TITLE: Vulnerability to heat wave-related mortality: a follow-up study of a cohort of elderly in Rome

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Words in the text: **3033**

Words in the abstract: **228**

Keywords: heat waves, mortality, elderly, risk factors, cohort study

ABSTRACT

Background

Few studies have identified specific factors that increase mortality during heat waves. This study investigated socio-demographic characteristics and preexisting medical conditions as effect modifiers of the risk of dying during heat waves in a cohort of elderly residents in Rome.

Methods

A cohort of 651,195 residents aged 65 yrs or older was followed from 2005 to 2007. During summer, heat wave days were defined according to month-specific thresholds of maximum apparent temperature. The adjusted relative risk of dying during heat waves was estimated using a Poisson regression model including all the considered covariates. Attributable risks were also calculated. All analyses were run separately for the 65-74 and 75+ age groups.

Results

A significant effect modification in the 65-74 age group was only observed for unmarried subjects and those with a previous hospitalization for chronic pulmonary disease or psychiatric disorders. In the 75+ age group, women, being unmarried and subjects with previous hospitalization for diabetes, diseases of the central nervous system, psychiatric disorders and cerebrovascular diseases were at higher risk of dying during heat waves.

Discussion

Results suggest that the composition of the population subgroups vulnerable to heat waves differ between the considered age groups. Moreover, compared with previous studies the pattern of susceptibility factors seems to have changed over time. For the purposes of public health programmes, susceptibility should be considered as time, space and population specific.

Introduction

High temperatures and heat waves have been associated with short term increases in mortality worldwide. In Europe, the exceptionally long and severe heat wave of summer 2003 found local communities substantially unprepared to cope with such an extreme event. Epidemiological research and public health efforts have been focused to a better understanding of the health impact of heat and of the individual factors that confer susceptibility to heat stress. Several countries throughout Europe have put into place a series of preventive measures, but only few are specifically targeted to high-risk individuals.[1]

Heat waves did not affect the entire population but specific subgroups are more susceptible to the effect of heat; they are represented by people with impaired physiological and behavioural responses to heat due to their old age,[2-5] to the presence of chronic illnesses,[3-7] to limited social contacts,[6] to living alone,[5,8] to low socio-economic conditions,[3,5] and limited access to air conditioning.[6] While for some of these factors, such as old age, there is strong evidence and physiological plausibility for their role in increasing the vulnerability to heat waves, for others, like specific health conditions and factors like social, behavioural and environmental conditions, evidence is still not conclusive and somewhat controversial and more research is needed.

Under a public health point of view a clear understanding of these factors is important to ensure a effectiveness of prevention programs.

In Italy the National Department of Civil Protection and the Ministry of Health implemented a national heat prevention program,[9] and national guidelines for the prevention of heat health effects have been defined, targeted to high risk subgroups (www.ccm-network.it). In the Lazio the region surrounding Roma, the heat response plan centered on active surveillance of high risk elderly (65+ years) identified using available health information systems.[10]

As a part of the Lazio prevention program for summer 2008, we carried out a longitudinal analysis of heat wave mortality between 2005 and 2007 with the primary aim of identifying vulnerability factors. The inclusion of the most recent years was to account for the possible changes in the spectrum of vulnerability factors, as well as changes in the impact of heat waves on mortality due to the effect of the heat prevention plan. We describe the results of these analyses, and discuss possible public health implications.

Materials and Methods

Study Population

We analyzed a cohort of residents in Rome aged 65 yrs or older as of the 1st of May 2005; this cohort was followed up for the subsequent two years. Each year new residents aged 65 years and older were added to the cohort, and subjects who died or changed residence by the 1st of May were removed. Information on resident's age, gender, and marital status was extracted from the Population Registry of the Roma Municipal Office. A small area-based (census tract) socio-economic status indicator using 2001 census data was also used.[11]

Health Status

We selected a list of 13 groups of diagnoses, known to be associated with a high mortality risk from high temperatures (Table 1).[3,5,7,12,13] Information about the prevalence of past hospitalization for each of these conditions in the study population was extracted by linking the regional hospital discharge files (Regional Hospital Information System) (HIS),[14] and the Municipality Population Registry, using individual social security numbers as the linkage key. We considered hospitalizations or day-hospital visits for each diagnostic group, reported either as primary causes of admission or as contributing diagnoses. Subjects were classified using 13 dichotomous variables, indicating if they sought medical treatment for each of the 13 diagnoses or not (Hospitalization Diagnosed Disease, HDD).

