## MEDICAL AND BIOLOGICAL ASPECTS RELATED TO ASSESSMENT OF IMPACTS EXERTED BY RISK FACTORS

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## UNIVERSAL THERMAL CLIMATE INDEX (UTCI) APPLIED TO DETERMINE THRESHOLDS FOR TEMPERATURE-RELATED MORTALITY

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Our research goal was to examine a response in mortality among population in Arkhangelsk caused by exposure to high and low temperatures. We determined the best available mortality predictor out of air temperature and Universal Thermal Climate Index that characterizes how people feel temperature and detected threshold temperatures depending on sex, age, and cause of death; under exposure to such temperatures there was a statistically authentic increase in mortality.

We analyzed data on daily mortality among population and meteorological data collected in 1999–2016. Relative preciseness in calculating attributive fractions of additional mortality during all hot and cold days was taken as a numeric criterion for selecting the best predictor. All the calculations were accomplished basing on Poisson's regression model taking into account a non-linear dependence between mortality and weather with a distributed lag up to 21 days long.

Although people in Arkhangelsk live in a climate with cold summer and moderately cold winter, we determined attributive fractions of mortality both for cold and heat. In summer high temperatures at night have greater effects on mortality than average daily ones. Differences in temperature-related mortality depend not only on age (people who are older than 65 are more vulnerable in this respect) but also on sex. We detected lower threshold heat temperatures for males as well as greater increase in mortality among them caused by exposure to cold. It is advisable to use different predictors to obtain the maximum precise characteristics for heat and cold stress. We recommend applying UTCI to determine threshold temperatures and additional mortality.

Key words: heat waves, cold waves, mortality, population, circulatory organs diseases, cerebrovascular diseases, respiratory organs diseases, Universal Thermal Climate Index (UTCI), Arkhangelsk.

At present there are a lot of data on an increase in mortality caused by exposure to extreme cold or hot temperatures. These data have been accumulated in various research; and issues related to influences exerted by climatic and weather conditions on population health still remain vital, especially taking into account abnormal climatic phenomena like extremely hot summer in 2019. Extreme cold or heat has been proved to be a risk factor that can cause additional death cases, primarily due to diseases in the circulatory system and respiratory organs [1-3]. Influence exerted by heat on population mortality has been studied profoundly, especially due to global warming [4] whereas exposure to cold and effects produced by it have been given much less attention [5].

Developing timely preventive activities requires better and more precise insight into all peculiarities of a relationship between mortality and air temperature. Among other things, it is important to reveal differences in suscepti-

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bility to temperature among various population groups depending on a sex and age; it is also necessary to improve prediction techniques applied to determine a response in mortality to changes in weather conditions. Recently bioclimatic indexes have been widely used as promising mortality predictors due to their ability to give a more precise insight into people's sensation of warmth or cold as compared with air temperature [6].

People who live in arctic regions in Russia where apparent climatic changes occur can be considered one of the most vulnerable population groups in this respect. Such people can have different adaptive capacities as regards exposure to heat or cold. Given all that, our research goal was to examine a response in mortality to exposure to heat and cold among population in Arkhangelsk. For several years Arkhangelsk has been a model territory where impacts exerted by air temperature and temperature waves on mortality among population have been examined. The first research was accomplished within a project of the WHO Regional Office for Europe and focused on adaptation of public healthcare systems to climatic changes. Experts who conducted the research applied Poisson's model to determine additional mortality caused by temperature exposures [7]. The consequent research yielded a significant result as it allowed obtaining a numerical forecast on expected additional mortality among population living in this city; it was also shown that by 2040-2059 a decrease in mortality in cold season will compensate for an increase in it during summer, and an overall effect produced by warming is quite favorable as there should be an approximately 2% decrease in average annual mortality [8]. Different bioclimatic indexes were assessed in Arkhangelsk, Murmansk, and Yakutsk when experts tried to determine relative rises in mortality during heat and cold waves [9]. Heat and cold waves are discrete weather phenomena; therefore, risks that occur during such waves are characterized not only with temperature-depending mortality, as is the case with the present work, but also with duration of uninterrupted exposure to extreme tempera-

