



REVIEW ARTICLE

The Impact of Heat Waves on Mortality among the Elderly: A Mini Systematic Review

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Abstract

The aim of this systematic review was to review the recent literature regarding the effect of heat waves on mortality in elderly adults. A systematic search of the literature, was conducted by two reviewers during March 2018, using three electronic databases (PubMed, Web of Science, and Scopus). The PRISMA guidelines were used for the quality assessment of the published studies. The literature search identified a total of 345 articles, while only 24 studies met the inclusion criteria and were included in this analysis. Overall, the results from these studies show that, although recent advances in technology allow scientists to predict heat waves, thereby enabling health agencies to alert the public with heat advisories, the number of heat wave-induced deaths remains high. The underlying reasons for these increases in heat-wave-induced mortality remains unclear, highlighting the need for developing evidence-based thresholds for the activation and implementation of actions plans to protect the health of heat-vulnerable elderly populations.

Keywords

Extreme heat events, Older, Aging, Deaths, Heat stress, Heat shock, Hyperthermia

Introduction

Extreme heat conditions are considered a major threat for public health and can induce many health complications to the urban populations. With a predicted rise in the frequency and intensity of extremely hot weather due to changing climate, heat exposure is presenting an increasing challenge to the health and safety

of heat-vulnerable populations such as elderly adults. Such extremes have resulted in the deaths of 70,000 in Europe in the summer 2003 [1] and 55,000 in Russia during the summer 2010 heat wave [2]. The immense burden placed on the health care systems worldwide as a result of these heat waves has been unequivocal [3]. When people are exposed to heat, especially when temperature remains atypically high for several days such as occurs during the summer months, they can suffer from potentially deadly illnesses such as heat exhaustion and heat stroke quickly [4]. Elderly with pre-existing health conditions are particularly vulnerable as exposure to even short periods of heat can aggravate their health conditions by worsening disease-specific symptoms [5]. Accordingly, a correlation between high ambient temperatures and negative health outcomes exists. Epidemiological evidence demonstrates a 2-5% increase in all-cause mortality for a 1 °C increase in average daily temperature during hot temperature periods [6]. However, extreme heat events occurring in spring or early summer pose an even greater threat to health in the elderly because of their lack of acclimation [7].

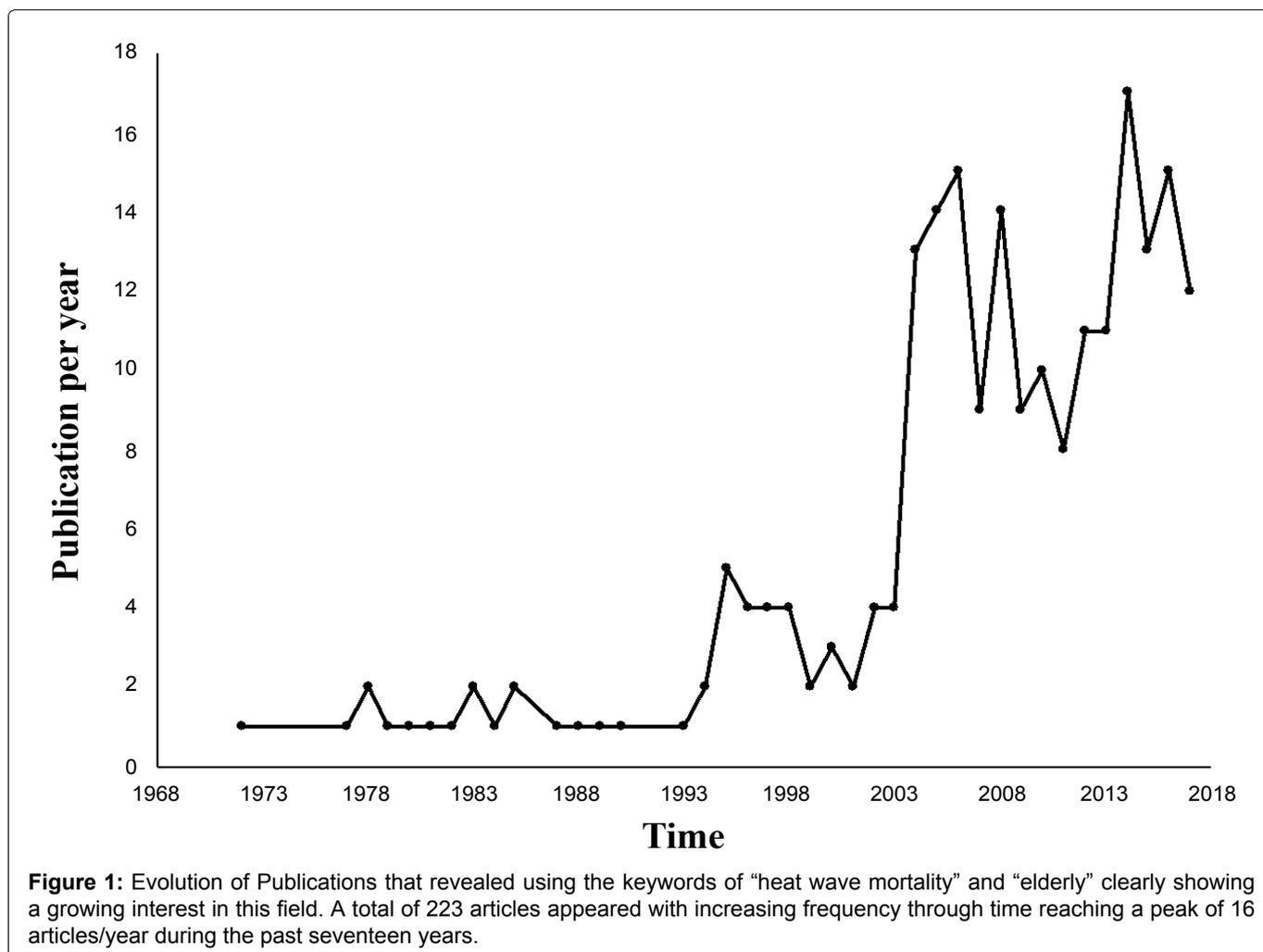
A heat wave is usually considered a prolonged period of excessive heat. According to Gasprarrini and Armstrong [8] a heat wave is defined as a period where for ≥ 2 repeated days the daily mean temperature is at or above the 98th percentile of the warm season daily mean temperature. Moreover, the intensity, the dura-

