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Health-Related Effects of Heat Exposure

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List of contents

Summary 3
1. Introduction 4
2. Definitions and glossary 4
   2.1. Heat wave 4
   2.2. Medical terms 4
3. Thermoregulation – basic principles 6
   3.1. Physiology of thermoregulation 6
   3.2. Aging and thermoregulation 9
4. Epidemiology of health-related effects of heat exposure 12
   4.1. Public health perspective 12
   4.2. Mortality 12
   4.3. Hospital admissions 14
5. Effects of heat on human body 15
   5.1. Physiological reactions to heat 15
   5.2. Vulnerability to heat and adaptation to overheating 16
   5.3. Heat-related symptoms 18
   5.4. Heat-related illness 20
   5.5. Comorbidities 22
   5.6. Heat exposure and medications 24
   5.7. Heat exposure and brain 25
6. Heat and exercise 25
7. Heat risk perception 27
8. Minimizing effects of heat exposure – examples of solutions 28
9. Conclusions 31
List of figures 32
List of tables 32
References 33

Summary

Climate change has produced extreme weather effects including prolonged and severe heat waves in regions with traditionally moderate climate. Heat wave is defined as a prolonged period of unusually hot weather, but there is no single accepted definition and multiple indicators of heat exposure are applied in research studies. The process of thermoregulation is complex and relies on central (cerebral) and peripheral mechanisms, mainly sweating and dilation of skin blood vessels. Aging as a physiological process may decrease the effectiveness and capability of heat control making older adults a heat vulnerable population. Heat-related events are perceived as public health issue of major and growing importance and excessive heat exposure contributes to increased morbidity and mortality worldwide. The risk of adverse effects of heat exposure depends on a variety of factors including age, comorbidities, environmental, social and economic factors. The sequelae of heat stress depend on the severity and duration of exposure and may vary from mild to life-threatening symptoms. Heat-related illness includes heat edema (leg swelling), heat rash, heat cramps, syncope (near-fainting or fainting), heat exhaustion and heat stroke. Heat-related illness is often associated with dehydration and electrolyte imbalance. Chronic diseases prevalent in the majority of older adults contribute to vulnerability to heat exposure and heat stress may cause exacerbation of many conditions. Adaptation to heat is one of the mechanisms to reduce heat-related illness. Exercise and physical activity performed in hot environment pose special challenges to physiological reserve. Raising awareness of heat-related illness and preventive strategies among health care workers, vulnerable populations, e.g. older adults and societies is of major importance. Solutions are based on local, national and international collaboration and there are multiple initiatives for urban environments. Climate change demands intensive research to better understand heat exposure challenges and develop effective strategies to minimize the risk for the Earth and its inhabitants.

1. Introduction

Climate change and consequently increasing heat exposure pose significant health risks for people in many parts of the world including these traditionally perceived as regions not affected by heat waves. Vulnerability of the human body to heat is related to many complex processes playing more important role than crude temperatures. One of the key factors of heat vulnerability is advancing age. Older adults are more susceptible to dangerous consequences of heat stress due to fading thermoregulatory control, less stable metabolic balance and comorbidities.

Symptoms of heat stress may vary from mild to severe and are reflected in many medical terms: heat-related illness, heat-related strain, heat stress etc. Exposure to heat is considered an important public health problem as it contributes to emergency room visits, hospitalizations and increases the risk of death. Multifactorial analysis of heat-related risks and individual factors contributing to heat stress may facilitate development of efficient solutions adjusted for various groups of people: children, workers and older adults. Urban areas, especially large cities are predisposed to extreme overheating. There is a need for general, e.g. nationwide and locally tailored ecological solutions to diminish the risk of detrimental effects of heat exposure.

2. Definitions and glossary

2.1. Heat wave

Heat wave (HW) is defined in the literature as an extended period of unusually high temperatures. Multiple definitions of a HW were developed by various authors and examples of HW definitions are presented in table 1. The simplest definitions are based on such variables as temperature thresholds and duration of the event. Moreover, different temperature variables may be used such as absolute temperature values, daily maximum temperatures, average daily temperatures or relative e.g. location specific values such as percentiles of monthly, seasonal or annual temperatures for a chosen region. Additionally, such variables as relative humidity, dew point temperature and wind velocity may have an impact on perceived temperature. For example, the term apparent temperature estimates the combined effect of heat and humidity and is calculated using mathematical equation (Davis 2018). Similarly, joined effect of temperature and humidity might be expressed as wet-bulb globe temperature, WBGT (Chen 2019, Erickson 2019) or pseudo-equivalent temperature (Percic 2018). To assess heat wave effects on certain outcomes, e.g. hospitalizations, it is necessary to apply mathematical transformation and parametrization (Liss 2017).

2.2. Medical terms

Heat waves create significant risk of heat exposure and may become a source of significant health problems. Consequences of heat exposure encompass a vast spectrum of symptoms of various intensity from mild to serious or even life-threatening. Medical vocabulary includes many terms related to consequences of overheating. General terms comprise the following:

- Heat-related conditions
- Heat-related illness
- Heat-related symptoms
- Heat strain
- Heat stress
- Heat stroke

Table 1. Definitions of heat exposure (based on Bobb 2014, Chen 2019, Davis 2018, Erickson 2019, Hopp 2018, Junk 2019, Li 2019, Percic 2018, Pfeifer 2020, Urban 2017)

Name	Abbreviation	Definition
Heat wave	HW	Daily max. temp. 27-32 °C for 2 consecutive days
		Daily max. temp. ≥33 °C
		Daily max, temp. >27 °C for 3 consecutive days
		Daily max temp. >30 °C for 3 consecutive days
		Daily max temp. >30 °C for 5 days or >33 °C for 3 days
		Daily mean temp. ≥95th percentile of the annual distribution for 3 days including 1 day ≥98 percentile
		Average daily temp. ≥99th percentile of the distribution of daily temp. for the given region for 2 consecutive days
		Average daily temp. ≥97th or ≥98th or ≥99th percentile for ≥2 consecutive days or ≥4 consecutive days
		Apparent temp. ≥95 percentile for 3 consecutive days
		Pseudo-equivalent daily temp. > 56 °C for 2 consecutive days
Measuring heat waves	HWDs	Heat wave days – number of annual heat wave days
	HW-D	Length of the longest HW (days)
	HW-F	Number of days contributing to HWs (days)
	HW-M	Mean temp. of all HWs in a year (°C)
	HW-N	Number of HWs per year (number)
	WSDI	Number of days contributing to events with >6 consecutive days with max. air temp. >90th percentile (days)
Apparent temperature, Heat Index	HI	Combined effect of heat and humidity, often referred to as “feels like” temperature
Psuedo-equivalent temperature	-	Sum of air temperature and 1.5 multiplied by partial pressure of water vapor
Wet-Bulb Globe Temperature	WBGT	Joint effects of temperature, humidity, air movement and radiant temperature
Simplified Wet-Bulb Globe Temperature	WBGT	Joint effects of temperature and humidity
Extremely hot days	EHD	Daily mean temp. ≥95 percentile per specific month and region

Max. – maximum; temp. – temperatures.

The global standard for diagnostic health information is the International Statistical Classification of Diseases and Related Health Problems (ICD). It provides a common language for standardized reporting and monitoring of health conditions. Currently, ICD 10th Revision is used in over 100 countries. The new ICD 11th Revision in a fully digital presentation was accepted by WHO in May 2019 and will come into force in 2022 with a 5 year period for translation and formal introduction in WHO member states. The list of medical consequences of exposure to heat according to ICD-10th Revision (ICD-10 Version: 2019) is presented in table 2.

Medical terms presented in table 2 may require explanation for readers without medical background: heat syncope – near-fainting or fainting due to excessive heat exposure; anhidrotic heat exhaustion – overheating due to diminished sweating; heat oedema – swelling of legs due to prolonged heat exposure and dilation of blood vessels.

Aside from problems caused directly by heat, exposure to high environmental temperature may cause exacerbation of chronic diseases and destabilization of health status especially in vulnerable populations such as older adults, people with multiple diseases and functional decline. Relationships between heat stress and comorbidities will be discussed in section 6.5 of the report.

Table 2. Diseases and health problems related to heat exposure according to the International Statistical Classification of Diseases and Related Health Problem, 10th Revision (ICD-10 Version 2019)

CODE	DESCRIPTION
CHAPTER XX External causes of morbidity and mortality (V01-Y98)	
T67	Effects of heat and light
T67.0	Heat stroke and sunstroke
T67.1	Heat syncope
T67.2	Heat cramp
T67.3	Heat exhaustion, anhydrotic
T67.4	Heat exhaustion due to salt depletion
T67.5	Heat exhaustion, unspecified
T67.6	Heat fatigue, transient
T67.7	Heat oedema
T67.8	Other effects of heat and light
T67.9	Effects of heat and light, unspecified
X30	Exposure to excessive natural heat

3. Thermoregulation – basic principles

To understand detrimental effects of heat exposure on human body and vulnerability to heat waves, it is necessary to take a look at the process of maintaining normal body temperature by healthy individuals.

3.1. Physiology of thermoregulation

Humans as other mammals are endotherms – organisms using thermoregulation to maintain consistent internal body temperature independently of the external environment. Thermoregulatory processes in the human body are complex and rely on many physiological mechanisms. Maintaining internal body temperature within a tolerable range (i.e. 36-39 °C) is crucial for the functioning of the human body. Internal heat production related to metabolic activity on cellular level as well as muscle contractions is counterbalanced by various mechanisms of heat exchange with the environment including sweating (evaporation) and dry heat exchange (conduction, convection, and radiation).

- Evaporation takes place when sweat glands in the skin produce sweat and heat vaporizes during perspiration.
- Convection means exchange of heat between the body surface and cooler air. Widening of skin vessels (vasodilation or vasodilatation) facilitates convection of heat from the body to the surrounding air. Internal heat is transported in blood to the skin where heat exchange takes place via dilated capillaries. The autonomic nervous system regulates blood flow to the skin. Convective heat exchange is greater when there is movement of body in the air or water or movement of air or water across the skin.
- Conduction occurs by a direct contact of the skin with a cooler object or surface.

- Radiation occurs when heat is moved from the skin to the surrounding air via electromagnetic waves (infrared radiation).

Out of the four processes listed above, perspiration and dilation of blood vessels are the main mechanisms of heat exchange. Additionally, some heat is exchanged via airways during the process of breathing. Optimal thermoregulation enables proper response to environmental and physical activity-induced thermal challenges. Overheating (hyperthermia) may have harmful effects on human body functioning and may lead to increased morbidity and mortality. (Balmain 2018, Oscilla 2018, Tansey 2015).

Adequate hydration as well as proper function of the cardiovascular system are crucial for the exchange of heat with the environment. Body fluid balance is a term used to describe balance between fluid input and output. Body fluid consists of water and molecules referred to as electrolytes such as sodium, potassium, chloride and magnesium. Fluids in the body are divided into two main compartments: intracellular space and extracellular space. The latter comprises of plasma in the blood and interstitial fluid (located in between cells of the body). Distribution and movement of water between spaces is regulated by laws of physics including hydrostatic pressure and osmotic pressure. Presence of protein molecules in the blood creates oncotic pressure which keeps water inside blood vessels.

Water intake comes from drinks and food in the diet. Some foods, especially fruit and vegetables, are rich in water, e.g. cucumbers, tomatoes, broccoli and melon contain above 90% of water, while oranges and apples above 85% of water. Water loss is mainly due to urine output, sweating, respiration and defecation. Body fluid balance is controlled by complex mechanisms involving mainly cardiovascular system, kidney function and hormones.

Fluctuations in fluid volume may cause dehydration or fluid overload. Main causes of dehydration include insufficient fluid intake and excessive fluid loss. Heat exposure causes sweating and, thus, may lead to dehydration if water intake is not adequately increased. Simple measures of hydration status include body mass change, urine output, assessment of skin elasticity and dryness of oral mucosa. It is important to note that skin elasticity is not a valid measurement in people in advanced age due to age associated skin changes. In the state of moderate dehydration, low blood pressure and fast resting heart rate (tachycardia) defined as pulse >100 per minute are often present on clinical examination. Another characteristic feature is a drop in blood pressure in standing position referred to as postural hypotension. It may cause dizziness and falls, especially dangerous for older adults. Figure 1 presents a simplified scheme of factors important in response to heat stress.