For each subject, the number of HDD over the previous two years for any other cause, other than those specified on our list, was also considered as an indicator of general health status.

Exposure

The exposure of interest is a heat wave episodes, measured by maximum apparent temperature (Tappmax), an index of discomfort based on air and dew point temperatures,[15] that indicates the level of physiological stress brought on by extreme summer conditions better than air temperature alone. When Tappmax rises above the monthly threshold, as defined by the Heat Health Watch Warning System (HHWWS),[9] a heat advisory is issued for that day. (May: 28.5, June: 32.5°C; July: 33.5°C; August/September: 34.5°C)). Our exposure variable was a heat wave episode: a minimum of two consecutive days with a heat advisory. Daily environmental data from **airport stations** were obtained from the Italian Air Force Meteorological Service, during summer (1st of May until the 15th of September).

Outcome

Vital status was determined each year as of the 15th of September, for each subject through a record linkage using individuals' social security number with the Regional Registry of Causes of Death (Regional Mortality Register).[16] We considered all deaths from non-injury causes (International Classification of Diseases, 9th Revision [ICD-9]: 1-799).

A heat wave related death was considered such if it occurred during the event itself or in the following three days, to take into account the lag effect of heat on mortality.

Statistical Analysis

We estimated the adjusted absolute risk and the adjusted modification effect measure of age, gender, socio-economic status, civil status, for each one of the selected groups of comorbidities and for the number of hospitalizations in the previous two years on the mortality-heat wave relationship, using a Poisson regression model.

A manual backward stepwise procedure was used to select the simple effects to be included in the final model. Age and gender were forced into the model. Finally an interaction term between heat-wave variables and the specific covariate was included in the selected model to compute the adjusted relative risk of dying on a heat wave day versus a non heat wave day for each of the modalities of the covariate considered. The analysis was performed using SAS.[17]

Adjusted attributable risk was computed to evaluate the number of cases attributable to each condition, for each modality of the covariates considered.

We assumed that age modifies the set of factors that interact with the heat-mortality relationship, therefore we analyzed the elderly in two separate groups, 65-74 and over 74 year olds.

We report the estimated absolute and relative risks of dying on heat wave and non heat wave days for each of the modalities of the covariates and the REM index, and risk differences for the two age groups separately. REM index is the ratio of the relative risk of dying during a heat wave for each of the covariates considered, comparing each category to the reference one.[5]

Results

We enrolled a total of 651,195 subjects over the three-year period, 574,192 of which were included in the first year. A total of 26,634 subjects were excluded from the analysis due to incomplete civil status information. The excluded subjects were comparable to the study population, except for a higher percentage of subjects over 95 years of age; no deaths were observed in this subgroup. The analyzed cohort represented 203,626 person-years of heat wave exposure (including the three post-heat wave lag days) and 437,520 person-years of non-heat wave exposure. Table 1 reports the population's characteristics. About 50% of the analyzed population was older than 75 and of these about 40% were male.

There were more females and a higher percentage of unmarried people in the over 75-year-old group than in the younger group. The 75+ group also had a higher prevalence of previous hospitalization for all the pathologies considered compared to the 65-74 age group. We observed 4,139 deaths in the 65-74 age group and 14,470 deaths among the over 74 year olds.

Table 2 reports the average Tappmax observed in the study period.

On average there was an 8°C difference between the median temperature on heat wave and non heat wave days in May and June, about a 5 °C difference in July, and 6 °C in August. A difference of 5-7°C was observed between the 90th percentile of heat wave and non heat wave days. There were no heat waves, and therefore no results reported for the month of September in the years we studied. According to the exposure definition single days with Tappmax over the monthly threshold were included in the "non heat waves days". This contributed to a slight overlap of temperatures observed between heat wave and non heat wave days.

The heat wave effect

We observed a crude relative risk of dying during heat waves compared to non heat waves of 1.09 (IC95%: 1.02-1.16) in the 65-74 age group, and of 1.15 (IC95%: 1.11-1.18) in the over 74 age group.