tion and the time in the season that it appears, are the main characteristics of each heat wave [8]. Moreover, as the rapidly aging population relocates to large urban centres to be closer to essential health and social care services, they are likely to experience some of the highest temperatures during hot weather periods. This is because of the urban heat island where temperatures within major metropolitan cities (e.g., London, England; Toronto, Canada, New York City, USA; Paris, France) can be as much as 10 °C greater than the surrounding rural areas [9-11]. These elevated temperature are primarily due to the design and density of buildings and by other manmade changes which includes asphalt roads and pathways, removal of trees, elimination of open green space areas, others [12].

Elderly persons are typically considered those who are aged 65 years or more [13]. Natural ageing can be characterized by a complex process, in which progressive age-specific deteriorations of internal physiological systems inevitably impair the body's capacity to respond appropriately to internal and external stressors [14-16]. As recent studies show, this includes deterioration in their ability to dissipate heat [17-19], a process pivotal in the maintenance of normal core temperature especially in extreme heat conditions. Specifically, older adults take longer to respond to increases in ambient air

temperature than their younger counterparts [20]. This response is due to age-related reductions in heat loss responses of sweating [21,22] and skin vasodilation [23-27], which are paralleled by marked impairments in the whole-body heat dissipation [18], and occur independently of the individual's level of acclimation [23]. As a consequence, elderly people are less heat tolerant and are at an increased risk of heat-related morbidity and mortality [17,28].

Given the fact that the population over age 65 years is steadily increasing [29] the numbers of heat related illnesses and deaths are likely to rise exponentially. Accordingly, there has been an increased urgency to address this important public health issue. This is evidenced by the fact that the number of articles (total of 507 based on search term "heat wave mortality" and "elderly") published in PubMed are appearing with increased frequency (~16 articles per year) over the past five years (Figure 1). Experts suggest that appropriate health prevention and management programs could greatly limit heat-related morbidity and mortality in heat vulnerable populations such as the elderly [30,31]. To contribute towards addressing these concerns, the aim of this systematic review was to review the recent literature regarding the effect of heat waves on mortality in elderly adults.