A part of the brain called hypothalamus controls thermoregulation. A thermogenic set point, which relates to a setting of thermoregulation center to a physiological range of inner body temperature, is responsible for maintaining optimal body temperature. If the body core temperature rises due to ambient conditions or vigorous exercise, brain receptors sense the temperature via afferent signals and produce efferent signals to cells of the skin to produce sweat. In case of fever, inflammatory or infectious agents trigger production of pyrogens (cytokines, prostaglandins and thromboxane) further causing up-regulation of the thermogenic set point in the hypothalamus and resulting in high body temperature. This is an adaptive role of thermoregulation in the reaction of the human body to infections with pathogenic bacterial and viral agents. Fever as a sign of immunologic system reactivity is a prove of proper function of the body. In cold environment, the body triggers a shivering reflex because contracting skeletal muscles produce heat (Osilla 2020).

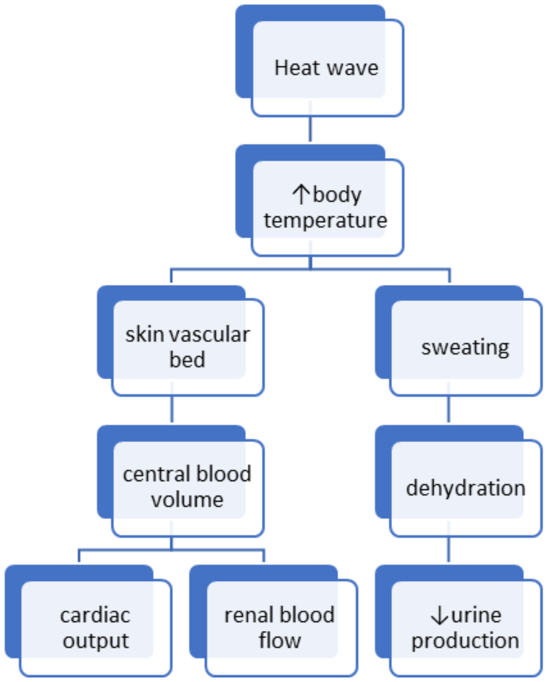

Figure 1. Factors involved in response to heat stress (adapted and simplified from Meade 2020). Meaning of arrows: ↑ - increased; ↓ - decreased.

Hypothalamus as the center for thermoregulation receives input from peripheral and central thermoreceptors of two types: responding to cold and to warmth. Peripheral thermoreceptors are located in the skin where cold receptors are more numerous. Central thermoreceptors are located in the hypothalamus, spinal cord, viscera and big veins and warm receptors outnumber the cold receptors. There is also an interplay between activity of two kinds of thermoreceptors (Tansey 2015). Acetylocholine is the main transmitter involved in vasodilator response to body heating as well as sweating regulation. A number of co-transmitters have been identified including vasoactive intestinal peptide (VIP), substance P, histamine, prostaglandins and nitric oxide. The scheme of skin blood control as well as further details may be found in the literature (Tansey 2015).

Sweat production enabling evaporation is the main mechanism of heat exchange during exercise and when ambient temperature rises. It is important to note that evaporative heat loss is the only possible physiological mechanisms when ambient temperature exceeds body temperature. There are several million of sweat glands over the entire surface of the body. In humid environments, less sweat might be evaporated from the skin surface and, therefore, hot and humid weather creates a particular challenge for thermoregulation.

In recent decades, advances in the understanding of thermoregulation have been made concerning central circuitry of thermoregulatory control and peripheral sensory mechanisms of temperature transduction (Tansey 2015). It is important to differentiate two types of body temperature: central core and peripheral shell temperature. The core temperature refers to internal organs and deep tissues, e.g. liver, heart, brain, while peripheral shell temperature means the external temperature measured at skin level of hands or feet. The difference between core and shell temperatures may reach 4 °C with the shell temperature being lower. The surface area-to-mass ratio of hands is several times greater than the same parameter for the whole body and it explains why hands chill (exchange heat) much faster than the torso.

Hormonal balance is important for maintaining optimal thermoregulation. A good example are thyroid hormones. They play a significant role in production of energy in the body, increase metabolism, augment thermogenesis and may influence central as well as peripheral mechanisms of thermoregulation. Nevertheless, the exact influence of thyroid hormones on the regulation of body temperature in humans has not been elucidated (Iwen 2018). It was calculated that human core body temperature had decreased by 0.03°C per decade since the beginning of industrialization era (Protsiv 2020). The authors suggest that this phenomenon might be due to decrease of infectious diseases and chronic inflammatory processes over time. There are also speculative hypotheses that environmental factors such as contact with chemicals due to industrialization may have a disruptive effect on thyroid hormone-dependent thermoregulation (Vancamp 2020).

3.2.Aging and thermoregulation

Physiological process of aging may influence efficacy of thermoregulation. Additionally, a lot of factors related to the health status of an older individual might affect the thermoregulatory control. As mentioned above, evaporation during perspiration and increased skin blood flow are two mechanisms that enable body to cool down. Older people have lower overall sweat rate than younger individuals due to sweat gland atrophy and altered function expressed as lower sensitivity of sweat glands. Furthermore, skin changes associated with aging may alter the physiological role of skin vascular bed due to skin thinning or atrophy. Thus, in older adults both human's body cooling mechanisms work less effectively than in younger individuals.

Decrease of functional reserves of cardiovascular system and kidneys are important factors limiting efficacy of thermotolerance in older adults. Figure 2 presents the main physiological mechanisms associated with aging leading to impaired thermoregulation in older adults. Central thermoregulatory response to heat stress may be slower and less effective in older in comparison to younger adults. Consequences of age-related decline are of little clinical significance in normal weather conditions, but when prolonged and intense heat waves occur, the physiological response of older adults might fail in an attempt to counteract extreme conditions.

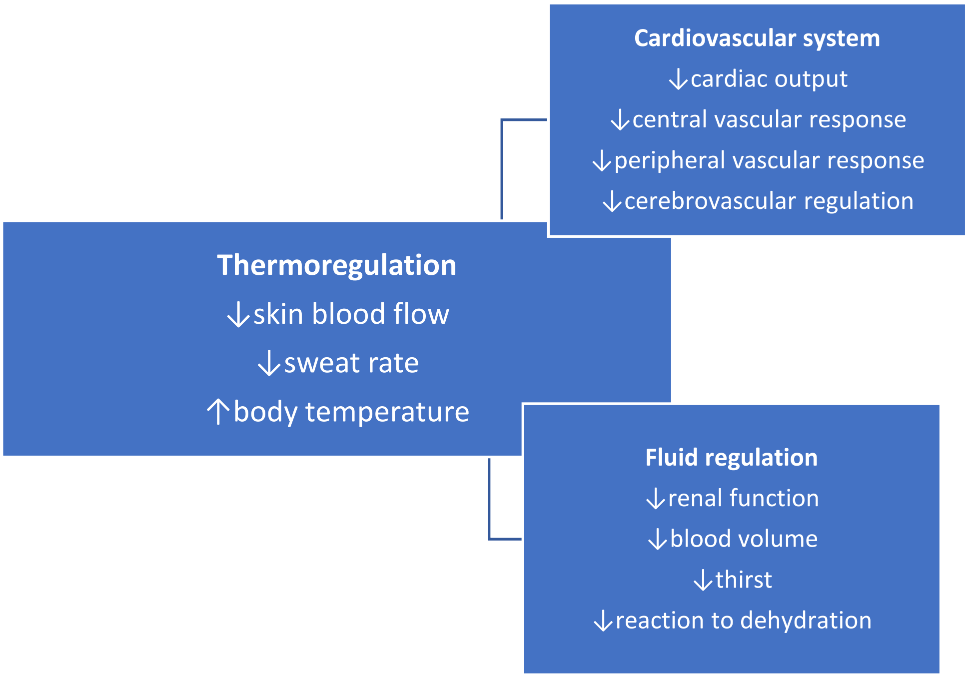

Figure 2. Age-related physiological changes contributing to less effective thermoregulation in older adults (adapted and simplified from Maede 2020). Meaning of arrows: ↓ - decreased; ↑ - increased.

Normal aging as a physiological process, even though universal, is quite often heterogenous. This heterogeneity is represented by different pace of aging between individuals and proves a well-known observation that chronological age is not parallel to biological age. Moreover an individual may age in a heterogenous way in terms of differences in aging of organ systems. For example, age-related changes in kidneys might advance faster than aging of the heart in a given individual.

Normal aging is accompanied by gradual loss of functional reserve of organs and systems of the human body over time. Most people represent this type of aging. Another frequent trajectory is so-called pathological or accelerated aging, when additional factors intensify the process of age-related decline. Two explicit examples of pathological aging are: increased loss of muscle strength and mass in physically inactive individuals and changes in the lungs and airways of cigarette smokers. Loss of vital capacity of the lungs might progress five times faster than in non-smokers. For example, results of respiratory function tests of a 60 year old heavy smoker might be worse than of a 90 year old non-smoker. People who show signs of accelerated aging reach the level of insufficiency of organ function and failure to maintain metabolic stability much faster than others and become vulnerable to external stressors including heat exposure.

Only about 10 percent of the population may take advantage of successful aging. In these people age-related changes are slower and their biological age younger than their actual age calculated in years. Preserved effective thermoregulation may be a sign of successful aging. Older people who respond with fever to infections are perceived as robust in terms of their immunological status, while those who do not react with fever have higher risk of complications and death.

Aging is very often accompanied by chronic diseases as the majority of people aged 65 years and over have at least one chronic condition and multimorbidity is not rare. The most prevalent disorders include:

- cardiovascular diseases (CVDs) such as arterial hypertension, arrythmias, chronic coronary syndrome, heart failure, atherosclerosis,
- degenerative arthritis (e.g. hip, knees and spine),
- type 2 diabetes or pre-diabetic states,
- visual loss due to cataract, age-related macular degeneration (AMD), diabetic retinopathy,
- hearing impairment,
- respiratory diseases: chronic obstructive pulmonary disease (COPD),
- chronic kidney disease (CKD) due to gradual loss of renal filtration rate,
- urinary problems and urinary incontinence affecting 30-50% of older women and 10-30% of older men.

Presence of comorbidities usually leads to polypharmacy and drug interactions, especially in patients treated by several specialists. Certain medications may interact with mechanisms of heat exchange (see section 6.6). On the other hand, age-related diseases often remain underdiagnosed until more advanced clinical stages. Examples include cognitive disorders and dementia, depression and impaired kidney function. Presence of comorbid diseases (even those undiagnosed) may further alter the process of thermoregulation. Particularly in the case of CVDs, environmental heat may have more deleterious effects than in healthy individuals. For example, acceleration of heart rate accompanying heat stress may trigger arrythmia or myocardial infarction in an individual with arterial hypertension, chronic coronary syndrome or heart failure.

Thermoregulation is a perfect example of how important it is to maintain certain physiological parameters in the normal range. The ability to maintain metabolic stability is referred to as homeostasis. Taking into account that homeostasis is reached by dynamic regulatory processes, it is useful to use the term homeodynamics, homeodynamic space or homeodynamic stability, and many authors perceive this concept as adequately describing the idea of maintaining the metabolic balance. The functional reserve of the human body declines with age and, subsequently, the homeodynamic space is shrinking. Mechanisms working efficiently in near-normal environmental conditions may fail when the older organism is exposed to more demanding conditions, e.g. a prolonged heat wave. Consequences of heat exposure in older adults encompass not only sub-optimal thermoregulation, but more often reveal severe dysregulation of fluid and electrolyte balance including dehydration, hyponatremia (low serum sodium concentration) or hypernatremia (high serum sodium concentration), low arterial pressure or, on the contrary, a hypertensive reaction. It is important to remember that water content in the human body is shrinking with age: from approximately 80% in childhood to 40% in older age. In clinical practice, visible signs of heat-related illness are often delayed an may occur after several days of heat exposure when compensatory mechanisms become insufficient. Taking all of the above into consideration, it becomes clear that older individuals are more susceptible to deleterious effects of heat exposure, but signs and symptoms of heat stress might be masked by symptoms of co-morbid diseases and impaired functional performance due to aging.