tures. Hence, it is advisable to apply specific models of mortality in such studies; for example, those that take into account an ordinal number of a day since a wave has started. In particular, it was shown that in Arkhangelsk ordinary temperature was more closely related to mortality during heat waves than effective one. In the present work we, for the first time in Russia, have examined a possibility to apply a bioclimatic index UTCI as a marker of a temperature-induced stress and also used standard statistical numerical procedures to test a hypothesis that has been often stated in multiple research, namely, that high nighttime temperature might exert greater influence than daytime one during hot season due to people being unable to get their usual night rest from heat.

We aimed to solve two major tasks in our research: (1) to determine the best available predictor out of the examined ones (air temperature and a bioclimatic index UTCI) separately for cold and hot seasons; (2) to determine threshold temperatures for the chosen predictor under exposure to which there is a statistically authentic increase in mortality; the temperatures were to be determined depending on a sex, age, and a cause of death.

### Data and methods

#### Examined region

Arkhangelsk is located in a geographical zone with moderate climate with some features of marine one, with a correction for the geographic latitude (64°n.l., approximately 220 km to the south from the Arctic Circle). Summers are usually short and cool there and winters are long and moderately cold. As the city is located on the sea, there can often be drastic changes in weather conditions (for example, caused by ultrapolar cold invasions from the Kara Sea). Annual temperature range amounts to 29.1°C [10], resulting from average monthly temperature in January, the coldest month (-12.8°C), and in July, the warmest one (16.3°C).

#### Statistical data on mortality

We took data on daily mortality (an absolute number of deaths) in Arkhangelsk for each day from 1999 to 2016. We analyzed mortality by all natural causes of death excluding any external impacts; we also studied mortality rates as regards circulatory system diseases (CSD) including ischemic heart disease (IHD), cerebrovascular diseases (CVD), and diseases of respiratory system (DRS). Statistical data on all the above mentioned parameters were examined separately for different sex and age groups, with spotting out separate age groups of people aged 30-64 and older than 65. Overall, we used 10 mortality rates separately for men and women.

# Testing sufficiency of mortality data for modeling

To test whether we had sufficient data for regression analysis, we calculated average daily mortality  $(\mu)$  over the examined period. Taking into account the overall number of degrees of freedom in the statistical model for mortality, we can state that  $\mu \lesssim 0.24$  is the bottom limit for conditions of Gauss-Markov theorem to be met. If µ has smaller values, statistical power of a sampling is not sufficient for obtaining reliable regression results. As regards parameters that we chose for our research,  $\mu$  values for them varied from 0.03 cases per day (mortality among women aged 30-64 caused by DRS) to 5.0 cases per day (mortality caused by all natural reasons among women older than 65).

We revealed that mortality caused by DRS among men and women in both age groups didn't have sufficient statistical power; it was also the case with IHD and CVD among women and CVD among men aged 30–64. We took this fact into account when interpreting our results further.

#### Temperature predictors of mortality

We applied two basic temperature predictors to examine impacts exerted by heat and cold on mortality among population; they were air temperature (T) and Universal Thermal Climate Index (UTCI). The latter has an advantage of being universal as it is calculated within a temperature range from -50 to  $+50^{\circ}$ C. This index takes into account a physiological model of human energy balance and is such an equivalent temperature for a given combination of wind speed, solar radiation, humidity, and air temperature that would give the same feeling of weather under etalon conditions [11]. A relevant estimation scale was developed on the basis of modeled physiological reactions and included 10 categories starting from extreme cold stress (lower than  $-40^{\circ}$ C) to extreme heat stress (higher than  $+46^{\circ}$ C).