65-74 age group

Tables 3 and 4 suggest there is no evidence of significant effect modification in the 65-74 age group. However, point estimates of relative risks suggest that the excess in mortality during heat waves is higher among those who were previously hospitalized for a chronic pulmonary disease, and to a lesser extent, for psychiatric disorders and among those not married, widowed or divorced. For chronic pulmonary diseases, there seems to be an increased excess in the absolute numbers of deaths during heat wave days compared to non heat wave days (RD: 12.9 IC95% (0.3 – 25.5) during heat waves; RD: 0.7 IC95% (0.0 – 1.5) during non heat waves). Subjects previously hospitalized for malignant neoplasm, for cardiac arrhythmias and renal failure had lower relative risks of dying during heat wave days. Although not statistically significant, having been previously hospitalized for diabetes, ischemic diseases or liver diseases seemed to produce a similar protective effect; while socio economic status does not seem to be an effect modifier of the relationship under study.

75+ age group

Relative risks show that the excess in mortality during heat waves is significantly higher in females, and for all those not married, widowed or divorced (Table 3). Rate ratios show that the effect of heat on mortality increases with age and was greater for those who had 4 or more hospitalizations for other causes in the previous two years, although they were not statistically significant. However, to have had 4 or more hospitalizations seems to produce a higher absolute number of deaths, as shown by the risk difference (Table 4).

There were more deaths attributable to heat waves in the in the 75+ age group among those who had a previous hospitalization for diabetes, diseases of the CNS, psychiatric disorders and cerebrovascular diseases; however the same factors do not represent multiplicative effect modifiers of the heat-mortality relationship.

Conversely, there was a protective effect observed among subjects with a previous hospitalization for a wide range of conditions, including malignant neoplasm, ischemic diseases, hearth rhythm disorders, heart failure, chronic pulmonary diseases, liver diseases and renal failure. As in the 65-74 age group, socio economic status did not modify the effect .

Discussion

This study analysed factors associated to heat-related mortality in a cohort of elderly subjects in the summers of 2005-2007 in Roma. In these years prevention programs for the effects of heat on health were active in the city. The analysis was performed separately for the 65-74 and the 75+ age groups. One important finding is that both the crude effect of heat waves on mortality and the set of factors modifying the heat-mortality relationship differed between the two age groups. These results confirm that age acts as an effect modifier of the associations under study, and suggest that the underlying mechanisms that determine degrees of vulnerability to heat waves may vary with age.

Results from the 65-74 age group did not identify any significant effect modifier, although subjects with at least one hospitalization for a chronic pulmonary disease or psychiatric disorders, and those not married, widowed or divorced, showed a higher excess in mortality on heat wave days. In the 75+ age group, women and unmarried people were more likely to die during heat waves. Although not significant, the effect of heat on mortality increased with age.

Results suggest that previous hospitalization for a wide range of diagnosis is associated with a minor relative risk of dying during heat waves, especially in the 75+ age group.

In the 65-74 age group, higher risk of mortality in subjects with previous hospitalization for a chronic respiratory illness was also found in previous case-only and case-crossover studies on the 65+ population,[13,18] and in time-series studies that found a significant mortality risk for respiratory causes in populations younger than 75 years of age.[19,20] Possible explanations have already been suggested.[21] The slightly higher risk of dying in 65-74 year old sufferers of psychiatric disorders supports previous studies,[3,13] and may be explained by the fact that persons suffering from these diseases are unable to care for themselves,[3] and by side effects of certain neuroleptic drugs.[22]

In the present study and in other studies[4,5,13] the population segment found to be more likely to be adversely affected by heat waves is the 75+ age group, and the mortality risk increases with age. This can be attributed to concurrent factors such as pre-existing chronic diseases, physical fitness level, and to the fact that the elderly typically exhibit attenuated physiological responses to heat such as lower sweat gland outputs, decreased skin blood flow and reduced cardiac outputs.[23]

Results from both age groups showed that those who were hospitalized in the previous two years had a lower risk of dying during heat waves than non previously hospitalized subjects. For some specific pathologies, such as cancer or other severe chronic illnesses, this lower mortality risk could be due to the fact that these patients received greater medical attention, which acted as protection against the adverse effect of heat waves. On the other hand, it has been suggested that the lower risk of dying during heat waves for pre-hospitalized people should be interpreted more as a protective than a multiplicative effect, since the absolute risk of dying among those who had an hospitalization during the previous two years subjects is presumably higher than in the not hospitalized group.[6]

We did not find any effect modification by socio-economic condition in either of the age groups. It should be noted that our indicator of socio-economic status is derived from a census tract level study,[11] therefore misclassification of individual exposure may have affected our findings toward the null.