Methods

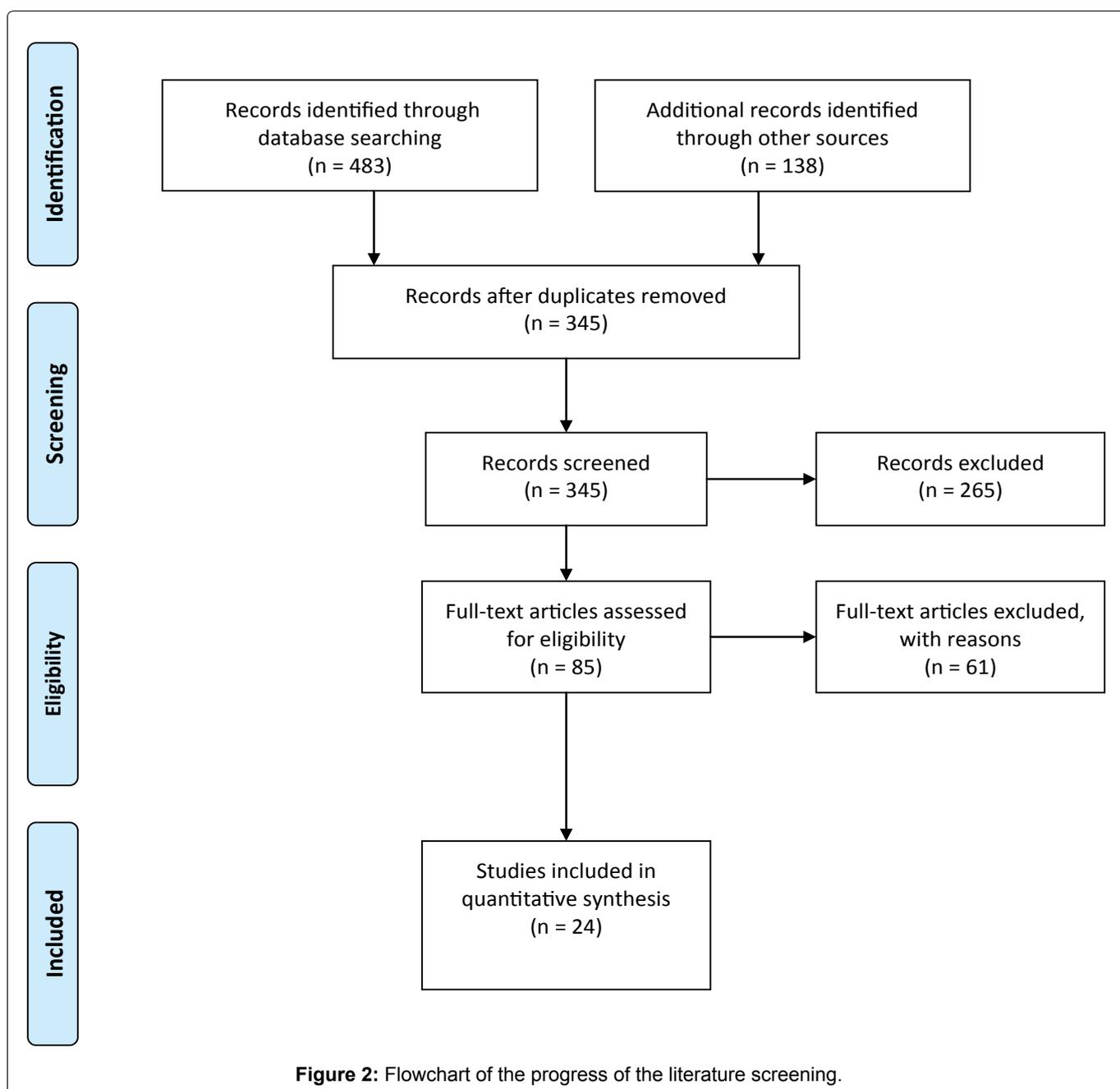
Literature search and identification

The current review included epidemiological studies that report on epidemiological data regarding the effect of heat waves on elderly mortality. A systematic search of literature was conducted by two reviewers during March 2018 using three electronic databases (PubMed, Web of Science and Scopus). The PRISMA guidelines were used for the quality assessment of the published studies [32]. Studies were selected using inclusion and exclusion criteria. Studies were included in the study if: 1) Results for elderly mortality rates during heat waves were presented; 2) Results for the effect of “heat waves” on “elderly mortality” as a sub-population were reported; and 3) The study was written in English. Studies were excluded when they: 1) Did not present the number of deaths during “heat wave” periods but

only the relative risk for mortality or models for the daily mortality prediction; 2) Did not evaluate the elderly mortality but mortality rates in other age groups and 3) Were studies published only in abstract form. Studies identified in the search were initially examined using the information presented in the title and abstract. Thereafter a full evaluation of the full-text copy of the article was conducted to determine if it met all inclusion criteria.

Results

A total of 345 articles were identified in the search. Of these, 85 full-text articles were reviewed for eligibility and only 24 studies met the inclusion criteria (Figure 2). Articles were excluded for the following reasons: 12 referred to animal, pregnancy, and infant mortality during heat waves; 22 examined the impact of heat waves mortality on specific chronic diseases; 5 studies were re-



view articles only; 16 studies evaluated the relative risk of mortality or presented models for the prediction of daily mortality; 6 studies evaluated the impact of heat waves in different aged groups but no on elderly. The

24 studies included in our review provided estimates of heat-related mortality in the elderly during heat waves that encompasses different geographically locations (Figure 3 and Table 1).

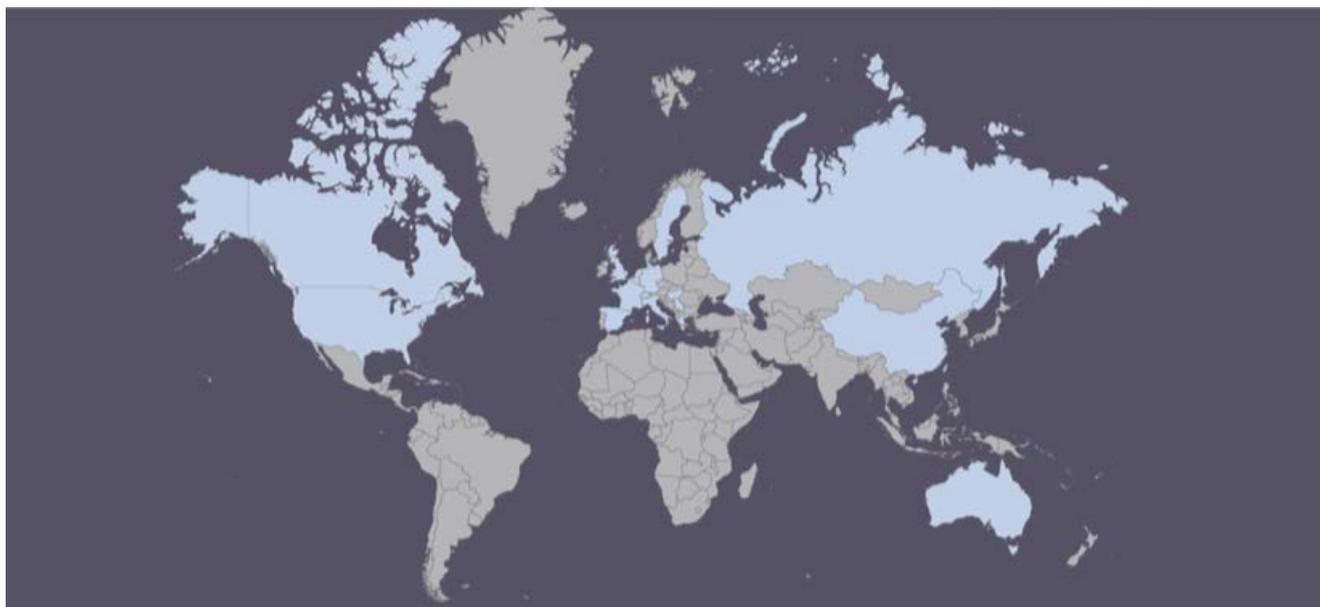


Figure 3: Geographical areas (marked with light blue) where the elderly mortality rates have been assessed in the studies evaluated in the current review.

Table 1: Epidemiological studies on elderly mortality during heat waves.