The increased risk of heat-related illness in older adults might also be due to behavioral factors. During the process of aging the sensation of thirst is suppressed and, thus, older individuals who do not control their fluid intake do not drink enough and might easily become dehydrated. Minimal fluid intake should be 1.5 liters per day and during hot weather this amount should be increased to at least two liters daily. Dehydration may be accompanied by unspecific symptoms, e.g. weakness, sleepiness, near-fainting experience, falls or delirium. Decreased production of urine in a dehydrated individual is an active process performed by the kidneys to protect body fluid volume and is controlled by complex physiological mechanisms. Prolonged dehydration is a risk factor for urinary tract infections, kidney failure, electrolyte imbalance, heart failure, thrombotic complications and death.

Climate change resulting in prolonged and more severe heat waves in countries considered to be regions with moderate weather conditions may catch older adults by surprise. People who were not used to hot weather in the past, do not acquire behaviors protecting them from excessive heat exposure. If combined with overestimation of one’s functional capabilities, it may easily lead to additional unnecessary heat stress and augmented risk of complications. It is not rare to see older people walking outside or working in the garden during midday of a heat wave. Suggestions to stay home during hot weather may not be readily implemented because older individuals (as well as majority of younger people) like to keep their usual daily schedule and dislike to be restricted in their activities.

Another important aspect is functional decline associated with aging. People who have problems with walking or transferring at home might become very reluctant about drinking water, because it is difficult for them to use the toilet. People who have urinary incontinence often avoid drinking at home as well as outdoors due to the shameful need to use the toilet and limited number of freely accessible public toilets. Important issue related to heat stress in older adults is the risk of falls and injuries. Falls belong to main geriatric problems (geriatric giants) and often result in potentially life-threatening injuries, fractures and complications. The risk of malnutrition also increases during prolonged periods of hot weather.

Combination of heat exposure and functional decline is especially dangerous for older people living alone. It is worth noting that in the process of population aging, number of people in advanced older age is growing rapidly and feminization as well as singularization of the societies (increasing percentage of widowed older females) becomes more and more apparent.

When reactions to heat were compared experimentally between young and older individuals, it became apparent that older adults store more heat in the body after sitting for two hours in hot and dry or hot and humid environment (Stapleton 2014). It implies that older adults may experience higher level of heat stress than younger people in the same thermal conditions.

4. Epidemiology of health-related effects of heat exposure

4.1. Public health perspective

From the public health perspective, heat waves present a challenge that will most likely increase in the coming decades. Heat wave events are often associated with other health hazards, such as increased air pollution, shortage of water supply, loss of electrical power supply and wildland fires (Kovats 2008). Spectacular heat wave lasting several weeks across many countries in Europe in 2003 resulted in death of tens of thousands of people. It triggered research in the area of health effects of heat exposure and analysis of contributing and preventive factors on population and individual level. A chain of heat effects includes heat exposure, heat stress, heat illness and, ultimately, heat death. The transitions of these phases depends on factors affecting the exposure, individual susceptibility to a given exposure and access to treatment (Kovats 2008).

In general, heat risk is higher in young children and older adults as well as people living alone or without social contacts. There is an ongoing discussion about the role of gender in vulnerability to heat stress, some studies indicate greater adverse effects in women, while other point out that men become more often victims of heat exposure. Institutionalized older adults living in retirement homes, care homes or nursing homes are at greater risk of heat-related complications and death, but these are rather due to their comorbidities and low functional status.

City dwellers may also experience increased heat during summers because of the Urban Heat Islands (UHIs), as metropolitan areas might be 1-3 °C warmer than surrounding rural areas. Heat islands are not necessarily stable in terms of space and time and might change in subsequent heat wave events. Reasons for UHIs formation are complex and include insulation caused by buildings constructed close together, dense populations and waste heat from cars, factories etc. UHIs are subject to statistical modelling (Gawuc 2020). One of the important characteristics of urban heat is a phenomenon of high nighttime temperatures due to little night cooling (Kovats 2008). It may adversely influence the quality of sleep and add to physiological age-related decline of sleep structure, resulting in multiple awakenings. Thus, staying in the city during a heat wave might translate into an increased risk of heat exposure.

4.2. Mortality

Heat exposure might contribute to the risk of death via both direct and indirect mechanisms. Vital statistics coding includes leading, underlying and contributing causes of death as well as comorbid diseases. Deaths related to excessive heat are rarely ascribed to heat itself, but usually recorded as caused by exacerbation of chronic diseases including cardiovascular diseases, especially in older adults (an der Heiden 2020). It is, therefore, necessary to apply mathematical models for data processing to calculate excessive mortality in hot periods and heat-related deaths. Table 3 presents results of epidemiological studies on heat-related mortality published in recent years. More data may be found in the literature (Kovats 2008).

Table 3. Mortality related to heat exposure

No.	Year	Author	Research place	Research period	Study Population	Heat-related criteria	Results
1.	2016	Chung	Taiwan Korea Japan	1994-2007 1992-2010 1972-2009	Population of 15 cities in 3 countries	Mathematical models for temp. analysis	Heat-related mortality rates have decreased over time, including older adults
2.	2016	Joe	USA	2006	Population of California	12-day heat wave + 6 following days in July 2006	Excess mortality 5%, mostly due to external causes at home
3.	2017	Urban	Czech Republic	2015 vs 1994	Population of Czech Republic	Daily mean temp. >95 percentile of annual distribution for 3 days	Excess mortality: 265% (2015) vs 240% (1994), excess mortality greater for older adults in 2015
4.	2018	Percic	Slovenia	2015 vs 2003	Population of Slovenia	Pseudo-equivalent daily temp. > 56 °C for 2 days	Increased mortality in the age group ≥75 years and for CVD
5.	2019	Can	Turkey	2013-2017	Istanbul	Daily mean temp. >95 percentile for 3 days	Increased mortality in 2015 (11%), 2016 (6%) and 2017 (21%)
6.	2020	an der Heiden	Germany	1992-2015	Total population of Germany	Weekly mean temperatures included in mathematical models	Estimated number of yearly heat-related deaths: min. 0 (1993), max. 10 200 (1994) and 9 600 (2003)
7.	2020	Kang	South Korea	2011-2017	Population of South Korea	Daily mean temp. above 85-99 percentiles for 2 days	Heat-associated mortality RR 1,1, slightly higher in urban areas RR 1.23
8.	2020	O'Lenick	USA	2000-2015	Population of Houston, Texas	Indoor conditions, building energy models	Increased mortality mainly due to CVDs
9.	2020	Pfeifer	Latvia	2009-2015	Population of Riga	Several definitions of HWs according to Latvian and Swedish HWS	Increase of mortality: all-cause 10-20%, older adults 12-22%, due to CVDs 15-26%
10.	2020	Vaidyan-athan	USA	2004-2018	Population of USA	Exposure to heat-related conditions not specified	10 527 deaths, 70% in males, 39% in people aged ≥ 65 yr., mortality rate per 100 000 increasing with age: 65-74 yr.: 0.2, 75-84 yr.: 0.4, ≥85 yr.: 0.7
11.	2021	Jacobson	Brazil	2000-2017	Older adults ≥60 yr. in 27 Brazilian cities	Daily mean temp.	Increase of mortality risk due to respiratory diseases by 27%, total deaths attributable to heat 2.8%

Temp. – temperatures; min. – minimum; max. – maximum; CVDs – cardiovascular diseases; HWs – heat waves; HWS – heat warning system.

4.3.Hospital admissions

Many studies show a short-time health impact of heat waves expressed as increased morbidity and growing use of healthcare (Li 2015). Magnitude and duration of heat exposure may have a direct effect on heat-related hospitalizations in terms of their occurrence and severity of heat-related illness. Chosen publications analyzing emergency room and hospital admissions due to heat-related causes are presented in table 4. In general, during and after a heat wave number of emergency room visits and hospitalizations increases for various reasons. Some studies showed increase in total admissions irrespective of age, some indicated augmented risk for older adults, while one study showed the highest emergency department admission rate for the age group 20-49 yr. (Davis et al. 2018). The authors of this study discuss surprisingly lower risk for older adults and explain that this result might be due to isolation of older individuals and inadequate access to immediate help as well as limited seniors' risk perception.

Analysis of heat-related morbidity indicators might be useful for heat wave early warning systems and contribute to the development of effective guidelines and policies in the area of public health. Health issues should play a central role in climate change negotiations (Rosati 2017).

Table 4. Emergency room and hospital admissions related to heat exposure

No.	Year	Author	Place	Research period	Study Population	Heat-related criteria	Results
1.	2014	Bobb et al.	USA	1990-2010	23.7 million ≥65 yr.	Hospitalization rate after 2 days of high temp.	Increased risk of hospitalization due to: fluid and electrolyte disorders, renal failure, urinary tract infection, septicemia, heat stroke BUT the absolute risk small
2.	2015	Ghirardi et al.	Italy	2012	Whole population	Temp. threshold 28-29 °C	Increase in emergency department visits 3.75% per 1 °C, high priority visits: children: 34/10000, 15-64 yr. 30/10000, ≥65 yr. 37/10000
3.	2017	Liss et al.	USA	1991-2006	Boston population	Nighttime temp. >65.5 °F for 3 consecutive nights	701 hospitalizations due to: heat exhaustion unspecified, heat stroke and sun stroke, heat exhaustion, anhydrotic
4.	2018	Davis et al.	USA	2005-2016	Virginia State, 720,000 admissions analyzed	Temp. >35 °C for 3 days	Increase in total admissions and admissions of females, males, whites, blacks and people aged 20-49 yr.
5.	2018	Hopp et al.	USA	1999-2010	23.7 million, age ≥65 yr.	High temp. for 2 consecutive days	Increased hospitalizations for sun stroke, electrolyte imbalance, age ≥85 yr. for volume depletion, heat exhaustion

6.	2018	van Loenhout et al.	Norway	2002-2007	Population of Norway	Temp. ≥ 21 °C	Increase in emergency room admissions
7.	2019	Li et al.	USA	2005-2013	New York State, 416 707 emergency room visits analyzed	Extremely hot day	Increased risk of admission for CVDs: ischemic heart disease on day 1 as well as hypertension and arrythmias on day 5 and 6 after a hot day
8.	2019	Xu et al.	Brazil	2000-2015	1814 Brazilian cities	Exposure to heat and hospitalization for undernutrition	15.6% of cases of undernutrition related to heat exposure, increased risk in people aged ≥80 yr.
9.	2020	O'Lenick et al.	USA	2003-2014	Population of Houston, Texas	Indoor heat exposure	Increased hospital admissions mainly due to cardiovascular diseases

Temp. – temperatures; CVDs – cardiovascular diseases.

5. Effects of heat on human body

5.1. Physiological reactions to heat

Physiology of thermoregulation has been described in detail in section 4. Two major mechanisms for heat exchange between human body and the environment are perspiration (sweat production and evaporation) and skin vessel dilation (vasodilation). Heat impacts multiple organ systems (presented in table 5) including the cardiovascular, respiratory, gastrointestinal, urinary, nervous systems as well as each organ separately and the overall metabolic regulation. Differences between responses to heat and cold may be found in the literature (Beker 2018), but both cold and heat can negatively impact the human body.

Table 5. Effects of heat on organ systems of the human body (Osilla 2018)

Organ system	Effect of heat-stress
Cardiovascular	Increased heart rate, increased heart output result in additional workload for the heart. Intravascular volume depletion possible
Respiratory	Hyperventilation, hyperpnea (increased frequency of breathing). In severe cases, pulmonary vasodilation may lead to acute respiratory failure
Gastrointestinal	Increased permeability of intestinal mucosa increasing the risk of gastrointestinal hemorrhage and infections.
Urinary	Increased risk of acute renal failure due to volume depletion and dehydration as well as impaired renal circulation. Increased risk of urinary tract infections
Central nervous system	The brain is at risk for ischemia or edema
Various organs	Risk of thrombosis and disseminated intravascular coagulation (DIC)
Overall metabolic regulation	Risk of dehydration, electrolyte imbalance including sodium (hypernatremia, hyponatremia) and potassium (hyperkalemia, hypokalemia), glucose imbalance (hyperglycemia, hypoglycemia), acid-base dysregulation (metabolic acidosis, respiratory alkalosis)

5.2.Vulnerability to heat and adaptation to overheating

Vulnerability to heat stress as a multifactorial phenomenon especially complex in older adults has been described in detail in section 4.2. Physiological adaptation to heat is understood as acclimatization in people staying in hot environments for longer periods of time. It includes higher sweat rate which might increase from maximum of 1 liter per hour in normal conditions to 2-3 l/h in acclimatized individuals. It is possible thanks to lower temperature threshold for sweating and increased sensitivity and capacity of sweat glands. Moreover, hormonal changes in renin and aldosterone levels contribute to lower sodium concentration in sweat, and, thus, prevent loss of natrium and hyponatremia (Tansey 2015). Behavioral adaptation plays an important role the acclimatization process as it encompasses intentional activities modifying heat exchange, such as staying in the shade, seeking shelter or drinking adequate amounts of water and electrolytes.