Our first research task was to select the most informative mortality predictor that would give the most exact forecast on a temperaturerelated component in mortality separately for all hot and cold days over the examined period. Temperature dependence of mortality has an apparent minimum, so called MMT or minimum mortality temperature. All days during which temperature was higher than MMT were considered to be "hot"; and those during which temperature was lower than MMT were "cold". We chose the best predictor out of six for hot days: average daily temperature, maximum temperature during a day and at night, and UTCI. We chose one of four predictors for cold days: average daily temperature, minimum daily temperature, and UTCI (Table 1). Night temperatures were taken between 10 p.m. and 8 a.m. next day. We took data obtained via eight routine observations over daily meteorological parameters at Arkhangelsk weather stations (Index WMO 22550). UTCI index was calculated with Rayman software package [12].

#### Table 1

Temperature predictors in examining influence exerted by heat and cold on mortality

Temperature	Influence	Influence
predictor	by heat	by cold
T <sub>day_max</sub>	1	—
T <sub>night_max</sub>	1	_
T <sub>mean</sub>	1	1
T <sub>min</sub>	-	1
UTCI <sub>day_max</sub>	1	—
UTCI <sub>night_max</sub>	1	—
UTCI <sub>mean</sub>	1	1
UTCI <sub>min</sub>	_	1

Notes:

"day\_max" means maximum temperature at daytime,

"night\_max" means maximum temperature at nighttime, "mean" is daily average,

"min" is minimum temperature during a day;

"✓" means an index was taken for research.

Our numeric criterion for selecting the best predictor was precision in calculating attribute fractions of additional mortality during all hot and cold days ( $AF_{heat}$  and  $AF_{cold}$ ). This precision was characterized with a relative standard error (RSE) in estimated value of these parameters calculated on the basis of comparable mortality models. RSE  $\leq 0.5$  means that AF estimation is authentic at 95% level and it corresponds to Student's t=1/RSE>1.96. We calculated population attribute fraction  $AF_x$  and attribute number of outcomes  $AN_x$  for a given exposure x on the basis of Poisson's model as per a procedure given in [13]. Attribute number of deaths was calculated relative to a hypothetic situation when a temperature during a day *i* was equal to MMT. It is possible to determine cumulative relative risk RRoverall accumulated within a population during a time period equal to L days after exposure to air temperature  $T_i$ , as an increase in mortality on average per 1 day in a period of exposure relative to a hypothetic situation given above. This possibility is provided by models with a distributed lag when it is assumed that an exposure lasts for L days and after this period is over any further exposure can be neglected. Attribute number of deaths  $AN(T_i)$  accumulated within a population during L days after an exposure to temperature  $T_i$ , is determined as an average excess of daily mortality  $M_i$  over minimum mortality MM:

$$AN(T_i) = \frac{\sum_{lag=0}^{L} (M_{i+lag} - MM)}{(L+1)} = (RR_{overall} - 1)MM.$$

To calculate an estimated value of attribute mortality  $\widehat{AN}_i$  over all days in the given period, we applied *a distributed lag non-linear model*-; it is described in details in [14]. There was previous research conducted in largest cities such as London and New-York where qualitative statistical data on daily mortality were available; that research revealed that three weeks were quite enough to be considered a maximum lag *L* during which an effect produced by exposure to extreme temperatures reached its maximum [15]. We applied the same lag in our work. We summed up  $\overline{AN_i}$  over all the days in the examined period and obtained total attribute mortality  $\widehat{AN_{tot}}$  which could be divided into two summands corresponding to all the days with temperatures higher than optimal ( $\widehat{AN}_{heat}$ ) and all days with temperatures lower than optimal ( $\widehat{AN}_{cold}$ ). After that we determined attribute fractions for heat and cold:

$$\widehat{AF}_{cold} = \frac{\widehat{AN}_{cold}}{M_{tot}}; \quad \widehat{AF}_{heat} = \frac{\widehat{AN}_{heat}}{M_{tot}},$$

where  $M_{tot}$  is total mortality over all the days in the examined period. User-defined function *attrdl.R* applied to calculate these parameters in R software (R-package *dlnm*2.2.0) and is available in online-application to the work [13]. This function also allows calculating empirical confidence intervals (CI) around attribute fractions with Monte-Carlo method assuming that model coefficients are normally distributed. Having looked through mortality models with alternative temperature predictors from Table 1, we found the best one that allowed minimizing a relative standard error in calculating attribute fractions.