We compared our results with previous studies on risk factors for heat-related mortality in the 65+ age group in Rome before 2003,[5,13] to detect possible changes in recent years in the spectrum of vulnerability factors in this population. The socio-demographic characteristics of this comparison revealed that very old people, women, and not married, divorced or widowed people have remained at higher risk.[5,13] In both studies chronic respiratory diseases, psychiatric disorders and cerebrovascular diseases were associated with a higher risk of mortality.[5,13] However, a slight change in the pattern of the concurrent clinical conditions seems to have occurred; heart failure and heart conduction disorders were not currently identified as risk modifiers as they had been previously,[5,13] whereas diabetes and diseases of the CNS were identified in this study as having a higher number of deaths during heat waves.

As far as we know, this is one of the few studies to analyze a prospective cohort with individual socio-demographic and health information on the elderly, stratified by age.

Compared to the more widely used case crossover design, our study has the advantage of allowing us to estimate comparable relative risk of dying during heat waves for different covariates of interest. Estimates were obtained from the interaction term of a model including the heat wave effect, the covariate effect and the interaction term, and adjusted for a pool of covariates.

Another advantage of the study design used is that it allowed us not only to compute the relative risk such as in a cross-over design but also the absolute risk . As a consequence we could evaluate both the multiplicative effect modification of the factors considered as well as the impact in terms of absolute number of excess of deaths during a heat wave. This has enabled us to identify a series of pathologies that do not modify the heat-mortality relationship but are associated with higher mortality rates during heat waves, in absolute numbers. In particular, in the 75+ age group, this was true for people with previous hospitalization for diabetes, diseases of the CNS, psychiatric disorders or cerebrovascular diseases. There were significant attributable risks also for chronic pulmonary diseases, psychiatric disorders and diseases of the CNS in the 65-74 age group.

We used cause-specific hospital admissions as markers of specific diseases. This has some intrinsic limitations since not all conditions considered result in a hospital admission and in this case the use of additional sources of health data (i.e. outpatient care, pharmaceutical care data) could have provided a more accurate measure of the prevalence of the disease in our population. Furthermore, it should be noted that the use of hospital admissions could provide a biased picture of morbidity since it reflects not only morbidity levels but also provider-specific factors and the availability of primary care and out-patient services.[24]

Our study aims to evaluate vulnerability factors and cannot disentangle the effect of heterogeneous susceptibility and/or probability of individual exposure.

Conclusion

Our study is one of the few to analyze the potential modification effects of a wide range of health conditions and of socio-demographic factors in a large cohort of elderly subjects in the years following the introduction of prevention programs aimed to prevent the health effects of heat waves. Results seem to suggest that heat surveillance should mainly target people over 74 years of age, and within this group in particular, to women and unmarried people. Regarding the younger group we studied, only those with a previous hospital diagnosis of specific pathologies, like chronic pulmonary diseases, should be specifically monitored during heat waves .

Previous contact with the hospital system seems to be a protective factor for heat wave-associated mortality. This might mean that greater attention to health problems in general, and more frequent contact with health services in particular, might enhance the effectiveness of prevention programs. Finally these results compared with previous studies underline the dynamic pattern of vulnerability factors to the effect of heat waves: for the purposes of public health programmes vulnerability should be considered time, space and population specific, not only from the point of view of relative effects but also of absolute impact.

Competing interests

The authors declare they have not competing interests.

Authors contributions

PS contributed to defining the objectives of the analysis, designed and supervised the analysis the analysis and drafted the paper; GC carried out the analysis and participated in the preparation of the paper; MDS contributed to writing and revised the paper; PM contributed to defining the objectives of the analysis and to writing and revising the paper; CM contributed to data management and revised the paper; AMB participated to the methodological discussion and revised the paper; CAP participated to the discussion of methodology and results and revised the paper. All authors read and approved the final version.

Funding : none.

Acknowledgements: Authors are grateful to the following institutions that provided the datasets used in the analysis: the Municipal Office of the City of Rome, the Agency for Public Health of Lazio Region, the Italian Air Force Meteorological Service, the LAit (Lazio Technological Innovation) S.p.a., and the Health Councillor of Lazio Region.

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Table 1. Person years and number of deaths by population characteristics and age group.