In a review published by researchers from Ireland, the authors showed paucity of scientific articles on heat-health and simultaneous significant increase of public interest in heat-related issues as measured by Google trends analysis (Paterson 2020). The number of Internet searches for such terms as “heat stroke” and “heat exhaustion” was closely correlated to the outdoor temperatures and reached peak values in the summer of 2018.

Research confirms the need to raise public awareness of the problem of heat exposure and overheating. For example, an interesting study was conducted in 10 cities in Quebec, Canada with over 3000 participants (Valois 2017). The participants were contacted by phone and asked about the following 18 adaptive behaviors:

1. Cover your head in strong sunlight;
2. Sponge or spray your face or neck with cool water;
3. Take showers or baths more often than usual;
4. Drink mainly plain water to cool down;
5. Consume frozen foods to cool down;
6. Swim in a public pool, lake or river to cool off;
7. Swim in a private poll to cool off;
8. Adopt preventive behaviors according to weather bulletins in the media or in the Internet;
9. Stay home during heat waves to avoid adverse health effects;
10. Keep a list of emergency phone numbers on hand;
11. Use air-conditioning during heat waves;
12. Use window shades to block strong sunlight and keep the home cool;
13. Use the dryer less to reduce heat sources at home;
14. Shut off the computer when not in use to reduce heat sources at home;
15. Use the stove less to reduce heat sources at home;
16. Spend time in air-conditioned spaces outside the home to cool off;
17. Use the balcony to cool off in the evening;
18. Use the yard to cool off in the evening.

On the basis of factor confirmatory analysis, a 12-item heat adaptation index was developed. The number of final items was lower than initial due to the fact that some of the strategies showed too high a relationship with another behavior. The results showed that individuals who perceived more adverse health-effects of heat, adopted more preventive behaviors (Valois 2017).

Vulnerability and adaptation to climate change may be perceived not only on an individual level, but also on the population or regional level. The World Health Organization (WHO) proposes following definitions (WHO 2017):

- Vulnerability - The propensity or predisposition to be adversely affected. Vulnerability encompasses a variety of concepts and elements including sensitivity or susceptibility to harm an lack of capacity to cope and adapt.
- Adaptation – The process of adjustment to actual or expected climate and its effects. In human systems, adaptation seeks to moderate or avoid harm or exploit beneficial opportunities. In some natural systems, human intervention may facilitate adjustment to expected climate and it effects.

Vulnerability and adaptation assessments (V&As) are important public health instruments to assess multifactorial impact of climate change on national and regional level (Berry 2018). They are conducted by health authorities on local or national scales with the aim to identify and interpret data needed to prepare health care systems for the challenges of climate change. The specific goals of these studies include: elucidating associations between weather and health outcomes including vulnerable populations, providing information on health risks, identifying vulnerabilities in the health care system, describing opportunities to include climate change concerns into existing policies and to develop new programs, serving as baseline analysis for future monitoring, promoting collaborations and investments for health protection. In the recent years, 34 V&As of climate change were conducted including 16 dedicated to heat and cold-related health issues (Berry 2018).

Another important term in the analysis of heat-related effects on the public health level is resilience defined as the capacity of health sector and populations to prepare and effectively respond to crisis. The requirements for studies on climate change include incorporation of the following topics: 1) indicators of health vulnerability, exposure and risk, 2) indicators of impacts on population health and health systems, 3) indicators of adaptation, health system resilience, coordination and collaboration with other sectors. Indicators for monitoring, evaluation and learning (M&E) should be promptly adjusted to the shifting environmental hazards and new challenges related to extreme temperatures and other climate change issues. A review of health risk indicators and adaptation strategies developed by health institutions, international organizations and academic coalitions was recently proposed by Ebi et al. (Ebi 2018).

The study by Levison et al. analyzed health hazards in a geographical region of Simcoe-Muskoka in Ontario, Canada. The results clearly show that heat exposure is related to other climate change processes and there are complex interrelationships of health consequences. The authors identified six categories of climate-sensitive health vulnerabilities as shown in figure 3. From the medical point of view, potential health consequences of extremely high temperatures in this region include heat-related illness, food-borne illness and water-borne illness due to bacterial contamination as well as vector-borne diseases such as mosquito-borne illness and tick-borne illness (Levison 2018). Adaptive capacity actions proposed in this study include the following:

- Implementation of extreme temperature notification system,
- Advocacy for healthy public policy,
- Public messaging on health impacts,
- Municipal emergency response planning,
- Access and preservation of green areas,
- Surveillance of health sensitivities and burden of illness,
- Inclusion of heat-related and climate change adaptation strategies into municipal planning.

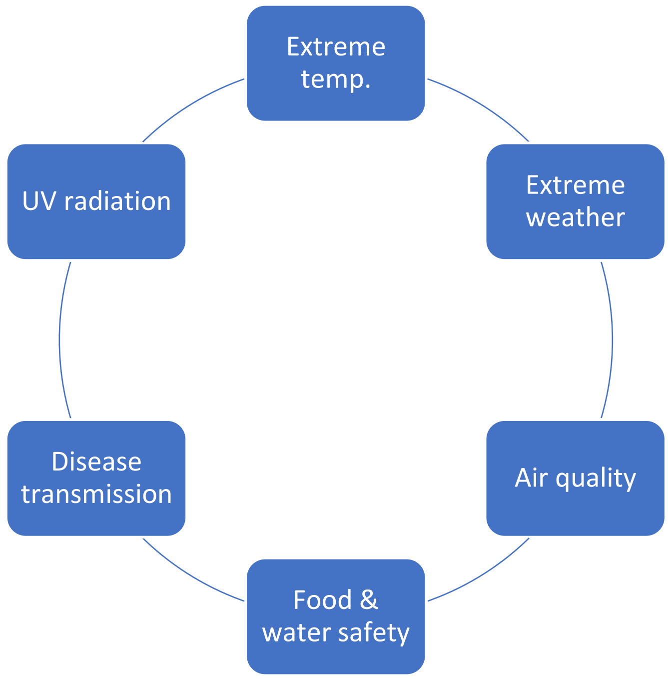

Figure 3. Health vulnerabilities related to heat exposure in relationship to climate change (adapted from Levison 2018). Abbreviation: temp. – temperatures.

In the light of global analyses and particular studies, it is necessary to consider environmental justice as an important aspect of excessive heat exposure. It should be taken into account not only in developing countries where poverty determines many of the health indicators of the population, but also in developed countries with relatively rich populations and good economic growth. For example, a study conducted in Portland, Oregon, USA showed that groups with limited adaptive capacity including those living in poverty, non-white populations and poorly educated people are at much greater risk for excessive heat stress (Voelkel 2018). The impacts of extremely hot weather have the potential to widen existing disparities in economically disadvantaged and health-compromised populations. A study conducted in a low-income cohort of older adults living in public housing in Cambridge, Massachusetts, USA showed that quality of sleep was decreased in seniors living in apartments with higher indoor temperature due to lack of central air conditioning (Williams 2019). An interesting additional finding of this study was that despite reporting hot conditions, older adults did not increase their intake of water. It clearly shows that awareness campaigns should be dedicated to senior residents, especially in historically cooler climates.

5.3. Heat-related symptoms

Heat exposure may cause a variety of symptoms from mild to severe with heat stroke being the ultimate and life-threatening condition. Heat accumulation in the body is a result of complex interplay between environmental exposure, metabolic requirements as well as impaired efficacy of heat exchange mechanisms. The highest risk of heat-related symptoms is found in outdoor workers, athletes, military personnel, older individuals and people affected with chronic diseases. High humidity is an important risk factor as well as lack of acclimatization (Gauer 2019).

The sequence of heat-related symptoms is presented in figure 4 and described below (The symptoms are listed following Gauer 2019).

- Heat oedema – soft tissue swelling of lower extremities caused by vascular leak related to skin vessels dilation. Intervention includes elevation of lower limbs and rest. Differential diagnosis of leg oedema includes a number of medical conditions.
- Heat rash – red papules or pustules on neck, arms, trunk, groin caused by obstructed sweat pores. Intervention includes removing cloths and evaporative cooling, it is recommended to avoid application of topical emollients. Skin infection is possible and requires treatment.
- Heat cramps – exercise-associated muscle spasms. Possible mechanisms include impaired neuromuscular control and fluid/electrolyte imbalance in overused muscles. Intervention includes fluid and electrolyte repletion, rest, leg elevation, stretching and massage.
- Heat syncope – usually associated with exercise. May manifest as pre-syncope (near-fainting) or syncope (fainting). Symptoms include: dizziness, lightheadedness, orthostatic reaction (symptoms increase in the standing position due to arterial pressure drop), passing out, transient loss of consciousness. Symptoms follow directly cessation of physical activity. Pathophysiological mechanisms include: profound peripheral vasodilation, blood volume depletion, decreased vasomotor tone resulting in low blood pressure. Intervention includes rest in supine position, leg elevation, evaporative cooling and oral or intravenous fluid supplementation (rehydration). In case of known cardiovascular risk factors or if symptoms persist in a healthy individual, further medical assessment is necessary.
- Heat exhaustion – a state of moderate thermoregulatory disfunction. Symptoms include weakness, fatigue, tachycardia (heart rate >100/min.), low blood pressure, cold and clammy skin, nausea and vomiting, diarrhea, syncope. Core temperature rises to 38-40 °C (rectal measurement recommended, other options include oral or ear (tympanic) temperature measurement). Mechanisms leading to heat exhaustion include hypovolemia (low fluid volume in blood vessels), hypotension (low blood pressure), constriction of skin vessels and internal organ vessels to maintain volemia, early organ damage. Treatments include rest in supine position with leg elevation, intravenous and oral rehydration, prolonged observation and monitoring.
- Heat stroke – a state of severe thermoregulatory disfunction. Symptoms include altered mental status, loss of consciousness, coma, seizures, tachycardia (heart rate >100/min.), hypotension (systolic blood pressure <90 mmHg), hyperventilation and hyperpnea (breathing rate >25/min), skin may be wet or dry, core temperature rises above 40 °C (rectal measurement recommended, other options include oral or ear (tympanic) temperature measurement). Pathophysiology includes acute systemic inflammatory response, endotoxin leakage, cell death, multiorgan dysfunction. Treatment includes immediate hospital admission, managing airways, breathing and circulation according to protocols and guidelines for resuscitation, constant monitoring, intravenous rehydration, cold water or ice water immersion and specialist treatment.

In all instances, the first action in the treatment of heat-related symptoms is to move the affected individual from heat.

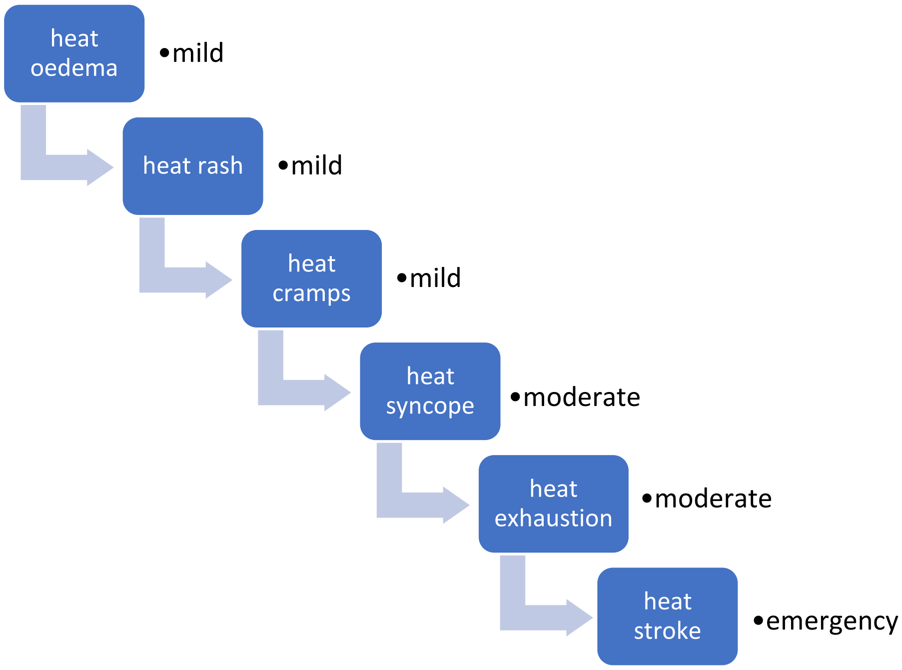

Figure 4. Heat-related symptoms (adapted from Gauer 2019)

Another and quite common manifestation of excessive heat related to solar exposure is sunburn defined as painful, red and warm skin with possible blisters. Treatment of this condition includes staying away from the sun and topical application of moisturizing lotions.

