

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

AUTHORS:

Patrizia Schifano¹, Giovanna Cappai¹, Manuela De Sario¹, Paola Michelozzi¹, Claudia Marino¹, Anna Maria Bargagli¹, Carlo A. Perucci¹

Authors affiliation:

¹ Department of Epidemiology, Local Health Authority Rome E, Rome, Italy

Correspondence to:

Dr. Patrizia Schifano

Department of Epidemiology Local Health Authority RM/E

Via di Santa Costanza 53

00198 Rome, Italy

Phone: +39-06-83060457

Fax: +39-06-83060374

e-mail : schifano@asplazio.it

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ABSTRACT

Background

Few studies have identified specific factors that increase mortality during heat waves. This study investigated socio-demographic characteristics and pre-existing 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. Risk differences were also calculated. All analyses were run separately for the 65-74 and 75+ age groups.

Results

In the 65-74 age group the risk of dying during heat waves was higher among unmarried subjects and those with a previous hospitalization for chronic pulmonary disease or psychiatric disorders. In the 75+ age group, women, and unmarried subjects were more susceptible to heat; furthermore a higher susceptibility to heat among those with previous hospitalization for diabetes, diseases of the central nervous system (CNS), psychiatric disorders and cerebrovascular diseases resulted from risk differences.

Discussion

Results show a higher susceptibility to heat among those older than seventy-five years, females and unmarried. Pre-existing health conditions play a different role among the two considered age groups. Moreover, compared with previous studies the pattern of susceptibility factors have slightly 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 better understand 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].

During heat waves the greatest burden in terms of mortality and morbidity is in specific population subgroups 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 as 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 the effectiveness of prevention programs.

Until now, most of the evidence regarding factors that modify the health effects of heat waves derives from case-control studies [6,9], and, more recently, from case-only and case-crossover studies [5,10-13]. However, in such studies the design itself doesn't allow to estimate comparable relative risks of dying during heat waves for different subgroups of interest [14].

Under a public health point of view a clear understanding of factors affecting heat wave related mortality is important to properly target prevention programs. Moreover after the 2003 heat wave in Europe the introduction of prevention programs may have modified the determinants of population's susceptibility to high temperature [15,16].

In Italy the National Department of Civil Protection and the Ministry of Health implemented a national heat prevention program [17], and national guidelines for the prevention of heat health effects have been defined, targeted to high risk subgroups (www.ccm-network.it). In 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 [18].

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 susceptibility factors. The inclusion of the most recent years was to account for the possible changes in the spectrum of susceptibility 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, until the 15th of September 2007. 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 [19].

Health Status

We selected a list of 13 groups of diagnoses, known to be associated with an increased mortality risk from high temperatures (Table 1) [3,5,7,12,20]. 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) [21], 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 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 episode, defined using maximum apparent temperature (Tappmax), an index of discomfort based on air and dew point temperatures [22]. Tappmax was defined as the maximum daily value of apparent temperatures.

A heat wave episode is defined when Tappmax rises above the monthly threshold, defined by the Heat Health Watch Warning System (HHWWS) [17], (May: 28.5, June: 32.5°C; July: 33.5°C; August/September: 34.5°C)). for two or more consecutive days. Daily weather data from Ciampino airport station 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, for each subject through a record linkage with the Regional Registry of Causes of Death (Regional Mortality Register) [23] using individual social security numbers. We considered all deaths from non-injury causes (International Classification of Diseases, 9th Revision [ICD-9]: 1-799).

Our outcome is represented by all deaths occurred during a heat episode or in the following three days, to account for the lag effect of heat on mortality.

Statistical Analysis

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 used a Poisson regression model to estimate the adjusted relative risk of mortality during heat wave days versus not heat wave days. We run a model including an indicator variable for heat wave days, age, gender, socio-economic status, civil status, presence or absence of each of the selected groups of diagnosis and the number of hospitalizations for conditions not included in the previous list.

Through a manual backward stepwise procedure we then selected a model including only variables significantly associated with mortality. Age, gender and presence/absence of heat wave were forced into the model. Interaction terms between each of the included covariates and heat-wave were added afterwards.

We calculated the relative risks (RR) of dying on heat wave and non heat wave days for each of the modalities of the covariates and the REM (Relative Effect Modification) index. REM index is the ratio of the relative risks of dying during a heat wave for each of the covariates considered, comparing each category to the reference one [5]. A significant REM index (p-

value lesser than 0.20) means that the specific covariate acts as an effect modifier of the heat-mortality relationship. Risk differences (RD) was also computed as the difference between the model estimates of absolute risks in presence and absence of heat wave for each modality of the considered covariates. A comparison between RDs relative to different modalities of the same variable was performed to evaluate a possible effect modification on an additive scale. The analysis was performed using SAS [24].

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 (5%) 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 characteristics. About 50% of the analyzed population was older than 75 and 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 hospitalizations for all the considered diseases 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. 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 1.08 (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

Results 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 smaller extent, for psychiatric disorders and among those not married, widowed or divorced (tables 3 and 4). For these same factors we observed also an increased excess in the absolute numbers of deaths during heat wave days compared to non heat wave days. Subjects previously hospitalized for malignant neoplasm, 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 showed a similar protective effect; while socio-economic status does not modify 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 is greater for those who had 4 or more hospitalizations for other causes in the previous two years, although they are not statistically

significant. However, having had 4 or more hospitalizations is associated to a higher absolute number of deaths, as shown by RDs (Table 4).