	All 65+ ages		65-74 ages		75+ ages	
	Person yrs	*Deaths*	*Person yrs*	*Deaths*	*Person yrs*	*Deaths*
	(n=641147) %	18609	*(n=348015) %*	4139	*(n=293132) %*	14470
Age						
65-74	*54.3*	4139				
75-84	*34.4*	7599				
85-94	*9.8*	5781				
95+	*1.6*	1090				
Gender						
Female	*59.1*	10112	*55.6*	1700	*63.3*	8412
Male	*40.9*	8497	*44.4*	2439	*36.7*	6058
Marital Status						
Married	*56.2*	8090	*68.5*	2825	*41.5*	5265
Not married,widowed, divorced	*43.8*	10519	*31.5*	1314	*58.5*	9205
SES						
Medium/High	*81.9*	15126	*80.5*	3144	*83.6*	11982
Low	*17.1*	3323	*18.6*	954	*15.4*	2369
Missing	*1.0*	160	*0.9*	41	*1.0*	119
HDD *(ICD9-CM)*						
Malignant neoplasm *(140-208)*	*3.9*	4510	*3.7*	1840	*4.1*	2670
Diabetes mellitus *(250)*	*3.9*	2237	*3.4*	576	*4.5*	1661
Other CNS disorders *(330-349)*	*1.9*	1530	*1.2*	335	*2.7*	1195
Ischaemic heart diseases *(410-414)*	*4.1*	2445	*3.3*	521	*5.1*	1924
Conduction disorders *(426)*	*1.1*	580	*0.6*	105	*1.5*	475
Cardiac dysrhythmias *(427)*	*3.5*	2557	*2.3*	437	*4.9*	2120
Heart failure *(428)*	*1.5*	1846	*0.8*	301	*2.4*	1545
Other cardiovascular diseases *(390-429 exept 410-414;426;427;428)*	*11.5*	5476	*9.3*	1221	*14.2*	4255
Chronic pulmonary diseases *(490-496)*	*3.1*	2344	*2.2*	495	*4.2*	1849
Acute and chronic liver diseases *(570-572)*	*0.7*	593	*0.7*	229	*0.7*	364
Renal failure *(584-588)*	*1.3*	1689	*0.7*	319	*1.9*	1370
Psychiatric disorders *(290-299;300.4;301.1;309.0;309.1;311)*	*1.2*	837	*0.8*	150	*1.6*	687
Cerebrovascular diseases *(430-438)*	*3.9*	2591	*2.4*	445	*5.6*	2146
Number of HDD for any other causes						
0-1	*97.6*	17774	*97.6*	3864	*97.6*	13910
2-3	*2.2*	715	*2.2*	213	*2.3*	502
4+	*0.2*	120	*0.2*	62	*0.2*	58

Table 2. Temperatures distribution and number of days by month and heat wave (years 2005-2007).

	May		**Jun**		**Jul**		**Aug**	
	Heat wave		Heat wave		Heat wave		Heat wave	
	no	yes	no	yes	no	yes	no	yes
min	14.3	28.8	17.3	31.2	24.4	32.6	20.8	32.9
max	27.3	33.5	32.4	38.4	34.2	39.1	34.3	39.7
20 pct	18.7	29.2	20.6	33.4	27.8	34.4	26.4	34.3
50 pct	21.1	29.9	26.7	34.6	29.9	35.3	28.8	35.5
90 pct	25.7	30.9	31.0	38.1	33.1	38.5	32.3	39.1
n(dd)	82	11	68	22	51	42	80	13

Table 3. Mortality rate (MR), risk difference (RD), adjusted mortality relative risks (RR) and REM index for socio-demographic covariates modalities by heat wave. 65-74 and 75+ age groups.