Reference	Region & population	Period	Temperature °C Mean, min-max	Results
Steul, et al. [41]	Frankfurt, Germany ≥ 60 years	2- 13 August 2003 18-22 July 2006 8-12 July 2010 1-5 July 2015	26.5, 19.1, 33.7 26, 19.7, 33.8 26.8, 19.6, 34.4 26.9, 20.1, 34.1	Mortality (cases of death/day): 32.7 20.6 22.6 25.4
Conti, et al. [34]	21 regions of Italy > 75 years	1 June-31 August 2003	> 40.0	No of deaths on 2002: 13.517 No of deaths on 2003: 16.393
Åström, et al. [39]	Rome & Stockholm > 50 years	15 May- 15 September the years from 2000- 2008	Rome: 29.5, 15.9-40.2 Stockholm: 18.6, 3.1-31.1	No of deaths in Rome: 47.180 No of deaths in Stockholm: 24.157
Borrell, et al. [44]	Barcelona, Spain > 65 years	June, July & August 2003 & 1998-2000	> 30.5	No of deaths from 1998-2002: 6.691 No of deaths on 2003: 1.489
Bogdanovic, et al. [45]	Belgrade, Serbia > 75 years	16 - 24 July 2007	34.6, 26.3-40.7	No of deaths: 350
Bustinza, et al. [65]	Quebec, Canada > 75 years	July 2010	18.5-34.0	No of deaths: 1.039
Canoui-Poitaine, et al. [66]	Paris, France > 75 years	1-20 August 2003 1-20 August 2000, 2001, 2003	-	No of deaths on 2003: 727 No of deaths on 2000, 2001, 2003: 215
Sartor [67]	589 communes of Belgium 65 years & older	27 June- 7 August 1994	21.9, 15.3-27.5	No of deaths on 1994: 990
Cerutti, et al. [68]	Ticino, Switzerland > 65 years > 75 years	June, July, August 2003	24.6	No of deaths on > 65 years: 558 No of deaths on > 75 years: 443

Conti, et al. [69]	Genoa, Italy > 74 years	16-31 August 2003	> 40.0	No of deaths: 968
D'Ippoliti, et al. [35]	Athens, Barcelona, Budapest, London, Milan, Munich, Paris, Rome, Valencia > 65 years	Athens 1997-2004 Barcelona 1991-2004 Budapest 1992-2003 London 1990-2004 Milan 1990-2003 Munich 1992-2004 Paris 1990-2003 Rome 1992-2004 Valencia 1994-2003	26.4- 37.6 23.2- 36.8 22.6- 32.8 16.8- 27.1 22.2- 36.2 15.9- 28.3 19.1- 30.9 21.6- 35.2 24.2- 39.9	No of deaths in Athens: 62 No of deaths in Barcelona: 30 No of deaths in Budapest: 46 No of deaths London: 117 No of deaths Milan: 21 No of deaths Munich: 24 No of deaths Paris: 82 No of deaths Rome: 42 No of deaths Valencia: 12
Huynen, et al. [70]	Netherlands ≥ 65 years	1990, 1994, 1995, 1997	25.0-30.0	No of deaths 1990: 301 No of deaths 1994: 1.043 No of deaths 1995: 214 No of deaths 1997: 230
Fouillet, et al. [71]	22 regions of France ≥ 75 years	1 - 20 August	25.0-37.0	No of deaths: 14539
Green, et al. [43]	England (East of England, East Midlands, London, North East, North West, South East, South West, West Midlands, Yorkshire & Humber) > 65 years	1 June- 15 September 2013	19.5, 16.5-21.6 19.1, 17.7-22.7	No of deaths: 195
Yang, et al. [53]	Guangzou, China > 65 years	13-24 July 2005 June, 9-14 August 2005	22.9, 19.7-27.6	No of deaths: 606 No of deaths: 453
Lan, et al. [38]	Harbib, China ≥ 65 years	7 -11 June 2010	> 35.0	No deaths: 284
Michelozzi, et al. [56]	Rome, Milan, Turin, Bologna, Italy ≥ 75 years	June-August 2003	35.2, 32.7, 32.7, 32.8,	No of deaths in Rome: 6089 No of deaths in Milan: 2958 No of deaths in Turin: 2331 No of deaths in Bologna: 1432
Ellis, et al. [47]	New York > 65 years	1- 7 August 1975	≥ 28.9	No of deaths: 136.3 ± 35.6
Revich, et al. [37]	Moscow, Russia 2001 > 75 years	15- 27 July 2001	> 22.7	No of deaths: 1200
Schifano, et al. [51]	Rome, Italy ≥ 65 years	May, June, July, August 2005-2007	May 29.2, 28.8-33.5 June 33.4, 31.2-38.4 July 34.4, 32.6-39.1 August 34.3, 32.9-39.7	No of deaths: 18.609
Schaffer, et al. [72]	Sydney, Australia ≥ 75 years	30 January- 6 February 2011	35.2, 32.0-38.5	No of deaths: 814
Huang, et al. [52]	Shangai, China > 65 years	19 July-6 August 2003	36.3	No of deaths: 2283
Smoyer [41]	St. Louis, Missouri, USA > 64 years	4-17 July 1980 12-17 July 1995	41.7 38.3	Average number of deaths on 1980: 14.61 ± 6.91 Average number of deaths on 1995: 9.07 ± 3.31
Sun, et al. [54]	Pudong New Area, China > 65 years	16 June- 15 September 2013	30.1, 27.0-31.6	No of deaths: 3.726

