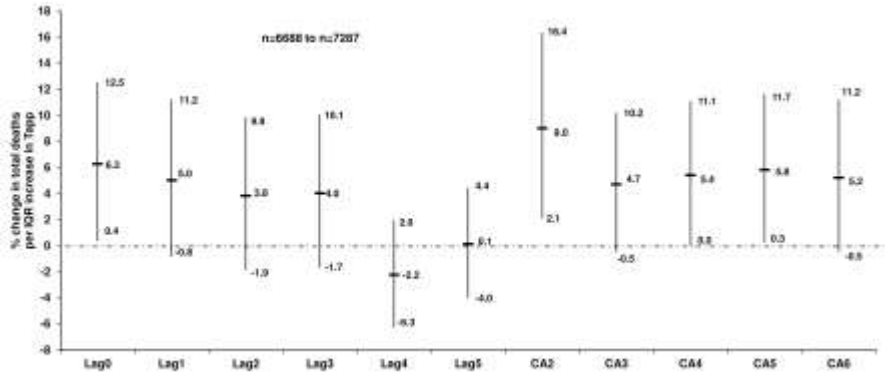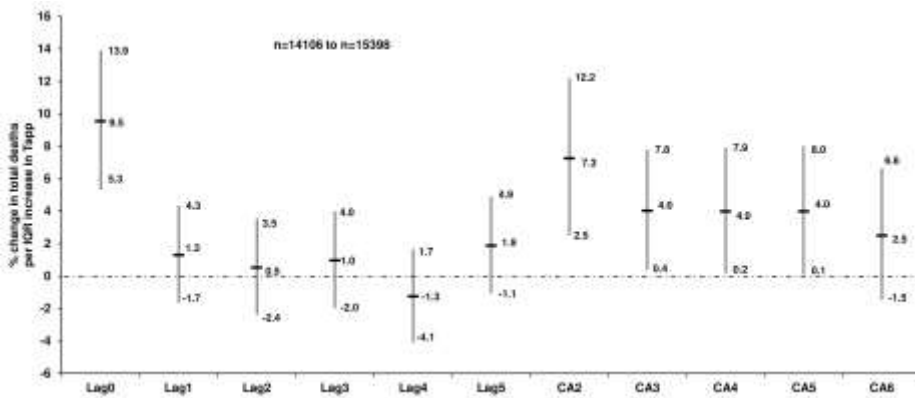
Supplementary figure 4. Percentage change (95% CI) in all-cause mortality in Durban per inter-quartile range increase in Tapp (≥24.8°C) during 2001 -2006, adjusted for public holidays and influenza (but not for PM_{10}): (a) 0-14 years, (b) 15-64 years, (c) ≥65 years

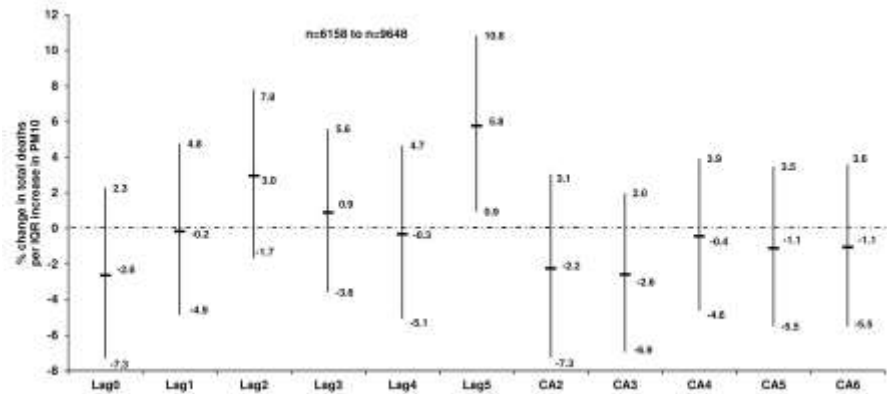CA=Cumulative average. CA2=lag0-1, CA3=lag0-2, CA4=lag0-3, CA5=lag0-4, CA6=lag0-5

(a)

(b)