Our second research task was to calculate heat and cold thresholds for the most informative predictors. Due to finiteness of a primary data array applied for modeling, MMT value was determined approximately as a model estimate. Given that, we applied an empirical procedure for assessing standard deviation and 95% confidence interval of MMT; the procedure was suggested in the work [16]. The right (upper) limit of MMT 95% confidence interval was considered to be a required "heat threshold"; an increase in mortality that exceeded it became statistically authentic. The left (bottom) limit of the interval was considered to be a required "cold threshold".

The final stage in our research involved linearizing obtained dependences of cumulative relative risks  $RR_{overall}(T)$  for predictors with the best predicting capacity. A relative increase in mortality during hot weather was calculated per 1 degree of an increase in a predictor value on average within a range from MMT to 97.5-percentile of its historical longterm distribution; for cold weather, it was calculated per 1 degree of temperature drop within a range from MMT to 2.5-percentile.

Results and discussion. Our assessment and analysis of average UTCI values over 1999-2016 revealed that bioclimatic conditions in Arkhangelsk tended to be comfortable since June till September as there was no temperature stress, and the index values varied within +9...+26 °C (Figure 1). There was a strong cold stress in January and February (-13...-27 °C); as for all the other months, a stress was moderate or slight  $(+9...-13 \ ^{\circ}C).$ 

Tables 2 and 3 contain data which we applied to select the best predictor via minimizing a relative standard error in determining an attribute fraction of mortality for cold and hot weather. We obtained convincing evidence both for cold and hot weather that allowed us to make a choice on the "best" one out of several possible predictors; that is, a predictor that was the most closely related to mortality from a statistical point of view.