Analysis and Discussion

The majority of the identified studies examining the effects of heat waves on mortality in the elderly present epidemiological data based on the European heat wave

of 2003, when temperature extremes were observed in many parts of Europe over a prolonged period varying from 10 days to one month [33]. Accordingly, an epidemiological study by Conti, et al. [34], which exam-

ined the impact of heat wave in 21 different regions in Italy, found that the number of deaths among people of 75 years of age and older increased by 21.3% during the heat wave occurring in 2003 compared to 2002, with similar mortality rates between men and women. However, the authors identified locations of high-risk such as in north-western cities of Italy where higher mortality rates were observed [34]. More precisely, elderly mortality rate was highest in Turin (44.9%), Trento (35.2%), Milan (30.6%) and Genoa (22.2%), which are generally characterized by cold weather [34]. The authors hypothesized that the underlying reason for this disparity was acclimatization, since hot weather in the aforementioned cities is less common and, thus, inhabitants are less likely to be tolerant to high temperatures. Indeed, another study by, D'Ippoliti, et al. [35] showed that cities in the Mediterranean region such as Athens Greece, which experience higher average ambient temperatures during heat waves, have a reduced mortality rate in the elderly as compared to more temperate northern European cities such as London, England [35]. This finding has been attributed to more frequent exposure to temperatures extremes and generally higher day-to-day ambient temperature conditions [36,37]. As shown by Lan, et al. [38], heat adaptation may be a more important determinant of heat-related mortality in heat vulnerable populations than previously thought. They reported a marked surge in mortality rate in older adults during the 2010 heat wave (> 35 °C) in the large metropolitan city of Harbin, China, which typically experiences cool ambient temperatures (- 18 °C to 23 °C) during the summer period. The authors surmised that the residents were likely less heat acclimated and consequently were at greater risk of heat-related illness or death [38]. In contrast, Åström, et al. [39] showed no differences in daily number of deaths (as assessed between the months of May through to September (the 15th of each month) from 2002 to 2008) in older adults (≥ 50 years) living in Rome and Stockholm, two very distinct regions in terms of climate type. In fact, the population of older adults were found to be equally vulnerable to detrimental health effects of a heat wave.

Another important determinant is the time of year that the heat waves occurs. When extreme heat events occur in late spring or early place, accordingly the elderly are at an increased risk of a heat-related injury or death. This is because they have not benefited from improvements in heat dissipation that occur with progressive exposure to heat that would typically occur over the spring and summer period [4,40]. Indeed, heat vulnerable individuals are likely to gain some level of acclimation by the mid-to-late summer period that would provide some level of protection against the detrimental health effects of exposure to extreme heat conditions [4,40]. Smoyer [41], who compared the elderly mortality rates during two different heat wave periods, showed that although the higher ambient temperature

was recorded in Missouri during an August heat event (1995), the number of deaths in July was comparatively higher despite a relatively lower ambient temperature. In addition, Son, et al. [8], who examined the impact of heat waves on mortality rates across various age groups in seven cities in Korea, showed that a one day delay in the occurrence of the heat episode was associated with a 0.2% reduction in the risk of a heat-related death.

Conti, et al. [34] showed that heat-related mortality in the elderly is also influenced by the duration of the heat wave. Similarly with the study by Conti, et al. [34], in Frankfurt, Germany the numbers of deaths during the heat wave in 2003 were high (32.7 case per day for a period of 11 days) and the following heat wave periods that occurred in the next decades did not reach these numbers [42]. However, this can be explained in large part by the fact that the duration of 2003 heat wave was 12 days as compared to the relatively shorter heat waves (4 days in 2006, in 2010 and in 2015), albeit of comparable intensity occurring thereafter within the recording period [42]. These findings highlight the cumulative effect on human health that can occur with prolonged heat events.

Since the European heat wave of 2003, extensive work has been done to implement appropriate heat alert systems as well as heat management strategies to protect the vulnerable populations. The implementation of these protective strategies appears to be having a positive impact on population health. This is evidenced by a study by Green, et al. [43] who found a relative reduction to prior events during the heat wave of 2013 (from 1st of June until 15th of September) [43]. These findings were thought to indicate that health officials in England had implemented health protection measures and prevention strategies that were successful in alleviating the level of thermal strain experienced by the elderly during the heat wave. The mean daily central England temperature was 22.7 °C with a peak recorded temperature of 29.7 °C. Given that temperatures in South European countries typically range above this level, it becomes clear that lack of acclimatization plays an important role in elderly heat waves-induced mortality in England.

A comparable pattern of response was also reported by Borrell, et al. [44], who showed that elderly women in Barcelona, Spain had a significantly greater mortality rate relative to men, indicating that the sex plays an important role in heat wave mortality. According to the authors, the main reason for this finding was the fact that in Barcelona the rate of women older than 75 years living alone is higher compared to men (13% of men and 30.9% of women). Moreover, another key factor, which was responsible for the increased mortality was the socioeconomic status as individuals with low educational level showed increased number of deaths. Similarly, Bogdanovic, et al. [45] reported higher mortality rates

in women 75 years of age and older compared to their age-matched male counterparts [45]. They attributed these results to the greater life expectancy for women compared to men [45]. Indeed, it is well established that women live 5 to 10 years longer than men [16]. Noteworthy, Diaz, et al. [46] who analysed the health-effects of summer heat waves on mortality rates in the elderly (> 65 years) in Madrid, Spain for the period of January 1, 1986 to December 31, 1997, showed that for every degree the temperature rises above 36.5 °C, the rate of mortality increased by as much as 28.4% with women being again the most vulnerable [46].

It has been suggested that ethnicity and skin color does not play a role in elderly mortality [47], while others found that people of African origin are at higher risk of a heat-related death [48]. Madrigano, et al. [49], showed that African non-Hispanic individuals were more likely to die during to heat waves. However, the differences were likely due to the disparity in socioeconomic status and not skin color. Indeed it has been shown, as previously reported, that low socioeconomic status is associated with an elevated risk for a heat-related death [49].