(c)
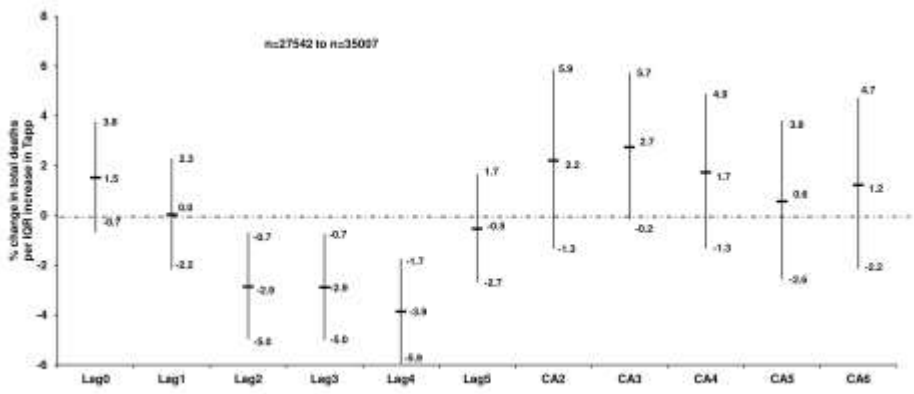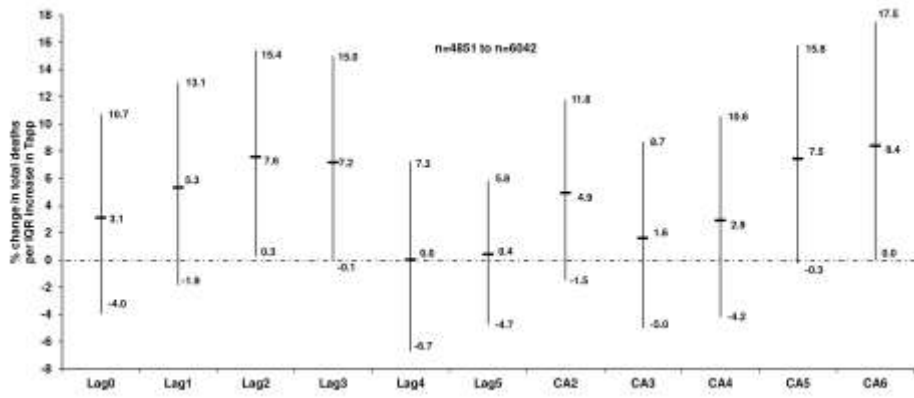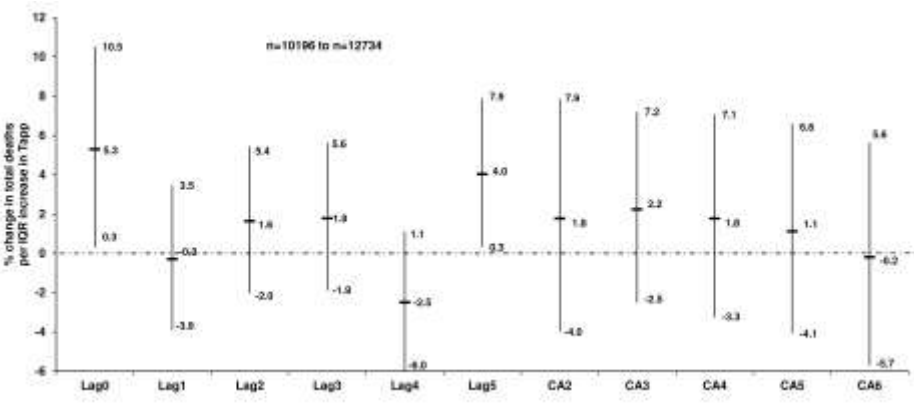
Supplementary figure 5. Percentage change (95% CI) in all-cause mortality in Durban per inter-quartile range increase in Tapp (≥24.8°C) during 2001 -2006, adjusted for PM_{10}, public holidays and influenza: (a) 0-14 years, (b) 15-64 years, (c) ≥65 years

CA=Cumulative average. CA2=lag0-1, CA3=lag0-2, CA4=lag0-3, CA5=lag0-4, CA6=lag0-5

(a)   (b)

