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ON SOME APPROACHES TO CALCULATION OF HEALTH RISKS CAUSED BY TEMPERATURE WAVES

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The paper dwells on techniques applied for assessing impacts exerted by environmental factors on population health which have become conventional all over the world over recent years. The greatest attention is paid to up-to-date approaches to calculating risks of additional mortality which occurs in big population groups during cold and hot temperature waves. The authors consider basic stages in direct epidemiologic research: temperature waves definition; statistics hypotheses formulation; models specification; statistical criteria sensitivity, and statistical validity of the obtained results. As per long-term research performed by us in various Russian cities, we constructed logistic curves which show probability of obtaining significant risk assessment results for small samplings. We recommend to apply percentiles of long-term average daily temperature distributions as temperature thresholds when identifying temperature waves; in our opinion, such thresholds correspond to perceptions of extreme (for this or that region) temperatures and provide comparable results in terms of expected waves quantity in different climatic zones. Poisson's generalized linear model for daily mortality is shown to be the most widely spread technique for calculating risks caused by hazardous environmental factors. It is advisable to allow for an apparent correlation between mortality and time and air contamination in any regression model. We can allow for meteorological conditions which influence heat balance (air humidity and wind speed) either via including them apparently into a model or via bioclimatic indexes application; research in this sphere is going on. When calculating risks, it is advisable to allow for time lags between extreme temperatures waves and changes in mortality. We revealed that minimal population of a typical city for which it is possible to obtain statistically significant assessment of risks caused by heat waves ensembles is about 200 000 people.

Key words: *population mortality, temperature waves, time rows analysis, risk assessment, Poisson's distribution, generalized linear model, mixing factors.*

Climatic changes we are witnessing at the moment lead to heat waves becoming more repeatable, longer, and more intense; cold waves, on the contrary, occur not so frequently, are less intense and don't last as long as they used to [1]. Consequences of impacts exerted by temperature waves on population health are being examined all over the world, and PubMed, the leading medical database, contains more than 1,000 works in the field. Serious health disorders which occur during temperature waves can cause not only its heavy losses but also a decrease in a number of healthy years of life. All this, in its turn, results in GDP losses, both on a country and regional level.

This paper focuses on contemporary biological statistic techniques which allow to reveal correlations between meteorological factors and public health. In particular, it dwells on how to calculate additional population mortality caused by heat and cold waves influence. Value of daily (every day) mortality for an examined population is a random function, and this randomness cannot be eliminated (for example, we can't consider it to be a measurement error). Epidemiologic research in the field is often re-

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lated to regression analysis performed on time series of daily mortality. Our goal was to describe up-to-date statistic mortality models which are applied to calculate mortality risks caused by temperature waves influences. The article is conditionally divided into three sections: the first one contains definitions of temperature waves; the second describes daily mortality modeling; the third one is about statistical validity of risk assessment results obtained for small samples.

Heat and cold waves: definitions. Some researchers put the following question: which waves stimulate greater growth in mortality, heat or cold ones? To answer it correctly, it is advisable to give "symmetric" definitions for heat and cold waves, both concerning their duration and temperature thresholds. Bearing this symmetry in mind, we are giving only a definition of heat waves here, and cold waves are to be defined by analogy.

Meteorology states that a heat wave is "a considerable temperature rise which spreads to a certain direction and is related to a warm mass advection" (Meteorological glossary, 1974). Rosgidromet (Federal Service on Hydrometeorology and Environmental Monitoring) gives the following definition of "abnormally hot weather": "... average daily temperature being 7ºC or more degrees higher than the climatic standard during a period from April to September"[1]. This definition for heat waves is to be applied by EMERCOM of Russia and other state organizations when they classify dangerous weather phenomena. If we apply this definition too, we can see that most heat waves come to central Russian regions in April, and in July their number is minimal. Heat waves in meteorology are defined analogically but there is no limitations "from April to September", so heat waves can occur during all four seasons [2]. However, the major problem concerning this definition is that probability of temperature waves occurrence (or their number) vary significantly in different climatic zones.