Differential diagnosis of heat-related symptoms requires careful assessment, especially in older adults and in case of multimoribidity, because the clinical picture may be blurred and symptoms caused by overheating may overlap with other pathologic findings. An example of diagnostic challenge may be weakness and feeling of exhaustion or syncope during a heat wave. The symptoms might be due directly to heat exposure or dehydration, but may also accompany such ailments as arrythmia, internal bleeding or infection. In case of any diagnostic doubts, prolonged observation, monitoring and further diagnostic procedures are warranted. Clinical presentation of hyperthermia may include altered mental status. In such cases differential diagnosis should encompass the following clinical entities: drug and alcohol associated conditions, infections including neuroinfections, neurologic conditions (stroke), venous thromboembolism and endocrine disorders (Gauer 2019).

5.4. Heat-related illness

Heat-related illness (HRI) or heat-related illnesses are a spectrum of conditions and have the same meaning as heat-related symptoms, but are more frequently used to describe consequences of heat exposure in the context of medical assessment and public health. Many studies have been dedicated to heat effects of professional exposure in people working outdoor in hot environment. The general notion is that HRI are underestimated and underdiagnosed. Several of recent research findings will be summarized below.

Sugarcane workers in Thailand work at high intensity because sugarcane must be cut promptly at peak maturity during harvesting season (Boonruksa 2020). Two groups of workers were examined: sugarcane cutters working outdoor in the fields (N=90, 58.9% males) and employees of sugarcane factories (N=93, 94.6% males). Exposure to environmental heat was assessed using a wet bulb globe temperature, WBGT (described in section 3.1, table 1). A number of physiological measurements were performed during work shift including blood pressure, heart rate, temperature. Additionally, urine sample analysis was performed and workers were asked to undertake a survey about heat-related symptoms. After a work shift, signs of heat strain were found in sugarcane cutters: temperature increased by 0.5 °C, systolic blood pressure and heart rate increased. Moreover half of the open air workers were dehydrated post-shift in comparison to one in seven pre-shift based on urine density measurement. Almost all sugarcane cutters experienced weakness/fatigue and heavy sweating, while over half reported headache, muscle cramps and skin rash. The prevalence of symptoms was significantly higher in outdoor than in factory workers.

An interesting study, although limited by a small number of participants, was conducted among Hispanic farmworkers in Iowa, USA (Culp 2019). A group of 148 seasonal workers were surveyed about HRI symptoms and 20 participants underwent repeated field trials with the use of multi-parameter monitoring wearable sensors (MPMWS) enabling calculation of physical intensity (PI) score. The most important symptom was extreme thirst reported by one in five workers, while less than 10 percent of participants reported muscle cramps and feeling dizzy during work. Field trials revealed rise in temperature, heart rate and breathing rate in high intensity workers. Interestingly, the study showed significant tachycardia (heart rate above 115/min) in three participants, a situation potentially requiring medical consultation. Additionally, relatively high consumption of salt tablets, carbonated drinks and sports drinks by the farmworkers was shown. The authors concluded with implications for the occupational health professionals to develop strategies to prevent HRI in practice.

A study of simulated heat wave effects on labor productivity and physiological strain was conducted recently in Slovenia (Ioannou 2021). Seven men performed work-shifts for 10 days experiencing three heat waves in a controlled environment in the Olympic Sports Center Planica. Heat-related strain expressed in multiple parameters increased as well as the number of mistakes committed by the subjects. Interestingly, the workers showed early adaptations on the second and third days of the heat wave. Heat stress provoked increased number of unplanned breaks taken by the participants and the authors interpret this finding as behavioral thermoregulation.

In April 2010, the BP Deep Water Horizon offshore oil drilling rid exploded near the coast of Louisiana, USA, causing the largest oil spill in the U.S. history. The disaster response was led by the U.S. Coast Guard with participation of 47 thousands of responders and the most intensive efforts took place during the summer 2010 considered one of the hottest in the century. A study assessed heat-related symptoms in 3,648 responders (84% males) who were exposed to heat stress (Erickson 2018). Heat exposure was based on Wet Bulb Globe Temperature (WBGT) and Heat-Index (HI) measurements (see section 3.1, table 1 for explanation). Heat-related symptoms correlated with the intensity of heat exposure and the results were similar for WBGT and HI metrics. Responders who used personal protective equipment (PPE) reported higher prevalence of heat-related symptoms. In conclusion, the authors recommend imperative refinement of existing protective guidelines and suggest introducing temperature-based guidelines such as WBGT and HI to provide optimal safety measures for disaster responders.

Summer of 2018 was the hottest in over a century in Korea. A survey research of 1000 adult Koreans including 24.8% aged 60 years and over was conducted to assess self-reported symptoms in correlation to air conditioning use (Lee 2020). Half of the respondents reported health problems induced by the heat wave and the most prevalent were sleep disorders, gastrointestinal disorders, skin problems and neurological disorders. Only 4.3% participants missed school or work, but 51.3% cancelled appointments due to hot weather. Using air conditioning correlated with lower prevalence of some of the health problems, e.g. neurological and cardiovascular disorders, but contributed to increased frequency of “conditioningitis” defined as the following symptoms during or after using an air conditioner: headache, myalgia, dry mucous membranes of the eye, nose, mouth or throat.

The examples of studies presented above indicate that heat-related stress is present in various environments: workplace, home and extreme situations. Studying complex relationships of heat exposure and health ailments is valuable for development of more effective strategies to prevent health consequences of heat strain.

5.5. Comorbidities

General health status and chronic diseases are important factors influencing individual susceptibility to deleterious effects of heat exposure. In people with chronic condition or with low functional reserve associated with advanced age, heat stress will most likely present as exacerbation of chronic diseases or acute disease states e.g. falls, dehydration and electrolyte imbalance rather than heat-related symptoms described above (section 6.3). Multimorbidity is characteristic for older adults and in this population, sequelae of heat strain depend on complex health-related, social, organizational and environmental issues described in detail in section 4.2.

Cardiovascular diseases (CVDs) are the main cause of morbidity and mortality worldwide and include mainly: arterial hypertension (AH), chronic coronary syndrome (CCS), myocardial infarction (MI), chronic heart failure (HF) and cerebrovascular diseases including stroke. The relationship between CVDs and heat-related illness may be seen as reciprocal influence. People with CVDs are more prone to harmful effects of heat due to impaired heart function and blood circulation, i.e. will develop heat related symptoms earlier than healthy individuals. On the other hand, heat stress may induce exacerbation of CVDs manifesting as severe hypertension or acute heart failure. Examples of studies assessing effects of heat exposure on mortality (Percic 2018, Pfeifer 2018) and hospital admissions due to CVDs (Li 2019, O’Lenick 2020) were presented in tables 3 and 4, respectively (sections 5.2, and 5.3).

Canadian scientists presented a useful analysis of relative risk (RR) or odds ratio (OD) for hospital admission and death comparing heat wave and normal conditions (Kenny 2010). Greater risk was found for respiratory diseases, CVDs, diabetes, hypertension, obesity and increasing age. The most important risk factor among social characteristics was living alone.

A community-based study conducted in Detroit, Michigan, USA examined history of heat-related illness in relationship to self-reported health (SRH), air conditioning (AC) and variety of built-environment factors (Cardoza 2020). Residents with poor/fair SRH suffered from HRI significantly more often as those with good/excellent SRH (OR = 3.15) as were those not using AC (OR 10.39). Interestingly, the study found a number of confounding factors related to housing and neighborhood characteristics. It is, therefore, important to remember that objective health measures (number and type of chronic diseases diagnosed by health professionals) as well as subjective evaluation of one’s health may influence susceptibility to deleterious effects of high environmental temperatures.

Climate change and global warming may influence respiratory health and contribute to respiratory tract bacterial and viral infections (Mirsaeidi 2016). Even though influenza and bacterial pneumonia are most prevalent in winter months, it was shown that significant oscillations in temperature during other seasons may increase the risk. Influenza outbreaks are more severe after mild winters. Rising temperatures may also facilitate growths of animal vectors necessary for the transmission of some diseases, e.g. leptospirosis. Changes in temperature are often accompanied by changes in humidity, rainfalls and air pollution, and all of these factors may be related to vulnerability of the respiratory system. For example, incidence of human cases of avian influenza (Bird Flu) was related to changes in concentration of carbon dioxide (CO_2) in the air (Mirsaeidi 2016). The above complex relationships prove that effects of heat waves encompass a broad range of potentially unpredictable consequences and go far beyond heat-related stress. Global warming must be interpreted in the broader context of climate change and its influence on the Earth ecosystem.

Chronic kidney disease (CKD) is emerging as one of the leading health problems in older adults and frequently accompanies AH, diabetes and obesity. Moreover, people are often unaware of impaired kidney function even though it might be easily revealed by blood tests (serum creatinine). Age-related decrease in kidney reserve and lowered glomerular filtration rate (GFR) make kidneys especially susceptible to heat-related disfunction. In adults, inadequate rehydration during work in outdoor conditions may be a significant risk factor for progressive loss of kidney function. Even though mechanisms leading to CKD are multifactorial, solutions for screening and protection of kidney function might be similar for younger and older populations and are of special importance in the light of climate change (Flatharta 2019).

A longitudinal cohort study in Taiwan showed higher risk of developing CKD in patients who suffered from heat stroke (Tseng 2020). During the 13 year observation period, CKD risk and end-stage CKD risk increased significantly in comparison to control group as calculated with hazard ratios (HR=4.346 and HR=9.078, respectively). The authors conclude that heat injury related CKD may be one of the future epidemics due to global warming. Another study conducted in Taiwan including long-term (14 years) observation of patients who suffered from heat-related illness showed a significant increase of the risk of CKD as well as CVDs including myocardial infarction and ischemic stroke (Wang 2019). It might be concluded that heat waves may result not only in acute symptoms following directly heat exposure, but also may contribute to progressive long-term changes in the function of organ systems, specifically cardiovascular system and kidneys.

Diabetes as the most prevalent metabolic disorder related to impaired glycemia control increases the risk of heat-related illness during heat waves. Diminished capacity to dissipate heat is related to lower skin blood flow and inadequate sweating responses (Kenny 2016). One of the mechanisms leading to impaired thermoregulation is diabetic neuropathy, the most common complication of long-term diabetes, manifesting as damage to peripheral nerves caused by high glucose levels. Impairments in skin blood flow regulation may be due to multiple factors related to dysfunction of vascular endothelium, the inner cellular level of blood vessels releasing vasoactive substances that control blood vessel dilation. The authors stress, however, that specific mechanisms underpinning heat exchange impairments in diabetes remain to be further elucidated (Kenny 2016). It is worth emphasizing that people with diabetes are more prone to develop cardiovascular events during excessive heat exposure. On the other hand, it is well known that regular physical exercise and maintaining aerobic fitness helps diabetic individuals to achieve beneficial metabolic effects and, to some extent, develop resilience against environmental stressors.

Thyroid hormones play important role in maintaining metabolic balance and production of energy. Therefore, changes in thyroid hormone level may, to some extend affect the process of thermoregulation. In clinical practice, mild or moderate hyperthyroidism (increased levels of thyroid hormones) and hypothyroidism (decreased levels of thyroid hormones) may cause lower tolerance to environmental temperature changes, but do not cause severe problems with thermoregulation. However, in cases of severe thyroid dysfunction, hyperthermia may occur in patients with hyperthyroid crisis (thyrotoxic storm), and hypothermia may be associated with severe hypothyroidism. These rare cases require emergency hospitalization and acute care.