(c)
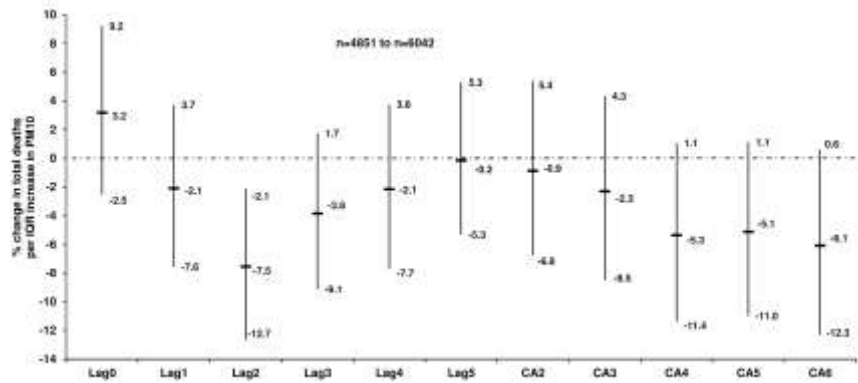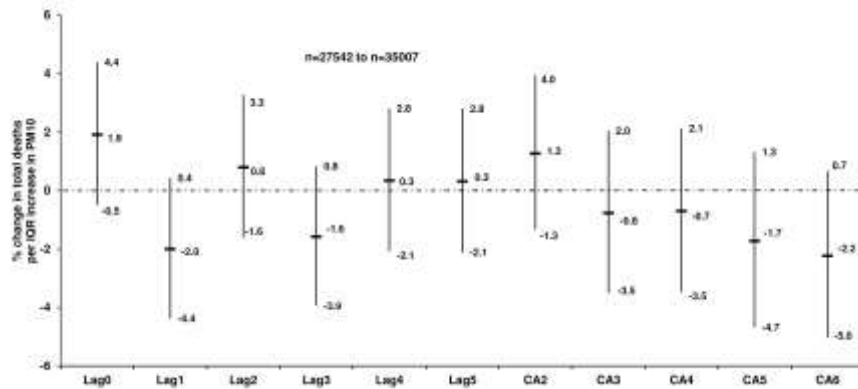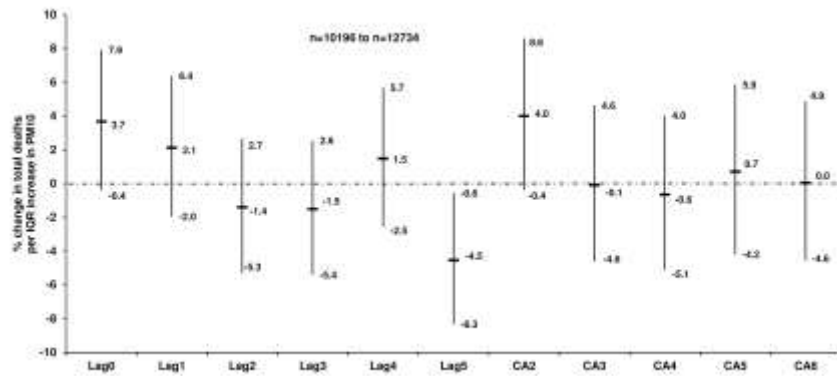
Supplementary figure 6. Percentage change (95% CI) in all-cause mortality in Durban per inter-quartile range increase in PM$_{10}$ during 2001 -2006, adjusted for Tapp (≥24.8°C

CA=Cumulative average. CA2=lag0-1, CA3=lag0-2, CA4=lag0-3, CA5=lag0-4, CA6=lag0-5

(a)

(b)

(c)

Supplementary figure 7. Percentage change (95% CI) in all-cause mortality in Johannesburg per inter-quartile range increase in Tapp (≥18.7°C) during 2001 -2006, adjusted for public holidays and influenza (but not for PM_{10}): (a) 0-14 years, (b) 15-64 years, (c) ≥65 years

CA=Cumulative average. CA2=lag0-1, CA3=lag0-2, CA4=lag0-3, CA5=lag0-4, CA6=lag0-5

(a)

(b)

(c)