We observed more deaths attributable to heat waves among those who had a previous hospitalization for diabetes, diseases of the central nervous system, psychiatric disorders and cerebrovascular diseases.

Conversely, there was a protective effect observed among subjects with a previous hospitalization for a wide range of conditions, including malignant neoplasm, ischemic diseases, heart 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. Overall, the impact of heat wave on mortality was higher among the older age group; moreover, females and unmarried subjects result to be more susceptible to heat waves effects.

Results from the 65-74 age group identify only previous hospitalizations for chronic pulmonary disease as a significant effect modifier; however, subjects with at least one hospitalization for psychiatric disorders showed a higher excess in mortality during heat wave days. In the 75+ age group, a higher susceptibility to heat was observed among those with previous hospitalization for diabetes, diseases of the central nervous system, psychiatric disorders and cerebrovascular diseases, but only from the risk differences analysis. Our results confirm that age acts as an effect modifier of the associations under study, and suggest that

the underlying mechanisms that determine degrees of susceptibility to heat waves might vary with age.

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. Furthermore, this study design 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 health conditions that modify the heat-mortality relationship on an additive scale but not on a multiplicative scale.

The higher relative risk of mortality during heat waves in subjects with previous hospitalization for a chronic respiratory illness is supported by previous case-only, case-crossover and time-series studies [10,12,25,26]. In patients with COPD an exposure to extreme heat might induce hyperventilation leading to dyspnea and to mechanical and cardiovascular effects [27]; furthermore, some heat-induced physiological changes such as dehydration might represent a risk factor of broncho-pulmonary disorders [28]. Such mechanism offers an explanation of the higher rates of hospitalization for respiratory causes observed by a European multicity study [29]. The higher risk of dying among people with psychiatric disorders is supported by previous studies [3,12], and may be explained by the inability of these people to care for themselves [3], and by the side effects of some neuroleptic drugs [30].

In this as in other studies [4,5,12], the effect of heat waves results stronger among those older than 75 years. This can be attributed to concurrent factors such as pre-existing chronic diseases, physical fitness level, and attenuated physiological responses to heat such as lower sweat gland outputs, decreased skin blood flow and reduced cardiac outputs [31].

Results from both age groups showed that those who were hospitalized in the previous two years had a smaller risk of dying during heat waves than non previously hospitalized subjects. For some specific health conditions, 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. 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 an additive than a multiplicative effect, since the absolute risk of dying among those who had an hospitalization during the previous two years is presumably higher than in the not hospitalized group [6].

As reported by previous studies [5], we did not observe any effect modification by socio-economic conditions in either of the two considered age groups. It should be noted that our indicator of socio-economic status is derived from a census tract level study [19], therefore misclassification of individual exposure may have affected our findings toward the null.

The comparison of our results with previous studies on risk factors for heat related mortality in the 65+ age group in Rome before 2003 [5,12] shows a slight change in the pattern of the concurrent clinical conditions associated to a higher susceptibility to heat; heart failure and heart conduction disorders were not currently identified as risk modifiers as they had been previously [5,12], whereas diabetes and diseases of the CNS were identified in this study as having a higher number of deaths during heat waves. These changes may have resulted from the implementation of prevention programs targeted to high risk population in Rome in recent years [17, 18] .

Some limitations of this study need to be discussed. Even if we have considered a three-year period cohort of all the residents in Rome, the high number of covariates included in the model determine a problem of power in the analysis. Among the 65-74 years old in particular we might not have had enough power to detect all the effect modifiers.

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) 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 [32].

In this study, we used “population-averaged” temperatures collected at a single monitor (the nearest airport), but no potential measurement error should have affected our effect estimates since it was possibly of the same entity in heat wave and non-heat wave days and cancelled by comparisons. Possible sources of exposure bias are however the micro-urban variations in heat effect that are influenced by the underlying socio-economic conditions and the summer migratory patterns that finds the elderly and ill people and those of low socio-economic status more often in the city. This bias is difficult to quantify and to be adjusted for from the available data.

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 suggest that prevention programs should mainly target people over 74

years of age, women and unmarried people. Specifically, in the 65-74 years old age group people with chronic pulmonary diseases should be particularly monitored during heat waves, while further analysis should be done to better understand the role of previous hospitalizations for cerebrovascular, CNS, psychiatric disorders and diabetes among those older than 75 years . In conclusion, for the purposes of public health programmes susceptibility should be considered time, space and population specific, and the identification of prognostic factors should be performed repeatedly over time.

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.

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

	All 65+ ages		65-74 ages		75+ ages	
	Person yrs (n=641147) %	Deaths 18609	Person yrs (n=348015) %	Deaths 4139	Person yrs (n=293132) %	Deaths 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 (Hospitalization Diagnosed Disease) (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 except 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. Temperature 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 risk (RR) and relative effect modification (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 risk (RR) and relative effect modification (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 risk (RR) and relative effect modification (REM) index for hospitalization diagnosed diseases (HDD) modalities by heatwave. 75+ age groups.

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