5.6.Heat exposure and medications

The most common groups of medications frequently used in the treatment of chronic diseases that might increase the risk of heat-related illness include (Gauer 2019):

- Anticholinergics
- Antidepressants
- Antihistamines
- Antipsychotics
- Beta blockers
- Benzodiazepines
- Calcium channel blockers
- Diuretics
- Laxatives
- Neuroleptics

Additionally, alcohol, amphetamines and illicit drugs may have deleterious effects on heat-related risk.

There are several ways in which medications may predispose people with chronic conditions to heat-related complications (Layton 2020). Thermoregulatory responses may be disrupted by medications acting in the brain (antidepressants, antipsychotics, neuroleptics, benzodiazapines) as well as affecting the autonomous nervous system (beta blockers). Medications with anticholinergic properties (suppressing acetylocholine transmission in the nervous system) including antihistamines may impair physiological reaction to heat. Several groups of medications may interfere with fluid and electrolyte balance (diuretics and laxatives). Additionally, many substances may impair cognitive processes and cause sedation, slowing down reactions to environmental heat (benzodiazepines, alcohol and illicit drugs).

Several hundred medications have photosensitizing properties and may cause cutaneous adverse reactions, e.g. skin redness, swelling, blisters, itching, hyperpigmentation after exposure to sunlight (some antibiotics, diuretics and botanical preparations). Drug-induced photosensitivity is due to photoallergy and phototoxicity (Kowalska 2021). People who take medications for chronic conditions should avoid direct exposure to sunlight and may benefit from careful reading of medication leaflets as well as consulting their health care providers.

In the study by Layton et al., medical records of over 377 thousands older adults (≥65 years) discharged from the hospital were followed for 5 years and subsequent heat-related summer hospitalizations were identified in 9721 cases (2.6%). During heatwaves, there was a 21-33% increased rate of hospitalizations of older adults with chronic conditions, but no direct correlations were found with their medication regimens. However, several medication classes were related to more frequent hospitalizations during summer even in non-heatwave periods, for example the use of diuretics was associated with hospitalizations in people with dementia or heart failure. These medications were referred to by authors “heat sensitizing” (Layton2020).

A survey of almost five hundred people aged ≥65 years was conducted after a massive heat wave which occurred in 2009 in Australia (Nitschke 2013). Three in four participants took medications on regular basis and one in four assessed their health as fair or poor. Factors associated with heat health outcomes included medications for the following conditions: mental health, heart failure, diabetes and respiratory health. Additionally, fair/poor reported health status, female sex and using mobility aids increased the heat health risk.

The above mentioned studies indicate that medication status should always be included when analysis of potential heat vulnerability is attempted. Implementation of pharmaceutical care provided by pharmacists and defined as direct and comprehensive assessment of medication needs and quality of life has the highest priority in public health. Engagement of pharmacists may play an important role in the evaluation of hazards related to heat exposure in people with chronic diseases and complicated medication regimens.

5.7. Heat exposure and brain

As mentioned previously, living alone and social isolation contribute to the increased risk of heat exposure and delayed response to heat-related symptoms, especially in vulnerable populations including older adults and people with impaired functional status and neurological conditions. A variety of neurological diseases may increase heat-related risk including post-stroke functional disabilities, Alzheimer's disease and other types of dementia, Parkinson's disease and multiple sclerosis . Pathophysiological mechanisms include autonomous nervous system instability, altered central and peripheral thermoregulation mechanisms, altered sweating, impaired thermal sensation, postural (orthostatic) hypotension, previous balance and gait disorders, cognitive impairment, behavioral problems, decreased ability to perform daily activities.

Heat waves may have a negative and prolonged effect on mental status, however studies dedicated exclusively to psychological consequences of heat exposure are scarce, especially in Europe. A systematic review of 17 studies was conducted to assess the prevalence and causes of mental health problems in population exposed to extreme weather events in the United Kingdom (Cruz 2020). Although only one of the analyzed publications was directly related to heat exposure and majority described psychological consequences of floods, it might be interesting to acknowledge the results as manifestation of human reactions to extreme weather. The most prevalent disorders included anxiety (19.8%), depression (21.3%) and post-traumatic stress disorder, PTSD (30.4%). These ailments may potentially affect people exposed to extreme temperatures as heat waves are often associated with floods and other intemperate events.

A study performed in over 500 primary care patients in Wisconsin, USA showed that patients frequently expressed concerns about climate change and this finding correlated with dysphoria experienced by 22.5% of the surveyed population (Temte 2019). A systematic review and meta-analysis confined to high ambient temperatures and heatwaves and their relationship with mental health problems was performed by a group from Australia and China and included analysis of 57 articles (Liu 2021). This huge analysis included 1.9 million mental health morbidity and 1.7 million mental health-related mortality. A positive association was found between rising temperatures and suicide as well as mental health emergency department visits. People with underlying mental and behavioral disorders showed higher vulnerability during extreme heat.

An international group of authors observed that self-isolation due to COVID-19 pandemic-related restrictions may significantly increase the risk of heat-related stress in patients with neurological conditions (Buoite Stella 2020). They proposed a protocol for heat-related symptoms prevention including physiological and environmental data collection via e-health system and teleassistance in case of increased heat-related risk.

6. Heat and exercise

Exercise causes increase of body core temperature in itself and when performed in a hot environment may pose a serious challenge for the thermoregulatory mechanisms. Exercise during heat results in lower exertional capacity and earlier fatigue. A circulatory conflict occurs between muscles and skin vascular bed, because during exercise a vasoconstriction of vessels leading to organs other than skeletal muscles provides the maximum blood flow to the active muscular tissue and, on the contrary, skin vasodilation is necessary for efficient heat exchange (Tansey 2015). Regular training along with acclimatization may improve the response of the cardiovascular system to exercise in heat and increase performance. These adaptation mechanisms develop over time, therefore, starting an exercise program during hot weather is contraindicated.

The thermoregulatory control in older people may be less efficient than in younger populations. Older adults have lower evaporative heat loss capacity due to altered morphology and function of sweat glands. Additionally, core temperature onset of sweating may be delayed and local sweat rate diminished in response to exercise. Impaired cutaneous vascular response is another factor limiting the capacity of older adults to counteract the consequences of overheating. The proposed mechanism is diminished sensitivity of the cholinergic active vasodilation system. Moreover, older individuals have lower cardiac output in response to exercise and decreased ability for effective redistribution of blood flow between internal organs and the skin. All of the above may lead to the accumulation of body heat and increase of core body temperature to dangerous levels. Low fluid intake and dehydration may exacerbate the detrimental effects of heat combined with exercise or physical activity in older individuals. Even though physical activity is promoted as an important component of a healthy lifestyle, no public health recommendations for older adults exist for performing physical activity in the heat. There is evidence from research studies that regular exercise performed by older adults may prevent age-associated impairment in thermoregulatory control. Fit older adults maintain more efficient sweat gland output than unfit people and this finding is important in the light of the fact that 1 gram of sweat liberates 2426 J of heat energy in the process of evaporation. Habitually active older adults may achieve similar level of acclimatization than younger people. (Balmain 2018).

In older individuals with chronic diseases, thermoregulatory control and efficacy of heat exchange process may be impaired due to multiple factors. It is important to remember that majority of people aged 65 years and over have at least one chronic condition and many suffer from several diseases. Multimorbidity is almost always associated with polypharmacy. Chronic diseases may diminish physiological reaction to heat stress and heat exposure may increase the risk of disease exacerbations and complications as well as medication side-effects and drug interactions. Studies of people with heart failure showed higher risk for heat-related illness. One of the potential reasons is impaired skin blood flow limiting heat exchange. Patients suffering from lung diseases including the most prevalent chronic obstructive pulmonary disease are also at higher risk of HRI (Balmain 2018). An example of diabetes was discussed above in the section 6.5. Therefore, it is advisable that older adults with chronic disease decrease to some extend their physical activity during heat wave and stay away from the outdoor and indoor heat. It is, however, not enough to prevent heat-related symptoms as multimorbidity makes older adults susceptible to deleterious effects of heat in many ways. Prevention of dehydration and electrolyte imbalance should be considered a priority in this group.

There are various definitions of hyperthermia, it may be described as rise in body temperature above a certain point when heat-dissipating mechanisms are impaired, or a certain level, e.g. ≥40.5 °C (severe hyperthermia), or >37 °C at rest and >38 °C during exercise of moderate intensity (Beker 2018, Douzi 2020). In athletes, an increase in muscle temperature may improve muscle power during short duration exercise, but this effect is not seen if the exercise is repeated, and thus hyperthermia has a negative effect on performance. Additionally, high ambient temperature may impair cognitive functions such as memory, attention, vigilance and reaction times. Poorer cognitive performance might be due to transient changes in oxygen supply to the brain and neurotransmitter abnormalities (Douzi 2020).

An interesting study was conducted in women aged ≥70 years after a brief 1-hour exposure to indoor temperature of 20 °C and 30 °C (Stotz 2014). Repeated blood pressure measurements were taken and participants performed a 6-Minutes-Walk-Test. Women staying in hotter conditions experienced greater systolic blood drop and had reduced aerobic capacity. The authors conclude that these findings need to be considered when recommending exercise to older individuals in summer months.

7. Heat risk perception

Climate change with extreme temperatures and longer heat waves in traditionally cooler places is a dynamic challenge for individuals, societies and governments. Heat-related illness is largely avoidable if adequate protective measures are proposed and accepted. Therefore, risk perception seems an inevitable prerequisite for efficient introduction of rules of behavior during heat waves. It is especially important in large cities where urban heat islands may augment the heat risks and city life may be regulated to some extend by public heat adaptation measures. Several studies addressed this issue in the context of urban dwellers as well as the patient-health care system axis.

Urban citizens in Augsburg, Germany were asked to participate in an on-line survey to assess their heat risk perception (Beckman 2020). Heat risk perception was related to the level of knowledge of heat risks, subjective heat risk sensitivity and external locus of control defined as the extent to which an individual thinks that everything that happens in his/her life depends on destiny or fate, or is under the control of others. No association with heat risk perception was found for such factors as gender, income, education, living alone and chronic diseases. Younger people had the highest heat risk perception and, therefore, the authors conclude that older adults are an important target group in heat risk communication.

An interesting study was conducted by the Department of Family Medicine at the University of Wisconsin, USA. Patients of community health clinics and physicians were asked about climate change and health in the family medicine setting (Boland 2019). Among patients, 95% believed that climate change is occurring, 57% were convinced that it is affecting their community and 44% agreed that it has impact on community health. Patients expressed trust in their physicians regarding environmental health. Among surveyed family physicians, 98% confirmed belief in climate change, 89% have seen its effects in their communities and 64% reported that climate change affected their patients' health. Additionally, 33% of physicians felt they were well informed about climate change, but only 17% felt comfortable counselling patients on health in the context of climate change. The authors underscore the opportunities for family physicians to educate patients in the primary health care setting.

Another study conducted in the same university setting, included over 500 patients of the primary care clinics (Temte 2019). Patients responded to a survey about attitudes toward climate change and global warming. Approximately half of the participants were concerned with global climate change, were troubled by lack of action on climate change by leaders and expressed a belief that this issue requires more attention. When asked about local impact of climate change, 27% of the surveyed patients were aware of environmental changes in their communities and 17% have noted health effects related to climate change in their families. There was a significant correlation between patients' concerns and symptoms of dysphoria.

The Royal Australian College of Family Medicine published a justification for active participation of primary care physicians in the context of climate change (Tait 2018). Recognizing the general practitioner's responsibility for action should result in heat stress prevention on various levels including the following:

- Patient level
    - primordial prevention: improving acclimatization through promoting exercise and fitness, providing information and education
    - primary prevention: developing personal care plans for heat events to reduce heat exposure, minimizing factors related to response to heat, e.g. pre-heatwave assessment, medication review
    - secondary prevention: reducing effects of heat through proper hydration, check and assess approach
- Societal level
    - Advocating to local and territorial governments for good urban planning and heat-adaptive building design
    - Participation in the development of heatwave warning systems and local response plans

8. Minimizing effects of heat exposure – examples of solutions

Public health interventions to reduce consequences of heat exposure include multidirectional activities including outreach to vulnerable populations, increasing awareness of heat-related risks and heat-related symptoms, providing guidelines on proper hydration and methods of staying cool in hot environment. Improved coordination across various health sectors is of great importance and examples of solutions include development and implementation of heat response plans, facilitating communication and providing educational activities (Vaidyanathan 2020). Since 2003 enormous heat wave causing death of tens of thousands of people, most countries in Europe introduced some public health measures e.g. Heat Health Warning Systems (HHWS) (Kovats 2008). In large countries like India heat alerts should be based on regional and local weather monitoring (Nori-Sarma 2019).