Supplementary figure 8. Percentage change (95% CI) in all-cause mortality in Johannesburg per inter-quartile range increase in Tapp (≥18.7°C) during 2001 -2006, adjusted for PM$_{10}$, public holidays and influenza: (a) 0-14 years, (b) 15-64 years, (c) ≥65 years

CA=Cumulative average. CA2=lag0-1, CA3=lag0-2, CA4=lag0-3, CA5=lag0-4, CA6=lag0-5

(a)

(b)

(c)

Supplementary figure 9. Percentage change (95% CI) in all-cause mortality in Johannesburg per inter-quartile range increase in PM_{10} during 2001 - 2006, adjusted for Tapp (≥18.7°C), public holidays and influenza: (a) 0-14 years, (b) 15-64 years, (c) ≥65 years

CA=Cumulative average. CA2=lag0-1, CA3=lag0-2, CA4=lag0-3, CA5=lag0-4, CA6=lag0-5

(a)   **(b)**   **(c)**
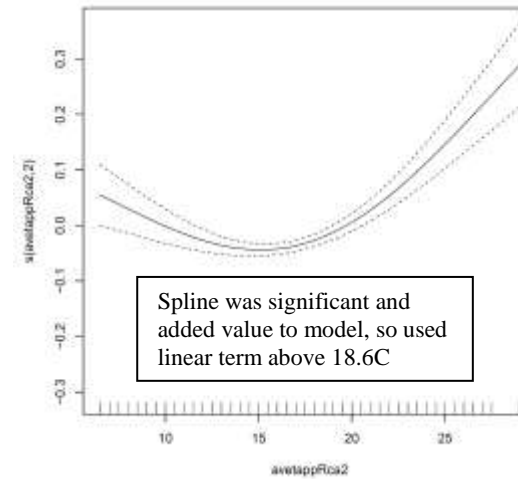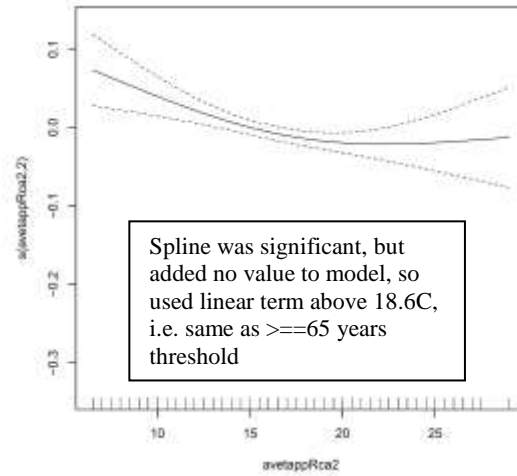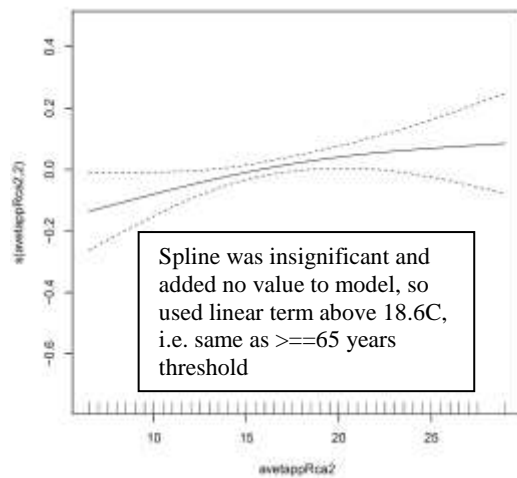
Supplementary figure 10. Linear or non-linear association between Tapp (lag0-1) and all-cause non-accidental mortality for (a) 0-14 years, (b) 15-64 years and (c) ≥65 year olds in Cape Town during 1 January 2006 – 31 December 2010.

avetappRca2=Tapp (lag0-1)

Note:

- For simplicity the threshold of the >=65 year group was used also for the 0-14 and 15-64 year groups in the case-crossover models. The latter two groups displayed a linear association between Tapp (lag0-1) and all-cause non-accidental mortality, hence their thresholds should actually be the minimum of Tapp (lag0-1). However, as the association is linear, so the slope of the linear curve at minimum of Tapp (lag0-1) is the same as at 18.6C.
- One threshold is needed to run case-crossover models with an interaction term between Tapp (lag0-1) and age group variable.
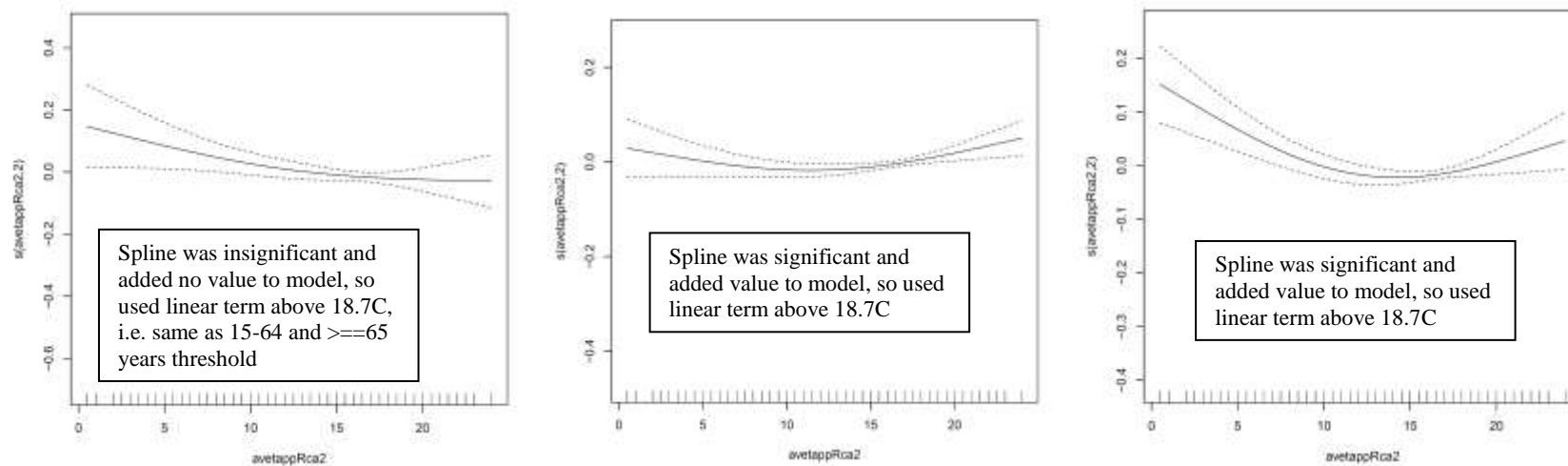
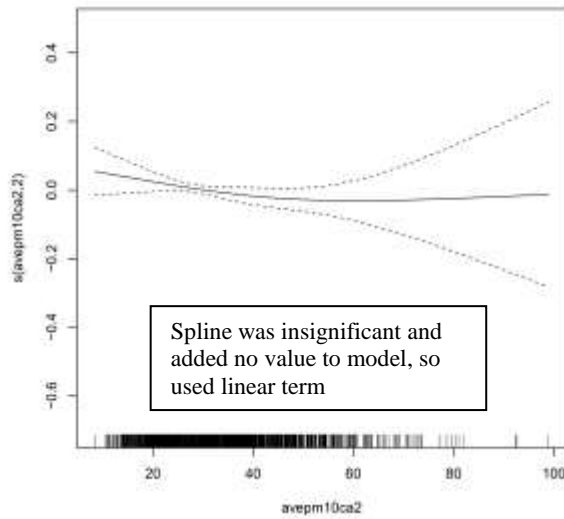**(a)**   **(b)**   **(c)**
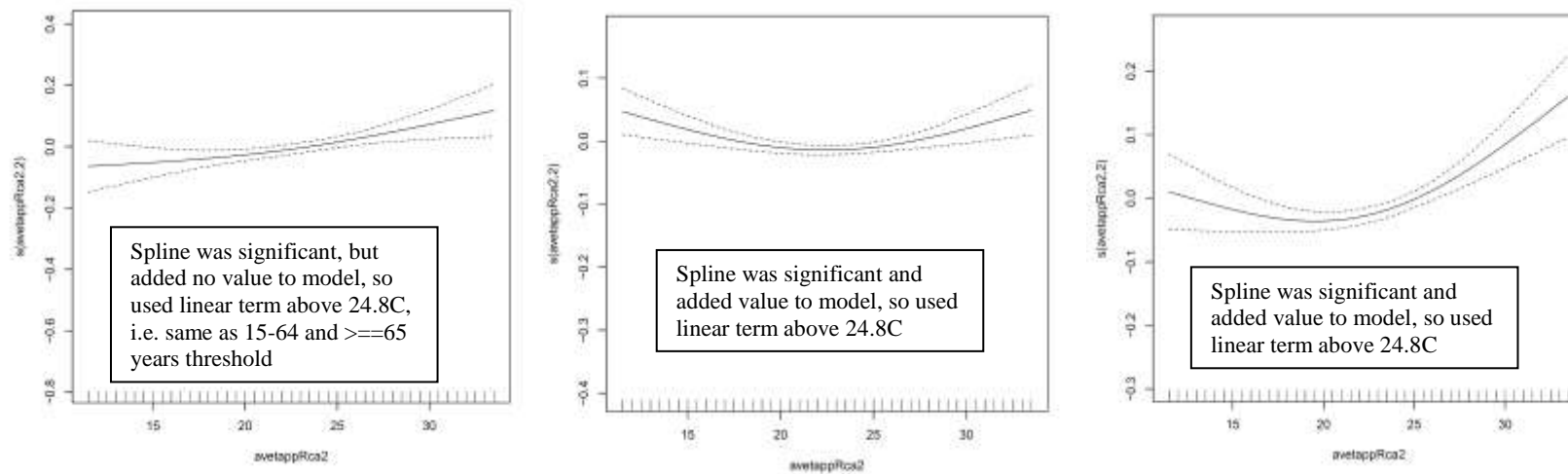
Supplementary figure 11. Linear or non-linear association between Tapp (lag0-1) and all-cause non-accidental mortality for (a) 0-14 years, (b) 15-64 years and (c) ≥65 year olds in Durban during 1 January 2006 – 31 December 2010.