	65-74 ages										75+ ages									
	Deaths		*MR *1000*		*RD *1000*	*(95% IC)*	*RR*	*(95% IC)*	*REM Index*	*p-value*	*Deaths*		*MR *1000*		*RD *1000*	*(95% IC)*	*RR*	*(95% IC)*	*REM Index*	*p-value*
	Heat wave		*Heat wave*								*Heat wave*		*Heat wave*							
	no	*yes*	*no*	*yes*							*no*	*yes*	*no*	*yes*						
Total	2753	1386	11.6	12.6	1.0	*(0.2 ; 1.8)*	1.08	*(1.02 - 1.16)*			9427	5043	47.2	54.1	6.9	*(5.1 ; 8.7)*	1.15	*(1.11 - 1.18)*		
Age																				
75-84											5004	2595	33.2	37.0	3.8	*(2.1 ; 5.5)*	1.11	*(1.06 - 1.17)*	*1.00*	
85-94											3733	2048	87.8	102.4	14.7	*(9.4 ; 19.9)*	1.17	*(1.11 - 1.23)*	*1.05*	*0.196*
95+											690	400	101.7	124.9	23.3	*(8.9 ; 37.7)*	1.23	*(1.08 - 1.39)*	*1.10*	*0.149*
Gender																				
Female	1124	576	8.5	9.4	0.9	*(0.0 ; 1.8)*	1.11	*(1.00 - 1.22)*	*1.00*		5406	3006	42.7	50.9	8.2	*(6.1 ; 10.3)*	1.19	*(1.14 - 1.24)*	*1.00*	
Male	1629	810	15.4	16.5	1.1	*(-0.3 ; 2.5)*	1.07	*(0.99 - 1.17)*	*0.96*	*0.666*	4021	2037	54.8	59.5	4.6	*(1.5 ; 7.7)*	1.08	*(1.03 - 1.14)*	*0.91*	*0.008*
Marital Status																				
Married	1891	934	11.6	12.3	0.7	*(-0.3 ; 1.6)*	1.06	*(0.98 - 1.15)*	*1.00*		3494	1771	42.2	45.5	3.3	*(0.7 ; 5.8)*	1.07	*(1.02 - 1.14)*	*1.00*	
Not married,widowed, divorced	862	452	11.5	13.1	1.6	*(0.2 ; 3.0)*	1.14	*(1.02 - 1.28)*	*1.08*	*0.323*	5933	3272	50.7	60.2	9.5	*(7.1 ; 12.0)*	1.18	*(1.13 - 1.24)*	*1.10*	*0.008*
SES																				
Medium/High	2088	1056	10.9	11.9	1.0	*(0.1 ; 1.8)*	1.09	*(1.01 - 1.18)*	*1.00*		7807	4175	46.7	53.5	6.8	*(4.9 ; 8.8)*	1.14	*(1.10 - 1.19)*	*1.00*	
Low	634	320	14.4	15.6	1.3	*(-0.8 ; 3.3)*	1.09	*(0.95 - 1.25)*	*1.00*	*0.999*	1531	838	49.7	58.1	8.4	*(3.7 ; 13.1)*	1.17	*(1.07 - 1.27)*	*1.03*	*0.668*
Missing	31	10	13.7	9.5	-4.2	*(-11.8 ; 3.4)*	0.69	*(0.34 - 1.40)*	*0.64*	*0.202*	89	30	46.6	33.6	-13.0	*(-28.4 ; 2.5)*	0.72	*(0.48 - 1.10)*	*0.63*	*0.031*

Table 4a Mortality rate (MR), risk difference (RD), adjusted mortality relative risks (RR) and REM index for hospitalization diagnosed diseases (HDD) modalities by heat wave. 65-74 age groups.