The most important approach to prevent heat-related illness is to raise public awareness and educate the public about simple measures of diminishing the risk of overheating. These methods include acclimatization, adequate hydration, appropriate clothing (light-colored and loose-fitting), avoidance of outdoor activities during extreme temperature events (Gauer 2019). Even though simple, these guidelines might be challenging to introduce because of low acceptance of measures requiring a change in lifestyle and daily functioning. An example of public-oriented message is an on-line poster developed by Center for Disease Control and Prevention addressing simple questions of “What to look for?” and “What to do?” in the context of heat-related illness presented in table 6 (CDC 2017).

An important aspect is to raise awareness and preparedness of the health care system to react to heat waves and prevent evolution of heat-related symptoms. Previously cited protocol for heat symptoms prevention in patients with neurological disorders proposes remote monitoring of physiological and environmental conditions by e-health systems (Buoite Stella 2020). Teleassistance protocol facilitates contact with an operator or a physician who can activate emergency system or instruct the patient to introduce interventions to reduce core temperature, e.g. using a fan, wetting the skin, drinking cold water and using cooling vests.

Environmental health policy may take advantage of mobile applications to inform digitally about appropriate behavior and activity in response to environmental stressors including heat waves. There are, however, very few published studies examining mobile apps in the context of chronic diseases and climate change (Black 2018).

Interesting results related to prevention of heat-related illness were obtained in Japan. Heat health warning and water delivery (HHW+W) was performed for older adults aged 65-84 yr. in Nagasaki (Takahashi 2015). Such approach resulted in improvements in nighttime air conditioning use, higher water intake, effective body cooling and reduced activities in the heat.

Reactions to global warming and extreme temperatures should always take into account a wider perspective of climate change and, thus, include initiatives dedicated to reduce urban heat as well as preserve water supplies and prevent floods. Solutions on larger scale implementing architecture and landscape design include Sponge City concept introduced in many cities in China (Zevenbergen 2018, Frontiers Forum - Healing the world's cities 2021, World Economic Forum 2020). Nature-based solutions (NBS) have been also developed in European Union, USA and Australia. Other large scale projects and integrative approaches include: Integrated Urban Water Management (IUWM), Water Sensitive Urban Design (WSUD), Green Infrastructure (GI) and many others (Zevenbergen 2018). The idea of planting trees to save the planet has proved to be less of a poetic metaphor and more of a necessary solution to prevent heat-related outcomes in areas deprived of trees.

The involvement of the scientific community in discussions on climate change may facilitate multidimensional collaboration with the aim to achieve better health and sustainable development. Frontiers Forum is an example of such efforts as it creates a platform for scientific exchange and discussions. In the last three years, several talks by eminent speakers were dedicated to climate change and solutions for a healthier life (Frontiers Forum 2021).

Table 6. Center for Disease Control guidelines on heat-related illness (adapted from CDC 2017 Recommendations)

Symptoms of heat-illness **WHAT TO LOOK FOR?**	**Recommended reactions** **WHAT TO DO?**
HEAT STROKE	
High body temperature (103°F or 39.5°C or higher) Hot, red, dry or damp skin Fast, strong pulse Headache Dizziness Nausea Confusion Losing consciousness (passing out)	Call **EMERGENCY** number right away (911 in USA, 112 in Europe) – heat stroke is a medical emergency Move the person to a cooler place Help lower the person's temperature with cool clothes or a cool bath Do not give the person anything to drink
HEAT EXHAUSTION	
Heavy sweating Cold, pale and clammy skin Fast, weak pulse Nausea or vomiting Muscle cramps Tiredness or weakness Dizziness Headache Fainting (passing out)	Move to a cool place Loosen your clothes Put cool, wet clothes on your body or take a cool bath Sip water **GET MEDICAL HELP RIGHT AWAY IF:** You are throwing up Your symptoms get worse Your symptoms last longer than 1 hour
HEAT CRAMPS	
Heavy sweating during intense exercise Muscle pain or spasms	Stop physical activity and move to a cool place Drink water or a sports drink Wait for cramps to go away before you do any more physical activity **GET MEDICAL HELP RIGHT AWAY IF:** Cramps last longer than 1 hour You are on a low-sodium diet You have heart problems
SUNBURN	
Painful, red and warm skin Blisters on the skin	Stay out of the sun until your sunburn heals Put cool clothes on sunburned areas or take a cool bath Put moisturizing lotion on sunburned areas Do not break blisters
HEAT RASH	
Red clusters of small blisters looking like pimples on the skin usually on the neck, chest, groin, in elbow creases	Stay in a cool, dry place Keep the rash dry Use powder (like baby powder) to soothe the rash

9. Conclusions

Heat Exposure has been recognized as a public health problem for decades, but in recent years the negative impact of climate change has been growing and meteorological analyses describe global warming as an advancing and accelerating process. Aging of the populations in many parts of the world augments the importance of heat-related illness as a public health challenge. The latest analysis published by an international group of experts show that the approximately linear global warming trend of 0.2 °C/decade results in a non-linear increase in the number of extreme weather events (Robinson 2021). Heat extremes increased 90-fold in 2011-2020 in comparison to the reference period of 1951-1980. Rich body of evidence published recently confirms health impacts of heat waves and supports activities for prevention on the local, national as well as global level. Nevertheless, more research is needed to elucidate specific factors underlying heat stress and to guide adequate solutions. Climate change and global warming are mostly due to human activity and potential solutions must address the complex issues related to human dwelling on Earth. EmCliC project (Embodying Climate Change – Transdisciplinary Research on Urban Overheating) may greatly contribute to our understanding of the effects of excessive heat on people's life.

List of figures

Figure 1. Factors involved in response to heat stress 8

Figure 2. Age-related physiological changes contributing to less effective thermoregulation in older adults 9

Figure 3. Health vulnerabilities related to heat exposure in relationship to climate change 18

Figure 4. Heat-related symptoms 20

List of tables

Table 1. Definitions of heat exposure 5

Table 2. Diseases and health problems related to heat exposure according to the International Statistical Classification of Diseases and Related Health Problem, 10th Revision 6

Table 3. Mortality related to heat exposure 13

Table 4. Emergency room and hospital admissions related to heat exposure 14

Table 5. Effects of heat on organ systems of the human body 15

Table 6. Center for Disease Control guidelines on heat-related illness....................................... 30

References

1. an der Heiden M, Muthers S, Niemann H, Buchholz U, Grabenhenrich L, Matzarakis A: Heat-related mortality. An analysis of the impact of heatwaves in Germany between 1992 and 2017. Dtsch Arztebl Int 2020; 117: 603-609; doi:10.3238/arztebl.2020.0603
2. Balmain BN, Sabapathy S, Louis M, Morris NR. Aging and thermoregulatory control: The clinical implications of exercising under heat stress in older individuals. BioMed Res Int 2018, art. ID 8306154; doi:10.1155/2018/8306154
3. Beckman SK, Hiete M. Predictors associated with health-related heat risk perception of urban citizens in Germany. Int J Environ Res Public Health 2020; 17, 874; doi:10.3390/ijerph1703087
4. Beker BM, Cervellera C, De Vito A, Musso CG. Human physiology in extreme heat and cold. Int Arch Clin Physiol 2018; 1:001
5. Berry P, Enright PM, Shumake-Guillemot J, Villalobos Prats E, Campbell-Lendrum D. Assessing health vulnerabilities and adaptation to climate change: A review of international progress. Int J Environ Res Public Health 2018; 15, 2626; doi:10.3390/ijerph15122626
6. Black DA, O'Loughlin K, Wilson LA. Climate change and the health of older people in Australia: A scoping review on the role of mobile applications (apps) in ameliorating impact. Australasian J Ageing 2018; 37(2):99-106; doi:10.1111/ajiag.12522
7. Bobb JF, Obermeyer Z, Wang Y, Dominici F. Cause-specific risk of hospital admission related to extreme heat in older adults. JAMA 2014; 312:1659-2667; doi:10.1001/jama.2014.15715
8. Boland TM, Temte JL. Family medicine patient and physician attitudes toward climate change and health in Wisconsin. Wilderness Environ Med. 2019; 30(4):386-93
9. Boonruksa P, Maturachon T, Kongtip P, Woskie S. Heat stress, physiological response, and heat-related symptoms among Thai sugarcane workers. Int J Environ Res Public Health 2020; 17, 6363; doi:10.3390/ijerph17176363
10. Buoite Stella A, Filingeri D, Ravanelli N et al. Heat risk exacerbation potential for neurology patients during the COVID-19 pandemic and related isolation. Int J Biometeorol 2020; doi:10.1007/s00484-020-02044-2
11. Can G, Sahin U, Sayaili U et al. Excess mortality in Istanbul during extreme heat waves between 2013 and 2017. Int J Environ Res Public Health 2019; 16, 4348; doi:10.3390/ijerph16224348
12. Cardoza JE, Gronlund CJ, Schott J, Ziegler T, Stone B, O'Neill MS. Heat-related illness is associated with lack of air conditioning and pre-existing health problems in Detroit, Michigan, USA: A community-based participatory co-analysis of survey data. Int J Environ Res Public Health 2020; 17, 5704; doi:10.3390/ijerph17165704
13. Center for Disease Control and Prevention. Warning signs and symptoms of heat-related illness. https://www.cdc.gov/disasters/extremeheat/warning.html Page last reviewed September 1, 2017; Access on September 30, 2021
14. Chen X, Li N, Liu J, Zhang Z, Liu Y. Global heat wave hazard considering humidity effects during the 21st century. Int J Environ Res Public Health 2019; 16, 1513; doi:10.3390/ijerph16091513
15. Chung Y, Noh H, Hond Y et al. Temporal changes in mortality related to extreme temperatures for 15 cities in Northeast Asia: Adaptation to heat and maladaptation to cold. Am J Epidemiol 2017; 185:907-913; doi:10.1093/aje/kww199

16. Cruz J, White PCL, Bell A, Coventry PA. Effect of extreme weather events on mental health: A narrative synthesis and meta-analysis for the UK. Int J Environ Res Public Health 2020; 17, 8581; doi:10.3390/ijerph17228581
17. Culp K, Tonelli S. Heat-related illness in midwestern Hispanic farmworkers: A descriptive analysis of hydration status and reported symptoms. Workplace Health Saf 2019; 67(4):168-178; doi:10.1177/2165079918813380
18. Davis RE, Novicoff WM. The impact of heat waves on emergency department admissions in Charlottesville, Virginia, U.S.A. Int J Environ Res Public Health 2018; 15, 1436; doi:10.3390/ijerph15071436
19. Douzi W, Dupuy O, Theurot D, Smolander J, Dugue B. Per-Cooling (Using cooling systems during physical exercise) enhances physical and cognitive performance in hot environments. A narrative review. Int J Environ Res Public Health 2020; 17, 1031; doi:10.3390/ijerph17031031
20. Ebi KL, Boyer C, Bowen KJ, Frumkin H, Hess J. Monitoring and evaluation indicators for climate change-related health impacts, risks, adaptation, and resilience. Int J Environ Res Public Health 2018; 15, 1943; doi:10.3390/ijerph15091943
21. Erickson EA, Engel LS, Christenbury K, Weems L, Schwartz EG, Rusiecki JA. Environmental heat exposure and heat-related symptoms in United States Coast Guard Deepwater Horizon Disaster Responders. Disaster Med Public Health Prep 2019; 13(3):561-569; doi:10.1017/dmp.2018.120
22. Flatharta TO, Flynn A, Mulkerrin EC. Heat-related chronic kidney disease mortality in the young and old: differing mechanisms, potentially similar solutions? BMJ Evidence-Based Medicine 2019; 24:45-47; doi:10.1136/bmjebm-2018-110971
23. Gauer R, Meyers BK Heat-related illness. Am Fam Physician 2019; 99(8):482-489
24. Gawuc L, Jefimow M, Szymankiewicz K, Kuchcik M, Sattari A, Struzewska J. Statistical medelling of urban heat island intensity in Warsaw, Poland using simultaneous air and surface temperature observations. IEEE J Sel Top Appl Earth Obs Remote Sens 2020; 13:2716-2728; doi:10.1109/JSTARS.2020.2989071
25. Ghirardi L, Bisoffi G, Mirandola R, Ricci G, Baccini M. The impact of heat on an emergency department in Italy: Attributable visits among children, young adults and the elderly during the warm season. PLoS ONE 2015; 10: e0141054; doi:10.1371/journal.pone.0141054
26. Hopp S. Medical diagnoses of heat wave-related hospital admissions in older adults. Prev Med 2018; 110:81-85; doi:10.1016/j.ypmed.2018.02.001
27. International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10 Version:2019). https://icd.who.int/browse10/2019/en#/ Access: Sept 30, 2021
28. International Statistical Classification of Diseases 11th Revision. https://icd.who.int/en Access: Dec. 30, 2021
29. Ioannou LG, Mantzios K, Tsoutsoubi L et al. Effect of a simulated heat wave on physiological strain and labour productivity. Int J Environ Res Public Health 2021, 18, 3011; doi:10.3390/ijerph18063011
30. Iwen KA, Oelkrug R, Brabant G. Effects of thyroid hormones on thermogenesis and energy partitioning. J Mol Endocrinol 2018; 60, R157-R170; doi:10.1530/JME-17-0319
31. Jacobson LdSV, Oliveira BFAd, Schneider R, Gasparrini A, Hacon SdS. Mortality risk from respiratory diseases due to non-optimal temperature among Brazilian elderlies. Int J Environ Res Public Health 2021; 18, 555; doi:10.3390/ijerph18115550
32. Joe L, Hoshiko S, Dobraca D et al. Mortality during a large-scale heat wave by place, demographic group, internal and external causes of death, and building climate zone. Int J Environ Res Public Health 2016; 13, 299; doi:10.3390/ijerph13030299