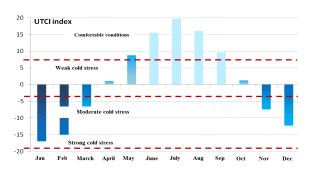


Figure 1. Average monthly values of UTCI (°C) in Arkhangelsk in 1999-2016

Table 2

is given in bold													
Cause	T <sub>day</sub>	max	T <sub>night max</sub>		T <sub>mean</sub>		UTCI <sub>day_max</sub>		UTCI <sub>night max</sub>		UTCI <sub>mean</sub>		best
of death	AF <sub>heat</sub>	RSE	AF <sub>heat</sub>	RSE	AF <sub>heat</sub>	RSE	AF <sub>heat</sub>	RSE	AF <sub>heat</sub>	RSE	AF <sub>heat</sub>	RSE	predictor
Women aged 30-64													
IHD	0.001	7.000	0.0000	NA	0.001	7.450	NA		0.004	2.563	0.0000	NA	UTCI <sub>night_max</sub>
CVD	NA		NA		NA		NA		NA		NA		
CSD	NA		NA		NA		NA		NA		NA		
DRS	0.025	0.600	0.25	1.090	0.27	1.056	0.015	1.283	0.016	1.438	0.010	2.025	T <sub>day_max</sub>
All natural	0.0025	1.800	NA		0.0003	6.333	0.0011	2.864	0.000	NA	0.000	NA	T <sub>day_max</sub>
					Wo	men ol	lder thai	n 65					
IHD	0.0016	2.141	0.0012						0.0019				UTCI <sub>night_max</sub>
CVD			0.004		0.0007								UTCI <sub>night max</sub>
CSD	0.0032	0.938	0.0034	0.787	0.0014	1.696	0.0010	1.850	0.0040	0.681	0.0010	1.925	UTCI <sub>night max</sub>
DRS			0.013		0.013								T <sub>day_max</sub>
All natural	0.0030	0.933	0.0036	0.681	0.0015	0.741	0.0010	1.850	0.0041	0.622	0.0013	1.500	UTCI <sub>night max</sub>
					1	Men ag	ed 30-6	4				-	
IHD	NA		NA		NA		NA		NA		NA		
CVD	0.002	3.625	0.20	0.913	0.20	0.838	0.25	0.670	0.13	1.404	0.22	0.716	UTCInight max
CSD	NA		NA		NA		NA		NA		NA		
DRS	NA		NA		NA		NA		NA		NA		
All natural	0.0033	1.053	0.0042	0.750	0.0035	0.893	0.0015	1.917	0.0042	0.851	0.0024	1.260	T <sub>night_max</sub>
Men older than 65													
IHD	0.007	0.893	0.0083	0.711	0.008	0.719	0.006	0.921	0.013*	0.442	0.008	0.719	UTCI <sub>night max</sub>
CVD	0.000	NA	0.003	3.250	0.003	2.833		3.250					UTCI <sub>nigh max</sub>
CSD	0.005	1.150	0.006	0.833	0.005	0.950	0.005	1.000	0.009*	0.500	0.0062	0.694	UTCI <sub>night max</sub>
DRS	NA		NA		NA		NA		NA		NA		
All natural	0.0010	4.100	0.002	2.250	0.002	2.000	0.0014	2.714	0.006	0.667	0.0033	1.144	UTCI <sub>night max</sub>
*means an AF value is authentic at 95%-th level.													

Attribute fractions for heat (AF<sub>heat</sub>), minimum relative standard error in estimation (RSE)

means an AF value is authentic at 95%-th level.

#### Table 3

Cause	T <sub>me</sub>	ean	T	nin	UTCI <sub>mean</sub>		UTCI <sub>min</sub>		best	
of death	AF <sub>cold</sub>	RSE	$AF_{cold}$	RSE	AF <sub>cold</sub>	RSE	$AF_{cold}$	RSE	predictor	
Women aged 30-64										
IHD	0.27	0.741	0.38	1.974	0.22	1.511	0.29	2.897	T <sub>mean</sub>	
CVD	0.75	0.360	NA	NA	0.79	0.320	NA	NA	<b>UTCI</b> <sub>mean</sub>	
CSD	0.50	0.460	NA	NA	0.50	0.505	0.72*	0.229	UTCI <sub>min</sub>	
DRS	0.031	0.452	0.038	0.434	0.23	2.554	0.031	0.863	T <sub>min</sub>	
All natural	0.22	0.443	0.49	0.383	0.23	0.467	0.39	0.571	$T_{min}$	
	Women older than 65									
IHD	0.29*	0.276	0.45	0.394	0.28*	0.393	0.56*	0.290	T <sub>mean</sub>	
CVD	0.19*	0.447	0.22	1.273	0.21	0.464	0.22	1.364	T <sub>mean</sub>	
CSD	0.22*	0.250	0.27	0.602	0.21*	0.310	0.32	0.477	T <sub>mean</sub>	
DRS	0.43	0.576	NA	NA	0.38	0.770	0.20	1.025	T <sub>mean</sub>	
All natural	0.15*	0.367	0.18	0.861	0.14*	0.411	0.23	0.630	T <sub>mean</sub>	
				Men a	ged 30-64					
IHD	0.37	0.534	0.32	0.867	0.42	0.458	0.24*	0.448	<b>UTCI</b> <sub>min</sub>	
CVD	0.001	6.750	0.000	NA	0.001	6.500	0.003	3.667	UTCI <sub>min</sub>	
CSD	0.21	0.940	0.16	0.750	0.22	0.977	0.15	0.550	<b>UTCI</b> <sub>min</sub>	
DRS	0.42	1.214	0.56	0.929	0.48	1.130	0.50	1.280	$T_{min}$	
All natural	0.14*	0.446	0.17*	0.368	0.14*	0.464	0.17*	0.353	<b>UTCI</b> <sub>min</sub>	
Men older than 65										
IHD	0.26*	0.385	0.26*	0.356	0.31*	0.315	0.27*	0.352	UTCI <sub>mean</sub>	
CVD	0.16	0.891	0.19	0.697	0.20	0.738	0.22	0.580	UTCI <sub>min</sub>	
CSD	0.20*	0.413	0.21*	0.369	0.25*	0.340	0.25*	0.300	UTCI <sub>min</sub>	
DRS	0.49	1.250	0.55	1.445	0.62	1.113	0.70	0.868	UTCI <sub>min</sub>	
All natural	0.10	0.725	0.12	0.563	0.15	0.483	0.15*	0.417	UTCI <sub>min</sub>	