In general, extreme temperatures can have dramatic consequences on human health. Prolonged exposure of elderly adults to heat wave can induce hyperventilation, dyspnea, dehydration [50], as well as cardiovascular events [51]. Heat-induced aggravation of underlying cardiovascular and respiratory conditions is considered a key factor increasing excess mortality during heat waves [52-54]. A number of studies are in agreement that the elderly populations are the most vulnerable to detrimental health effects of heat waves due in large part to their impaired ability to dissipate heat and therefore regulate body core temperature [28]. This is exacerbated by the fact that elderly individuals have a reduced thirst sensation and experience greater levels of dehydration [55], which is exacerbated by medication use. However, apart from age, the socioeconomic and educational status seems to play a role, because people with low socioeconomic and educational status proved to have greater risk of mortality [53,56,57,]. For example, during heat waves access to centers or buildings with air-conditioning plays an important role in circumvent the risk of heat-related illness and deaths in vulnerable populations. Residences or buildings without air conditioning can reach excessively high ambient temperatures that can exceed the physiological adaptive capacity of vulnerable population groups [58,59]. Indeed, studies show that the number of deaths during heat waves increases for people outside hospitals compared to people in hospitals who have access to air-conditioned facilities [57,60]. In addition, in large cities where the density of the buildings is high, the temperatures are even more increased compared to the countryside, creating the well-known heat island effect [61,62]. Furthermore, it has been found that elderly people who live in places with little green-space and/or in

old buildings are more vulnerable to heat mortality [63]. Moreover, the low economic status could lead to limiting access to health care departments, and this could in turn increase the risk for heat wave mortality [59]. Finally, it has been found that when elderly adults are exposed to high temperatures during the day and nighttime for several days continuously, heat-related mortality increases. This is likely due to the prolonged nature of the exposure where the individual is unable to recover adequately during the typically cooler night period [64].

Concluding Remarks

As temperatures continue to rise due to the climate change, the frequency of heat waves will likely increase in the future [61]. Although the recent advances in technology allow scientists to identify when extreme weather temperatures will occur in the different regions and public messaging of heat related events has improved over the past decade, the number of deaths due to heat wave mortality remains high. The underlying reasons for this trend is unclear albeit better education and increased awareness of the detrimental health effects of heat waves may help reverse this trend. Considering all these factors, additional policy actions are required to enhance the public health awareness regarding the deleterious effects of heat waves on human health. Finally, the results of all these studies strengthen the need to review and update heat waves mitigation plans in each country as well as the need for National Health Departments to develop new prevention strategies in order to protect the people and minimize the consequences of extreme heat. Moreover, in many regions the reason for the heat waves mortality was the acclimatization and accordingly strategies that could reduce this risk should be developed. Thus established systems for preventing the effects of heat waves should be developed and implemented across the world.

References

1. Robine JM, Cheung SL, Le Roy S, Van Oyen H, Griffiths C, et al. (2008) Death toll exceeded 70,000 in Europe during the summer of 2003. *C R Biol* 33: 171-178.
2. David Barriopedro, Erich M Fischer, Jürg Luterbacher, Ricardo M Trigo, Ricardo García Herrera (2011) The hot summer of 2010: Redrawing the temperature record map of Europe. *Science* 332: 220-224.
3. Knowlton K, Rotkin Ellman M, Geballe L, Max W, Solomon GM (2011) Six climate change-related events in the United States accounted for about \$14 billion in lost lives and health costs. *Health Aff (Millwood)* 30: 2167-2176.
4. Anderson GB, Bell ML (2011) Heat waves in the United States: Mortality risk during heat waves and effect modification by heat wave characteristics in 43 U.S. communities. *Environ Health Perspect* 119: 210-218.
5. Glen P Kenny, Ronald J Sigal, Ryan Mc Ginna (2016) Body temperature regulation in diabetes. *Temperature (Austin)* 3: 119-145.
6. Yu W, Mengersen K, Wang X, Ye X, Guo Y, et al. (2012) Daily average temperature and mortality among the elderly:

- A meta-analysis and systematic review of epidemiological evidence. *Int J Biometeorol* 56: 569-581.
7. Kalkstein LS, Smoyer KE (1993) The impact of climate change on human health: Some international implications. *Experientia* 49: 969-979.
 8. Gasparrini A, Armstrong B (2011) The impact of heat waves on mortality. *Epidemiology* 22: 68-73.
 9. Cathy Aniello, Ken Morgan, Arthur Busbey, Leo Newland (1995) Mapping micro-urban heat islands using LANDSAT TM and a GIS. *Computers & Geosciences* 21: 965-967.
 10. CP Lo, DA Quattrochi, JC Luvall (1997) Application of high-resolution thermal infrared remote sensing and GIS to assess the urban heat island effect. *International Journal of Remote Sensing* 18: 287-304.
 11. JA Voogt, TR Oke (2003) Thermal remote sensing of urban climates. *Remote Sensing of Environment* 86: 370-384.
 12. TR Oke, GB Maxwell (1975) Urban heat island dynamics in Montreal and Vancouver. *Atmospheric Environment* 9: 191-200.
 13. Orimo H (2006) Reviewing the definition of elderly. *Nihon Ronen Igakkai Zasshi* 43: 27-34.
 14. Rose MR (1991) *Evolutionary Biology of Aging*. Oxford University Press, New York.
 15. Chodzko-Zajko WJ, Ringel RL (1987) Physiological fitness measures and sensory and motor performance in aging. *Exp Gerontol* 22: 317-328.
 16. Andreas D Flouris, Carla Piantoni (2015) Links between thermoregulation and aging in endotherms and ectotherms. *Temperature (Austin)* 2: 73-85.
 17. Jill M Stapleton, Martin P Poirier, Andreas D Flouris, Pierre Boulay, Ronald J Sigal, et al. (2015) Aging impairs heat loss, but when does it matter? *J Appl Physiol* (1985) 118: 299-309.
 18. Kenny GP, Poirier MP, Metsios GS, Boulay P, Dervis S, et al. (2016) Hyperthermia and cardiovascular strain during an extreme heat exposure in young versus older adults. *Temperature (Austin)* 4: 79-88.
 19. Stapleton JM, Poirier MP, Flouris AD, Boulay P, Sigal RJ, et al. (2015) At what level of heat load are age-related impairments in the ability to dissipate heat evident in females? *PLoS One* 10: e0119079.
 20. Dufour A, Candas V (2007) Ageing and thermal responses during passive heat exposure: Sweating and sensory aspects. *Eur J Appl Physiol* 100: 19-26.
 21. Kenney WL, Fowler SR (1988) Methylcholine-activated eccrine sweat gland density and output as a function of age. *J Appl Physiol* 65: 1082-1086.
 22. Hellon RF, AR Lind (1956) Observations on the activity of sweat glands with special reference to the influence of ageing. *J Physiol* 133: 132-144.
 23. Armstrong CG, Kenney WL (1993) Effects of age and acclimation on responses to passive heat exposure. *J Appl Physiol* 75: 2162-2167.
 24. Kenney WL, Morgan AL, Farquhar WB, Brooks EM, Pierzga JM, et al. (1997) Decreased active vasodilator sensitivity in aged skin. *Am J Physiol* 272: 1609-1614.
 25. Inoue Y, Shibasaki M, Hirata K, Araki T (1998) Relationship between skin blood flow and sweating rate, and age related regional differences. *Eur J Appl Physiol Occup Physiol* 79: 17-23.
 26. Minson CT, Wladkowski SL, Cardell AF, Pawelczyk JA, Kenney WL (1998) Age alters the cardiovascular response to direct passive heating. *J Appl Physiol* 84: 1323-1332.
 27. Holowatz LA, Thompson-Torgerson C, Kenney WL (2010) Aging and the control of human skin blood flow. *Front Biosci* 15: 718-739.
 28. Kenney WL, Hodgson JL (1987) Hodgson, Heat tolerance, thermoregulation and ageing. *Sports Med* 4: 446-456.
 29. http://www.who.int/features/factfiles/ageing/ageing_facts/en/index.html
 30. Fouillet A, Rey G, Wagner V, Laaidi K, Empereur-Bissonnet P, et al. (2008) Has the impact of heat waves on mortality changed in France since the European heat wave of summer 2003? A study of the 2006 heat wave. *Int J Epidemiol* 37: 309-317.
 31. Boyson C, Taylor S, Page L (2014) The national heatwave plan - A brief evaluation of issues for frontline health staff. *PLoS currents* 6.
 32. Moher D, Liberati A, Tetzlaff J, Altman DG (2009) Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med* 6: e1000097.
 33. Kosatsky T (2005) The 2003 European heat waves. *Euro Surveill* 10: 148-149.
 34. Conti S, Meli P, Minelli G, Solimini R, Toccaceli V, et al. (2005) Epidemiologic study of mortality during the Summer 2003 heat wave in Italy. *Environ Res* 98: 390-399.
 35. D'Ippoliti D, Michelozzi P, Marino C, de'Donato F, Menne B, et al. (2010) The impact of heat waves on mortality in 9 European cities: Results from the EuroHEAT project. *Environ Health* 9: 37.
 36. Khaw KT (1995) Temperature and cardiovascular mortality. *Lancet* 345: 337-338.
 37. Revich B, Shaposhnikov D (2008) Excess mortality during heat waves and cold spells in Moscow, Russia. *Occup Environ Med* 65: 691-696.
 38. Lan L, Cui G, Yang C, Wang J, Sui C, et al. (2012) Increased mortality during the 2010 heat wave in Harbin, China. *Ecohealth* 9: 310-314.
 39. Astrom DO, Schifano P, Asta F, Lallo A, Michelozzi P, et al. (2015) The effect of heat waves on mortality in susceptible groups: A cohort study of a mediterranean and a northern European City. *Environmental Health* 14: 30.
 40. Hajat S, Kovats R, Atkinson R, Haines A (2002) Impact of hot temperatures on death in London: A time series approach. *J Epidemiol Community Health* 56: 367-372.
 41. Smoyer KE (1998) A comparative analysis of heat waves and associated mortality in St. Louis, Missouri--1980 and 1995. *Int J Biometeorol* 42: 44-50.
 42. Steul K, Schade M, Heudorf U (2018) Mortality during heatwaves 2003-2015 in Frankfurt-Main - the 2003 heatwave and its implications. *Int J Hyg Environ Health* 221: 81-86.
 43. Green HK, Andrews N, Armstrong B, Bickler G, Pebody R (2016) Mortality during the 2013 heatwave in England--How did it compare to previous heatwaves? A retrospective observational study. *Environ Res* 147: 343-349.
 44. Borrell C, Marí-Dell'Olmo M, Rodríguez-Sanz M, Garcia-Olalla P, Caylà JA, et al. (2006) Socioeconomic position and excess mortality during the heat wave of 2003 in Barcelona. *Eur J Epidemiol* 21: 633-640.
 45. Bogdanovic DC, Milosević ZG, Lazarević KK, Dolićanin ZC, Randelović DM, et al. (2013) The impact of the July 2007