avetappRca2=Tapp (lag0-1)

Note:

- For simplicity the threshold of the 15-64 and >=65 year group was used also for the 0-14 year group in the case-crossover models. The latter group displayed a linear association between Tapp (lag0-1) and all-cause non-accidental mortality, hence its thresholds should actually be the minimum of Tapp (lag0-1). However, as the association is linear, so the slope of the linear curve at minimum of Tapp (lag0-1) is the same as at 24.8C.
- One threshold is needed to run case-crossover models with an interaction term between Tapp (lag0-1) and age group variable.

(a)   **(b)**   **(c)**

Supplementary figure 12. Linear or non-linear association between Tapp (lag0-1) and all-cause non-accidental mortality for (a) 0-14 years, (b) 15-64 years and (c) ≥65 year olds in Johannesburg during 1 January 2006 – 31 December 2010.

avetappRca2=Tapp (lag0-1)

Note:

- For simplicity the threshold of the 15-64 and >=65 year group was used also for the 0-14 year group in the case-crossover models. The latter group displayed a linear association between Tapp (lag0-1) and all-cause non-accidental mortality, hence its thresholds should actually be the minimum of Tapp (lag0-1). However, as the association is linear, so the slope of the linear curve at minimum of Tapp (lag0-1) is the same as at 18.7C.
- One threshold is needed to run case-crossover models with an interaction term between Tapp (lag0-1) and age group variable.