Attribute fractions for cold (AF<sub>cold</sub>), minimum relative standard error in estimation (RSE) is given in bold

\* means an AF value is authentic at 95%-th level

The most convincing results were obtained for hot weather. It was possible to select the best predictor only for 14 parameters (we didn't obtain any temperature-related dependences for high temperatures for the remaining 6 parameters). The UTCI nighttime maximum (UTCI<sub>night\_max</sub>) which we chose out of 6 alternative predictors turned out to be the best one in 11 cases out of 14.

We obtained reliable  $AF_{heat}$  estimations only for two parameters out of 20, namely IHD and CSD in men older than 65; it proves that elderly people are too sensitive to negative impacts exerted by heat as it was also confirmed in some previous research [3, 17, 18].

During cold days predictors turned out to have different predictive capacity depending on a sex. Average daily temperature  $T_{mean}$  was a better

predictor for women (for 6 mortality parameters out of ten). As for men, the best predictor for them was minimum daily  $UTCI_{min}$  (for 8 out of 10 parameters). At the moment we can't give any authentic explanation for the detected sexdependent differences in predictors. Among other things, they can be caused by differences in physical and social activity of men and women in winter. UTCI was chosen as a probable mortality predictor during a cold season in research conducted in Czech Republic [19] and Iran [20].

We obtained a lot more statistically authentic estimations of AF for exposure to cold (both for men and women); these estimations were detected for all the chosen pathologies excluding DRS. And not only elderly people but also younger age groups (30-64 years) were sensitive to this exposure.

#### Table 4

	Heat						Cold						
Cause of death	MMT (%)	MMT (°C)	Heat threshold (°C)	Relative in- crease in mortal- ity (% per 1°C)	MMT (%)	MMT (°C)	Cold threshold (°C)	Relative increase in mortality (% per 1°C)					
predictor		1	UTCI <sub>night ma</sub>	IX	T <sub>mean</sub>								
IHD	93	22.1	NA	2.0	95 19.2 -12.6		2.9						
CVD	NA	NA	NA	NA	NA	NA	-8.4	NA					
CSD	NA	NA	NA	NA	NA	NA	-8.1	NA					
DRS	90	20.3	NA	8.6	NA	-12	-17	NA					
All natural	98**	27	NA	NA	97	20.7	-12.5	1.3*					
				Women older th	an 65								
IHD	94	23.1	NA	1	97	20.4	17.1	1.8*					
CVD	93	21.8	NA	1.6	95	19.3	-10.5	1.4*					
CSD	93	21.9	30.6	1.7	95	18.8	16.8	1.4*					
DRS	90	20.1	NA	10.2	90	16.2	NA	3.8					
All natural	92	21.5	26.7	1.5	95	18.4	-11.8	1.0*					
	Men aged 30-64												
predictor	vredictor UTCI <sub>night max</sub>						UTCI <sub>min</sub>						
IHD	NA	NA	NA	NA	98	16.1	10.3	2.0*					
CVD	NA	NA	NA	NA	NA	NA	NA	NA					
CSD	99**	28.6	NA	NA	95	13.5	-20.2	1.1*					
DRS	NA	NA	NA	NA	NA	NA	-21.1	NA					
All natural	92	21.4	NA	1.5	93	12	-20.7	1.0*					
Men older than 65													
IHD	90	20.2	23	4.7*	93	11.7	8.9	2.2*					
CVD	91	21	NA	0.8	89	10.1	-6.3	3.4*					
CSD	90	20.3	24.7	3.1	91	11.1	8.9	2.6*					
DRS	NA	NA	NA		NA	NA	9.6	NA					
All natural	90	20.4	NA	1.8	91	11	0.5	1.4*					