- heat wave on daily mortality in Belgrade, Serbia. *Cent Eur J Public Health* 21: 140-145.
46. Diaz J, Jordán A, García R, López C, Alberdi J, et al. (2002) Heat waves in Madrid 1986-1997: Effects on the health of the elderly. *Int Arch Occup Environ Health* 75: 163-170.
47. Ellis FP, Nelson F (1978) Mortality in the elderly in a heat wave in New York City, August 1975. *Environ Res* 15: 504-512.
48. Schwartz J (2005) Who is sensitive to extremes of temperature?: A case-only analysis. *Epidemiology* 16: 67-72.
49. Madrigano J, Ito K, Johnson S, Kinney PL, Matte T (2015) A Case-Only Study of Vulnerability to Heat Wave-Related Mortality in New York City (2000-2011). *Environ Health Perspect* 123: 672-678.
50. Kettaneh A, Fardet L, Mario N, Retbi A, Taright N, et al. (2010) The 2003 heat wave in France: Hydration status changes in older inpatients. *Eur J Epidemiol* 25: 517-524.
51. Schifano P, Cappai G, De Sario M, Michelozzi P, Marino C, et al. (2009) Susceptibility to heat wave-related mortality: A follow-up study of a cohort of elderly in Rome. *Environ Health* 8: 50.
52. Huang W, Kan H, Kovats S (2010) The impact of the 2003 heat wave on mortality in Shanghai, China. *Sci Total Environ* 408: 2418-2420.
53. Yang J, Liu HZ, Ou CQ, Lin GZ, Ding Y, et al. (2013) Impact of heat wave in 2005 on mortality in Guangzhou, China. *Biomed Environ Sci* 26: 647-654.
54. Sun X, Sun Q, Zhou X, Li X, Yang M, et al. (2014) Heat wave impact on mortality in Pudong New Area, China in 2013. *Sci Total Environ* 493: 789-794.
55. Kenney WL, Munce TA (2003) Invited review: Aging and human temperature regulation. *J Appl Physiol* (1985) 95: 2598-2603.
56. Michelozzi P, E Donato F, Bisanti L, Russo A, Cadum E, et al. (2005) The impact of the summer 2003 heat waves on mortality in four Italian cities. *Euro Surveill* 10: 161-165.
57. Son JY, Lee JT, Anderson GB, Bell ML (2012) The impact of heat waves on mortality in seven major cities in Korea. *Environ Health Perspect* 120: 566-571.
58. Henschel A, Burton LL, Margolies L, Smith JE (1969) An analysis of the heat deaths in St. Louis during July, 1966. *Am J Public Health Nations Health* 59: 2232-2242.
59. McGeehin MA, Mirabelli M (2001) The potential impacts of climate variability and change on temperature-related morbidity and mortality in the United States. *Environ Health Perspect* 109: 185-189.
60. Medina-Ramon M, Zanobetti A, Cavanagh DP, Schwartz J (2006) Extreme temperatures and mortality: assessing effect modification by personal characteristics and specific cause of death in a multi-city case-only analysis. *Environ Health Perspect* 114: 1331-1336.
61. WHO (2004) Heat-waves: Risks and responses. Health and Global Environmental Change Series, Copenhagen, Series No 2.
62. Vandentorren S, Bretin P, Zeghnoun A, Mandereau-Bruno L, Croisier A, et al. (2006) August 2003 heat wave in France: Risk factors for death of elderly people living at home. *Eur J Public Health* 16: 583-591.
63. Gronlund CJ, Berrocal VJ, White-Newsome JL, Conlon KC, O'Neill MS, et al. (2015) Vulnerability to extreme heat by socio-demographic characteristics and area green space among the elderly in Michigan, 1990-2007. *Environ Res* 136: 449-461.
64. Laaidi K, Zeghnoun A, Dousset B, Bretin P, Vandentorren S, et al. (2012) The impact of heat islands on mortality in Paris during the August 2003 heat wave. *Environ Health Perspect* 120: 254-259.
65. Bustinza R, Lebel G, Gosselin P, Bélanger D, Chebana F (2013) Health impacts of the July 2010 heat wave in Quebec, Canada. *BMC Public Health* 13: 56.
66. Canoui-Poitaine F, Cadot E, Spira A (2006) Excess deaths during the August 2003 heat wave in Paris, France. *Rev Epidemiol Sante Publique* 54: 127-135.
67. Sartor F, Snacken R, Demuth C, Walckiers D (1995) Temperature, ambient ozone levels, and mortality during summer 1994, in Belgium. *Environ Res* 70: 105-113.
68. Cerutti B, Tereanu C, Domenighetti G, Cantoni E, Gaia M, et al. (2006) Temperature related mortality and ambulance service interventions during the heat waves of 2003 in Ticino (Switzerland). *Soz Praventivmed* 51: 185-193.
69. Conti S, Masocco M, Meli P, Minelli G, Palummeri E, et al. (2007) General and specific mortality among the elderly during the 2003 heat wave in Genoa (Italy). *Environ Res* 103: 267-274.
70. Huynen MM, Martens P, Schram D, Weijenberg MP, Kunst AE (2001) The impact of heat waves and cold spells on mortality rates in the Dutch population. *Environ Health Perspect* 109: 463-740.
71. Fouillet A, Rey G, Laurent F, Pavillon G, Bellec S, et al. (2006) Excess mortality related to the August 2003 heat wave in France. *Int Arch Occup Environ Health* 80: 16-24.
72. Schaffer A, Muscatello D, Broome R, Corbett S, Smith W (2012) Emergency department visits, ambulance calls, and mortality associated with an exceptional heat wave in Sydney, Australia, 2011: A time-series analysis. *Environ Health* 11: 3.