Spline was insignificant and added no value to model, so used linear term

Spline was significant, but added no value to model, so used linear term
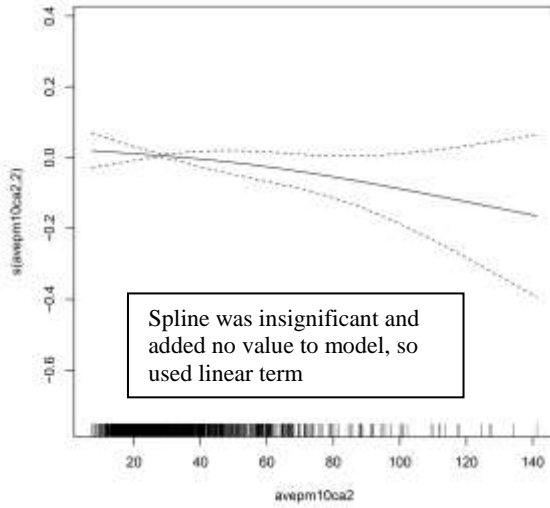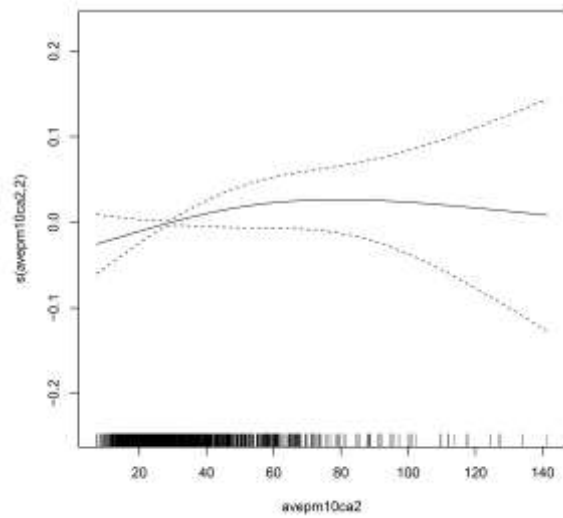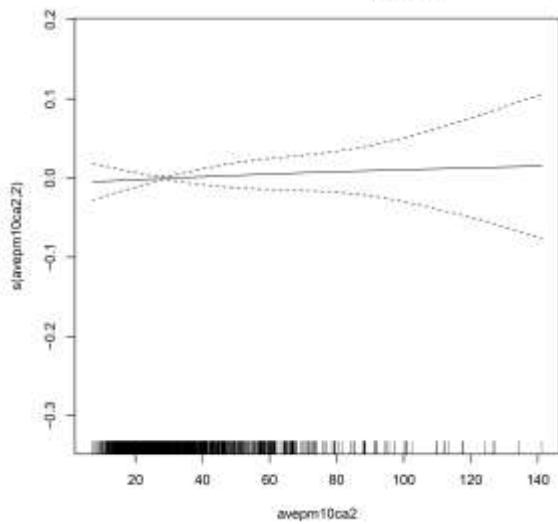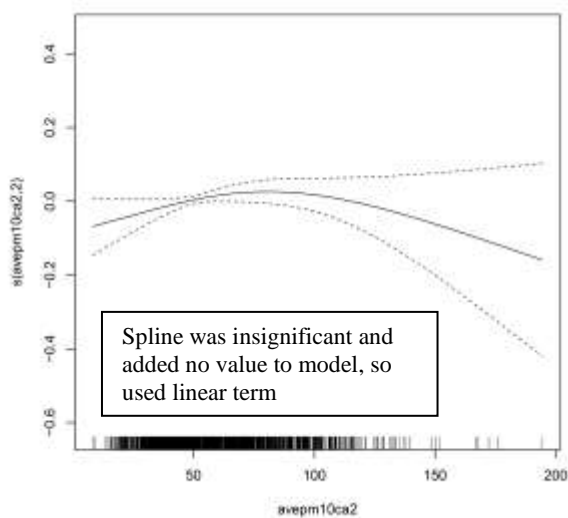
(a)   (b)