#### Temperature that corresponds to MMT; heat and cold thresholds, relevant increases in mortality (%) per 1°C increase in exposure

Note:

\* is an authentic increase per 1 1°C at 95%-th level;

\*\* are suspect (too high) MMT values that are higher than 97.5-th percentile of UTCI<sub>night max</sub> distribution.

There are heat and cold weather thresholds; when they are reached, there occurs a statistically significant increase in mortality. These thresholds are of great practical interest. The results in Table 4 are given for the best predictors chosen at the previous stage in our research, namely UTCI<sub>night max</sub>, T<sub>mean</sub>, UTCI<sub>min</sub>

MMT values and heat values are given for UTCI<sub>night\_max</sub>. Overall, MMT parameter was determined for 15 mortality parameters (Table 4). Having excluded suspect values, we concluded that MMT value was most frequently expected between 90 and 94 percentile. It corresponded

to  $UTCI_{night_max}$  index reaching 20–21°C. We can't possibly expect more exact calculation here. Lower MMT values for  $UTCI_{night_max}$  were detected for men than for women, especially among people older than 65; therefore, men are more sensitive to heat exposure. It confirms the results we obtained in our previous research in Rostov-on-Don that men were more sensitive to a temperature factor than women. Especially in older age groups [14].

Statistically authentic threshold values for heat were determined only for four mortality parameters (CSD and all natural death causes for women older than 65 as well as IHD and CSD for men older than 65) that varied from  $23.0^{\circ}$ C to  $30.6^{\circ}$ C for UTCI<sub>night\_max</sub>. Naturally, the minimum value +23.0°C was the most interesting one since in case there were such maximum UTCI values at nighttime we could expect an authentic increase in mortality caused by IHD among men older than 65 in Arkhangelsk. We didn't detect any authentic heat threshold for age groups that included people aged 30–64.

We calculated a relative increase in mortality in % per 1 degree Celsius and revealed that they varied from 0.8 to 10.2% for hot days depending on a specific pathology and sex and age group; but still, practically all obtained results were not significant except from mortality caused by IHD among men older than 65 (4.7% per 1°C).

When interpreting cold thresholds for *women*, we should take into account that "extreme cold threshold" which we require to determine a temperature range for linearizing temperature dependence is equal to  $T_{2.5\%}$ =-22.8 °C for  $T_{mean}$ . As we applied another predictor for men, the relevant 2.5 percentile was UTCI<sub>2.5%</sub>=-31,5°C. The most complicated task was to explain why the determined cold thresholds were heterogeneous and varied from -12.6 to +17.1°C (a 92-th percentile) among women and from -21.1 to 10.3°C (a 89-th percentile) among men depending on a parameter.

There can be two possible explanations for this spread. The first is that there is a long "plateau" below MMT within a range of transient year temperatures. It confirms a typical temperature dependence of mortality for Arkhangelsk (Figure 2). In this case differences in plateau length estimations should be considered a modeling artifact (it can be eliminated via greater degrees of freedom when modeling temperature dependence of mortality; however, authenticity of obtained results decreases drastically in this case due to very few lethal outcomes in Arkhangelsk).