33. Junk J, Goergen K, Krein A. Future heat waves in different European capital based on climate change indicators. Int J Environ Res Public Health 2019; 16, 3959; doi:10.3390/ijerph16203959
34. Kang C, Park C, Lee W et al. Heatwave-related mortality risk and the risk-based definitions of heat wave in South Korea: A Nationwide Time-Series Study for 2011-2017. Int J Environ Res Public Health 2020; 17, 5720; doi:10.3390/ijerph17165720
35. Kenny GP, Yardley J, Brown C, Sigal RJ, Jay O. Heat stress in older individuals and patients with common chronic diseases. CMAJ 2010; 182(10):1053-1060; doi:10.1503/cmaj.081050
36. Kenny GP, Sigal RJ, Mc Ginn R. Body temperature regulation in diabetes. Temperature 2016; 3: 119-145; doi:10.1080/23328940.2015.1131506
37. Kovats RS, Shakoor H. Heat stress and public health: A critical review. Ann Rev Public Health 2008; 29:41-55.
38. Kowalska J, Rok J, Rzepka Z, Wrzesniok D. Drug-induced photosensitivity – from light and chemistry to biological reactions and clinical symptoms. Pharmaceuticals 2021; 14, 723; doi:10.3390/ph14080723
39. Layton JB, Li W, Yuan J, Gilman JP, Horton DB, Setoguchi S. Heatwaves, medications, and heat-related hospitalization in older Medicare beneficiaries with chronic conditions. PLoS ONE 2020; 15(12): e0243665; doi:10.1371/journal.pone.0243665
40. Lee YH, Bae S, Hwang SS et al. Association between air conditioning use and self-reported symptoms during the 2018 heat wave in Korea. J Prev Med Public Health 2020; 53:15-25; doi:10.3961/jpmph.19.171
41. Levison MM, Butler AJ, Rebellato S, Armstrong B, Whelan M, Gardner C. Development of a climate change vulnerability assessment using a public health lens to determine local health vulnerabilities: An Ontario health unit experience. Int J Environ Res Public Health 2018; 15, 2237; doi:10.3390/ijerph15102237
42. Li M, Gu S, Bi P, Yang J, Liu Q. Heat waves and morbidity: Current knowledge and further direction – a comprehensive literature review. Int J Environ Res Public Health 2015; 12:5256-5283; doi:10.3390/ijerph120505256
43. Li M, Shaw BA, Zhang W, Vasquez E, Lin S. Impact of extremely hot days on emergency departments visits for cardiovascular disease among older adults in New York State. Int J Environ Res Public Health 2019; 16:2119; doi:10.3390/ijerph16122119
44. Liss A, Wu R, Kwan Ho Chui K, Naumova EN. Hear-related hospitalizations in older adults: An amplified effect of the first seasonal heatwave. Sci Reports 2017; 7:39581; doi:10.1038/srep39581
45. Liu J, Vargese BM, Hansen A et al. Is there an association between hot weather and poor mental health outcomes? A systematic review and meta-analysis. Environ Int 2021; 153, 106533; doi:10.1016/j.envint.2021.106533
46. Meade RD, Akerman AP, Notley SR et al. Physiological factors characterizing heat-vulnerable older adults: A narrative review. Environ Int 2020; 144, 105909; doi:10.1016/j.envint.2020.105909
47. Mirsaeidi M, Motahari H, Khamesi MT, Sharifi A, Campos M, Schraufnagel DE. Climate change and respiratory infections. Ann Am Thorac Soc 2016; 13(8): 1223-1230; doi:10.1513/AnnalsATS.201511-729PS
48. Nitschke M, Hansen A, Bi P et al. Risk factors, health effects and behaviour in older people during extreme heat: A survey in South Australia. Int J Environ Res Public Health 2013; 10, 6721-6733; doi:10.3390/ijerph10126721

49. Nori-Sarma A, Benmarhnia T, Rajiva A et al. Advancing our understanding of heat wave criteria and associated health impacts to improve heat wave alerts in developing country settings. Int J Environ Res Public Health 2019; 16, 2089; doi:10.3390/ijerph16122089
50. O'Lenick CR, Baniassadi A, Michael R et al. A case-crossover analysis of indoor heat exposure on mortality and hospitalizations among the elderly in Houston, Texas. Environ Health Perspect 2020; 128:12707-1-17; doi:10.1289/EHP6340
51. Osilla EV, Marsidi JL, Sharma S. Physiology, Temperature Regulation. 2021 May 7. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan–. PMID: 29939615
52. Paterson SK, Godsmark CN. Heat-health vulnerability in temperate climates: lessons and response options from Ireland. Glob Health 2020; 16:29; doi:10.1186/s12992-020-00554-7
53. Percic S, Kukec A, Cegnar T, Hojs A. Number of heat wave deaths by diagnosis, sex, age groups and area, in Slovenia, 2015 vs. 2003. Int J Environ Res Public Health 2020; 15, 173; doi:10.3390/ijerph15010173
54. Pfeifer K, Astrom DU, Martisone Z, Kaluznaja D, Oudin A. Evaluating mortality response associated with two different Nordic Heat Warning Systems in Riga, Latvia. Int J Environ Res Public Health 2020; 17, 7719; doi:10.3390/ijerph17217719
55. Protsiv M, Ley C, Lankester J, Hastie T, Parsonnet J. Decreasing human body temperature in the United States since the industrial revolution. eLife 2020; 9: e49555; doi:10.7554/eLife.49555
56. Robinson A, Lehmann J, Barriopedro D et al. Increasing heat and rainfall extremes now far outside the historical climate. npj Clim Atmos Sci 2021; 4, 45; doi:10.1038/s41612-021-00202-w
57. Rossati A. Global Warming and its health impact. Int J Occup Environ Med. 2017; 8-7-20; doi:1015171/ijoem.2017.963
58. Stapleton JM, Larose J, Simpson C, Flouris AD, Sigal RJ, Kenny GP. Do older adults experience greater thermal strain during heat waves? Appl Physiol Nutr Metab 2014; 39:292-298; doi:10.1139/apnm-2013-0317
59. Stotz A, Rapp K, Oksa J et al. Effect of a brief heat exposure on blood pressure and physical performance of older women living in the community – A pilot-study. Int J Environ Res Public Health 2014; 11, 12623-12631; doi:10.3390/ijerph111212623
60. Tait PW, Allan S, Katelaris AL. Preventing heat-related disease in general practice. Aust J Gen Pract 2018; 47(12): 835-840
61. Takahashi N, Nakao R, Ueda K. Community trial on heat-related illness prevention behaviors and knowledge for the elderly. Int J Environ Res Public Health 2015; 12, 3188-3214; doi:10.3390/ijerph120303188
62. Tansey EA, Johnson CD. Recent advances in thermoregulation. Adv Physiol Educ 2015; 39:39-148; doi:10.1152/advan.00126.2014
63. Temte JL, Holzhauer JR, Kushner KP. Correlation between climate change and dysphoria in primary care. WMJ 2019; 2:71-74.
64. Tseng MF, Chou CL, Chung CH et al. Risk of chronic kidney disease in patients with heat injury: A nationwide longitudinal cohort study in Taiwan. PLoS One 2020; 15(7): e0235607; doi: 10.1371/journal.pone.0235607.
65. Urban A, Hanzlikova H, Kysely J, Plavcova E. Impacts of the 2015 heat waves on mortality in the Czech Republic – A comparison with previous heat waves. Int J Environ Res Public Health 2017; 14, 1562; doi:10.3390/ijerph14121562
66. Vaidyanathan A, Malilay J, Schramm P, Shubhayu S. Heat-related deaths – United States, 2004-2018. Morb Mortal Wkly Rep 2020; 69(24):729-734

67. Valois P, Talbot D, Caron M et al. Development and validation of a behavioural index for adaptation to high summer temperature among urban dwellers. Int J Environ Res Public Health 2017; 14, 820; doi:10.3390/ijerph14070820
68. Vancamp P, Demeneix BA. Is the observed decrease in body temperature during industrialization due to thyroid hormone-dependent thermoregulation disruption? Front Endocrinol 2020; 11, 470; doi:10.3389/fendo.2020.00470
69. van Loenhout JAF, Delbiso TD, Kiriliouk A, Rodriguez-Llanes JM, Segers J, Guha-Sapir D. Heat and emergency room admissions in the Netherlands. BMC Public Health 2018; 18:108; doi:10.1186/s12889-017-5021-1
70. Volkel J, Hellman D, Sakuma R, Shandas V. Assessing vulnerability to urban heat: a study of disproportionate heat exposure and access to refuge by socio-demographic status in Portland, Oregon. Int J Environ Res Public Health 2018; 15, 640; doi:10.3390/ijerph15040640
71. Wang JC, Chien WC, Chu P, Chung CH, Lin CY, Tsai SH. The association between heat stroke and subsequent cardiovascular diseases. PLoS ONE 2019; 14(2): e0211386; doi:10.1371/journal.pone.0211386
72. Williams AA, Spengler JD, Allen JG, Cedeno-Laurent JG. Building vulnerability in a changing climate: Indoor temperature exposures and health outcomes in older adults living in public housing during an extreme heat event in Cambridge, MA. Int J Environ Res Public Health 2019; 16, 2373; doi:10.3390/ijerph16132373
73. World Health Organization. Regional Office for Europe. Protecting health in Europe from climate change: 2017 update. https://www.euro.who.int/__data/assets/pdf_file/0004/355792/ProtectingHealthEuropeFromClimateChange.pdf Access on September 30, 2021
74. Xu R, Zhao Q, Coelho MSZS et al. The association between heat exposure and hospitalizations for undernutrition in Brazil during 2000-2015: A nationwide case-crossover study. PLoS Med. 2019; 16: e1002950; doi:10.1371/journal.pmed.1002950
75. Zevenbergen C, Fu D, Pathirana A. Transitioning to Sponge Cities: Challenges and opportunities to address urban water problems in China. Water 2108; 10, 1230; http://dx.doi.org/10.3390/w10091230
76. Frontiers Forum. Healing the world's cities 2021; https://www.youtube.com/watch?v=g2tl3zC6wX4 Access on September 30, 2021
77. World Economic Forum. Pioneers for our planet. This man is turning cities into giant sponges to save lives 2020; https://www.weforum.org/videos/this-man-is-turning-cities-into-giant-sponges-to-save-lives Access on September 30, 2021
78. Frontiers Forum. Accelerating science-led solutions for healthy lives on a healthy planet 2021; https://forum.frontiersin.org/ Access on September 30, 2021