(c)
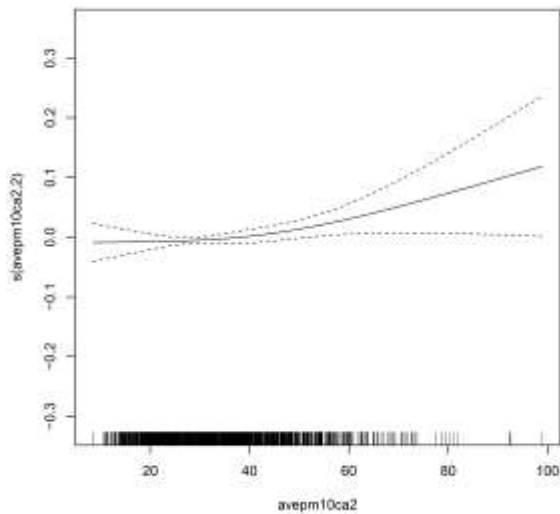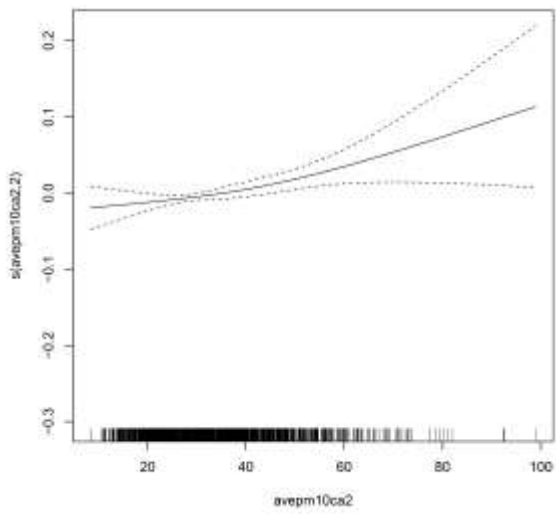
Supplementary figure 13. Linear or non-linear association between PM10 (lag0-1) and all-cause non-accidental mortality for (a) 0-14 years, (b) 15-64 years and (c) ≥65 year olds in Cape Town during 1 January 2006 – 31 December 2010.

avepm10ca2=PM10 (lag0-1)

Spline was insignificant and added no value to model, so used linear term

Spline was insignificant and added no value to model, so used linear term

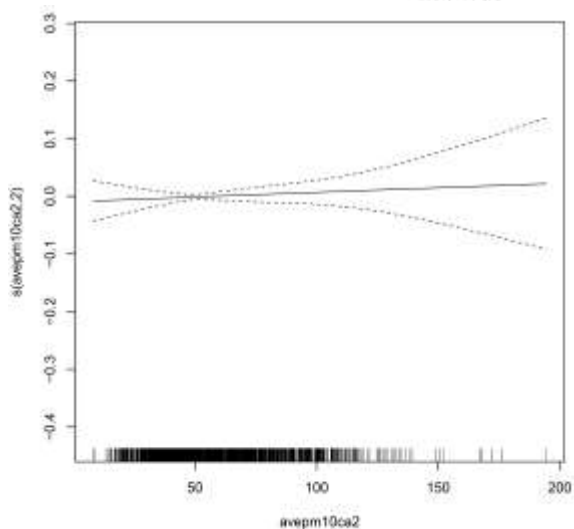**(a)**   **(b)**

       (c)

Supplementary figure 14. Linear or non-linear association between PM10 (lag0-1) and all-cause non-accidental mortality for (a) 0-14 years, (b) 15-64 years and (c) ≥65 year olds in Durban during 1 January 2006 – 31 December 2010.

avepm10ca2=PM10 (lag0-1)

Spline was insignificant and added no value to model, so used linear term
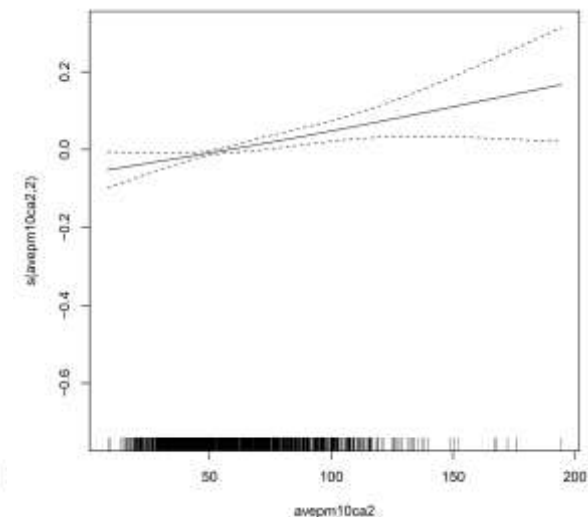
Spline was significant, but added no value to model, so used linear term

(a)   (b)

   (c)

Supplementary figure 15. Linear or non-linear association between PM10 (lag0-1) and all-cause non-accidental mortality for (a) 0-14 years, (b) 15-64 years and (c) ≥65 year olds in Johannesburg during 1 January 2006 – 31 December 2010.

avepm10ca2=PM10 (lag0-1)