The second explanation is that a "true" dependence should be U-like without any plateau; then "true" cold thresholds should be near MMT, that is, they are close to the following maximums:  $+17.1^{\circ}$ C for T<sub>mean</sub> and  $+10.3^{\circ}$ C for UTCI<sub>min</sub> (percentiles of these values are close, 92% and 89%). This or that explanation can be chosen only after testing whether modeling results for MMT CI are stable; such testing can be accomplished only on a big data array on mortality (for example, in a large city with millions of population, for example, in Moscow or Saint Petersburg).

The most significant difference in modeling results for heat and cold is much greater evidence obtained for authentic influence exerted by cold temperatures. For example, Table 4 contains 5 statistically significant results of linearization for women (out of ten) and 7

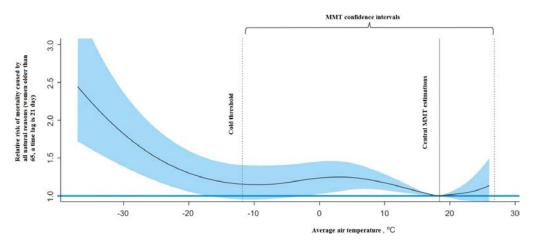


Figure 2. Temperature-dependent mortality caused by all natural reasons among women older than 65 in Arkhangelsk: we can see a plateau within a period of transient autumn and spring temperatures. Solid vertical line shows central MMT estimation, and broken lines show its confidence intervals. A broken line to the left is a cold threshold

(out of 10) for men. As a rule, results that are not statistically significant are related to insufficient statistical power of mortality samplings (see above). Average increases in mortality per 1-unit decrease in a predictor within cold temperatures range varied from 1.0% to 1.8% for women (out of authentic estimations); from 1.0% to 3.4%, for men. Effects produced by cold were greater for men than for women as it was shown by comparing all the authentically detected increases in mortality in an older age group.

Results which we obtained in this work allow comparing damage to health of population in Arkhangelsk caused by exposure to heat and cold, taking into account specific features of a local climate; it is well in line with bioclimatic conditions existing in the city. People in Arkhangelsk are rarely exposed to heat stress during summer; therefore, we didn't obtain many authentic results about a response in mortality during hot days. High temperatures at nighttime are likely to be the most significant factor that makes its contribution into an increase in mortality during hot weather.

People in Arkhangelsk live under exposure to cold stress during the most part of a year and it causes additional cold-related mortality that was numerically estimated in our research. It is in line with previously obtained results [8, 9]. For example, experts detected an increase in mortality caused by IHD and natural causes in Archangelsk during cold waves occurring in 1999-2008 [7]. Similar results were obtained in another northern city, Stockholm; research conducted there revealed that a number of additional death cases caused by heat had been decreasing over the last ten years whereas a number of additional death cases caused by cold remained stably high [21]. Most additional death cases caused by CSD and ROD were related to cold days in some cities in the USA [22], China [23, 24], and many other regions [1]. Therefore, impacts exerted by cold weather on population mortality still remain an outstanding issue in public healthcare.

**Conclusion.** Although people in Arkhangelsk live in a climate with cool summer and moderately cold winter, we can't neglect impacts exerted by heat on additional death cases. Such impacts become extremely apparent when there are high temperatures at night. It is necessary to work out and implement action plans for both extremely high and cold weather conditions and pay attention to individual precautions, including medications [25, 26].

Differences in temperature-related mortality are not only age-dependent (people who are older than 65 are more vulnerable in this respect) but also sex-dependent. As we detected lower heat thresholds for men as well as higher increases in mortality among them during exposure to cold, we can state that their health is more susceptible to such exposure.

As regards heat and cold stresses, it is advisable to apply different predictors. When we analyze heat exposure, we should apply a night maximum for UTCI; when analyzing cold exposure, we should take an average daily temperature (as a mortality predictor for women) and minimum daily UTCI value (as a mortality predictor for men). It is advisable to use UTCI to determine temperature thresholds and additional mortality values.

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