	65-74 ages									
	Deaths		*MR *1000*		*RD *1000*	*(95% IC)*	*RR*	*(95% IC)*	*REM Index*	*p-value*
	Heat wave		*Heat wave*							
	no	*yes*	*no*	*yes*						
HDD										
Malignant neoplasm										
no	1503	796	6.6	7.5	0.9	*(0.3 ; 1.5)*	1.14	*(1.05 - 1.24)*	*1.00*	
yes	1250	590	141.9	143.7	1.8	*(-12.2 ; 15.8)*	1.02	*(0.93 - 1.13)*	*0.89*	*0.092*
Diabetes mellitus										
no	2363	1200	10.3	11.3	1.0	*(0.2 ; 1.7)*	1.10	*(1.02 - 1.17)*	*1.00*	
yes	390	186	47.7	48.9	1.2	*(-7.3 ; 9.6)*	1.03	*(0.87 - 1.23)*	*0.94*	*0.550*
Other CNS disorders										
no	2534	1270	10.8	11.7	0.9	*(0.1 ; 1.6)*	1.08	*(1.01 - 1.16)*	*1.00*	
yes	219	116	75.2	87.0	11.7	*(-7.0 ; 30.4)*	1.15	*(0.92 - 1.44)*	*1.07*	*0.615*
Ischaemic heart diseases										
no	2396	1222	10.4	11.5	1.0	*(0.3 ; 1.8)*	1.10	*(1.03 - 1.18)*	*1.00*	
yes	357	164	45.0	44.6	-0.4	*(-8.7 ; 7.9)*	1.01	*(0.84 - 1.21)*	*0.92*	*0.398*
Conduction disorders										
no	2683	1351	11.4	12.3	1.0	*(0.2 ; 1.7)*	1.08	*(1.02 - 1.16)*	*1.00*	
yes	70	35	45.7	49.7	4.0	*(-15.7 ; 23.6)*	1.09	*(0.73 - 1.61)*	*1.00*	*0.992*
Cardiac dysrhythmias										
no	2443	1259	10.5	11.7	1.2	*(0.4 ; 1.9)*	1.11	*(1.04 - 1.19)*	*1.00*	
yes	310	127	57.2	50.5	-6.7	*(-17.6 ; 4.1)*	0.90	*(0.73 - 1.10)*	*0.81*	*0.055*
Heart failure										
no	2552	1286	10.8	11.7	0.9	*(0.2 ; 1.7)*	1.09	*(1.02 - 1.16)*	*1.00*	
yes	201	100	106.9	115.0	8.2	*(-18.8 ; 35.1)*	1.10	*(0.87 - 1.40)*	*1.01*	*0.892*
Other cardiovascular diseases										
no	1935	983	9.0	9.8	0.8	*(0.1 ; 1.6)*	1.09	*(1.01 - 1.18)*	*1.00*	
yes	818	403	37.0	39.4	2.4	*(-2.2 ; 7.0)*	1.06	*(0.95 - 1.2)*	*0.97*	*0.697*
Chronic pulmonary diseases										
no	2435	1209	10.5	11.2	0.7	*(0.0 ; 1.5)*	1.07	*(1.00 - 1.15)*	*1.00*	
yes	318	177	59.9	72.8	12.9	*(0.3 ; 25.5)*	1.23	*(1.03 - 1.48)*	*1.15*	*0.155*
Acute and chronic liver diseases										
no	2595	1315	11.0	12.0	1.0	*(0.2 ; 1.8)*	1.09	*(1.02 - 1.17)*	*1.00*	
yes	158	71	95.7	93.1	-2.7	*(-28.9 ; 23.6)*	1.00	*(0.76 - 1.33)*	*0.92*	*0.567*
Renal failure										
no	2529	1291	10.7	11.8	1.1	*(0.3 ; 1.8)*	1.10	*(1.03 - 1.18)*	*1.00*	
yes	224	95	127.7	115.7	-12.0	*(-40.6 ; 16.7)*	0.93	*(0.73 - 1.18)*	*0.85*	*0.177*
Psychiatric disorders										
no	2658	1331	11.3	12.2	0.9	*(0.1 ; 1.7)*	1.08	*(1.01 - 1.15)*	*1.00*	
yes	95	55	47.2	59.2	12.0	*(-6.3 ; 30.2)*	1.27	*(0.91 - 1.77)*	*1.18*	*0.350*
Cerebrovascular diseases										
no	2455	1239	10.6	11.5	0.9	*(0.2 ; 1.7)*	1.09	*(1.02 - 1.17)*	*1.00*	
yes	298	147	51.8	54.9	3.1	*(-7.5 ; 13.8)*	1.08	*(0.88 - 1.31)*	*0.99*	*0.907*
Number of HDD for any other causes										
0-1	2555	1309	11.0	12.1	1.1	*(0.4 ; 1.9)*	1.11	*(1.04 - 1.18)*	*1.00*	
2-3	151	62	29.4	26.2	-3.2	*(-11.2 ; 4.8)*	0.89	*(0.66 - 1.20)*	*0.80*	*0.161*
4+	47	15	98.4	68.9	-29.5	*(-74.3 ; 15.3)*	0.68	*(0.38 - 1.21)*	*0.61*	*0.099*

Table 4b. Mortality rate (MR), risk difference (RD), adjusted mortality relative risks (RR) and REM index for hospitalization diagnosed diseases (HDD) modalities by heatwave. 75+ age groups.

	Deaths		*MR *1000*		*RD *1000*	*(95% IC)*	*RR*	*(95% IC)*	*REM Index*	*p-value*
	Heat wave		*Heat wave*							
	no	*yes*	*no*	*yes*						
HDD										
Malignant neoplasm										
no	7627	4173	39.8	46.7	6.9	*(5.2 ; 8.5)*	1.17	*(1.13 - 1.21)*	*1.00*	
yes	1800	870	217.4	224.3	6.9	*(-11.0 ; 24.9)*	1.03	*(0.95 - 1.12)*	*0.88*	*0.006*
Diabetes mellitus										
no	8340	4469	43.7	50.1	6.5	*(4.7 ; 8.2)*	1.15	*(1.10 - 1.19)*	*1.00*	
yes	1087	574	122.2	137.8	15.6	*(2.2 ; 29.0)*	1.12	*(1.02 - 1.24)*	*0.98*	*0.734*
Other CNS disorders										
no	8657	4618	44.5	50.9	6.4	*(4.6 ; 8.1)*	1.14	*(1.10 - 1.18)*	*1.00*	
yes	770	425	144.8	171.4	26.6	*(7.4 ; 45.9)*	1.18	*(1.04 - 1.32)*	*1.04*	*0.625*
Ischaemic heart diseases										
no	8126	4420	42.8	49.9	7.1	*(5.3 ; 8.8)*	1.16	*(1.12 - 1.20)*	*1.00*	
yes	1301	623	127.6	131.3	3.7	*(-8.7 ; 16.1)*	1.03	*(0.94 - 1.13)*	*0.89*	*0.020*
Conduction disorders										
no	9107	4888	46.3	53.2	6.9	*(5.2 ; 8.7)*	1.15	*(1.11 - 1.19)*	*1.00*	
yes	320	155	104.0	108.6	4.6	*(-15.9 ; 25.2)*	1.04	*(0.86 - 1.26)*	*0.91*	*0.337*
Cardiac dysrhythmias										
no	7999	4351	42.1	49.0	7.0	*(5.2 ; 8.7)*	1.16	*(1.12 - 1.21)*	*1.00*	
yes	1428	692	147.3	152.7	5.4	*(-8.3 ; 19.2)*	1.03	*(0.94 - 1.13)*	*0.89*	*0.019*
Heart failure										
no	8385	4540	43.0	49.9	6.9	*(5.2 ; 8.6)*	1.16	*(1.12 - 1.20)*	*1.00*	
yes	1042	503	215.7	221.7	6.1	*(-17.3 ; 29.5)*	1.03	*(0.92 - 1.14)*	*0.89*	*0.035*
Other cardiovascular diseases										
no	6643	3572	38.8	44.6	5.9	*(4.2 ; 7.6)*	1.15	*(1.11 - 1.20)*	*1.00*	
yes	2784	1471	97.9	110.9	13.0	*(6.2 ; 19.7)*	1.13	*(1.07 - 1.20)*	*0.98*	*0.643*
Chronic pulmonary diseases										
no	8186	4435	42.8	49.6	6.9	*(5.1 ; 8.6)*	1.16	*(1.11 - 1.20)*	*1.00*	
yes	1241	608	146.1	154.7	8.6	*(-6.1 ; 23.4)*	1.06	*(0.96 - 1.17)*	*0.91*	*0.095*
Acute and chronic liver diseases										
no	9172	4934	46.2	53.3	7.0	*(5.3 ; 8.8)*	1.15	*(1.11 - 1.19)*	*1.00*	
yes	255	109	188.4	172.5	-15.8	*(-55.6 ; 24.0)*	0.91	*(0.73 - 1.14)*	*0.79*	*0.041*
Renal failure										
no	8503	4597	43.4	50.2	6.9	*(5.2 ; 8.6)*	1.16	*(1.12 - 1.20)*	*1.00*	
yes	924	446	243.3	249.6	6.3	*(-21.7 ; 34.3)*	1.03	*(0.92 - 1.15)*	*0.89*	*0.048*
Psychiatric disorders										
no	8980	4803	45.7	52.3	6.7	*(4.9 ; 8.4)*	1.14	*(1.10 - 1.18)*	*1.00*	
yes	447	240	136.5	158.2	21.7	*(-2.0 ; 45.4)*	1.16	*(0.99 - 1.35)*	*1.02*	*0.894*
Cerebrovascular diseases										
no	8033	4291	42.6	48.7	6.2	*(4.4 ; 7.9)*	1.14	*(1.10 - 1.19)*	*1.00*	
yes	1394	752	125.5	144.3	18.8	*(6.6 ; 31.1)*	1.15	*(1.05 - 1.26)*	*1.00*	*0.896*
Number of HDD for any other causes										
0-1	9061	4849	46.5	53.3	6.8	*(5.0 ; 8.6)*	1.14	*(1.10 - 1.18)*	*1.00*	
2-3	331	171	72.4	81.5	9.1	*(-5.4 ; 23.6)*	1.11	*(0.92 - 1.34)*	*0.97*	*0.772*
4+	35	23	93.2	134.5	41.3	*(-21.7 ; 104.4)*	1.44	*(0.85 - 2.44)*	*1.27*	*0.388*