The problem can be solved if we abandon "7ºC" criterion and apply percentiles of long-term "historical" average daily temperatures distribution instead; or we can apply root-mean-square deviation for this distribution, that is, statistic (probabilistic) features which are calculated as per a common sample comprising either all days in a year, or all days in a warm (cold) period. The World Meteorological Organization suggest to apply the upper 90th or 95th percentile of temperatures distribution during warm time of the year as a local specific threshold in the following definition: "A heat wave is a clearly defined two- (or more)-day period of extreme heat measured in daily maximum, average, and minimal temperatures, during warm time of the year" Thresholds are suggested to be set allowing for local climate [3].

A similar definition is used in epidemiologic literature [4]. For example, methodical guidelines issued by Rospotrebnadzor state that a wave heat is five and more consequent days during which average daily temperature is higher than 97th percentile of the average daily temperatures distribution over an examined long-term period[2]. Such threshold will on average "cut off" 3,65×3≈11 of the hottest days per year and

[1] Guidelines 52.27.724-2009. Guidelines on general short-term temperature forecasts. Obninsk, IG-SOZIN Publ., 2009, 66 p.

[2] MG 2.1.10.0057-12. Population health related to the environmental situation and living conditions. Assessment of risks and damages caused by climatic changes which influence morbidity and mortality in population groups running increased health risks: methodical guidelines. Moscow Federal Service for Surveillance over Consumer Rights Protection and Human Well-being Publ, 2012, 37 p. Available at: http://36.rospotrebnadzor.ru/documents/rekdoc1/9374 (11.10.2017).

not all of them will be included into heat waves. We say "on average", because heat waves are not distributed evenly over years, and two or three cooler years are usually followed by a year when summer is hot and there are several heat waves during it. Most waves come in July which is usually the hottest month of the year.

Which of two definitions given above is stricter, that is, gives less waves due to a higher hot weather threshold? Let us consider Moscow as an example. Over 2000-2009 average June temperature in Moscow amounted to 16.5ºC; July, 19.9ºC; August, 17.5ºC. Therefore, hot weather thresholds for three summer months according to Rosgidromet definition are to be approximately (as we apply average monthly temperatures here) equal to 23.5ºC; 26.9ºC; 24.5ºC. The 97th percentile of average daily temperatures in Moscow taken for the same period amounted to 23.5ºC. We can see that the first definition is stricter: we can expect only 14 days during 10 years when temperatures will be higher than these thresholds, that is, only one or (unlikely) two heat waves will occur. The second definition, as our research performed in moderate climatic zones showed [5–8], gives on average about 8 heat waves over a ten-year period. Such quantity of waves naturally gives more data for epidemiologic research and simultaneously coincides with an intuitive idea of extreme temperatures.

Bioclimatic indexes. Statistical mortality models can include temperature, humidity, wind speed and other meteofactors as independent variables; that is, risks caused by temperature are calculated with an adjustment for other meteorological variables. However, there is another approach when models incorporate a certain combination of these variables, when temperature is given a dimension and is called, for example, "an effective temperature" (in case of heat) or wind-cold index (in case of cold). Epidemiologists are still searching for the most relevant combination of meteorological variables; it should be such a combination when a statistic test would reveal the strongest correlation with a chosen health parameter [9, 10]. Accordingly, heat waves can be defined not with a usual air temperature (measured by a dry thermometer) but with an effective one. Methodical guidelines issued by Rospotrebnadzor give the following definition for effective temperature [11]:

$$AT = -2{,}653 + 0{,}994\,T + 0{,}0153\,D^2,$$

where AT is effective temperature; T is air temperature; D is dew point temperature.

We showed in one of our works that effective temperature is more closely connected with morality occurring during heat waves, and wind-cold index is a better mortality predictor during cold ones than just usual air temperature [5]. But as for this paper, here we apply usual air temperature as a variable to identify temperature waves (that is, heat and cold ones), without limiting generality in statement.

Statement and testing of statistic hypotheses. Any statistic research starts from stating statistic hypotheses which should correspond to its specific goals. If we want to examine influences exerted by temperature waves on population health we should prove there is a statistic correlation between such waves and a number of daily outcomes for a selected health parameter. Although we apply the same statistic procedures to examine both cold and heat waves, there is one significant difference between influence on mortality exerted by cold waves and heat ones. And this difference is a time aspect: cold effects are rather long-term and come with a delay while heat acts almost instantly. This difference should be explained by pathophysiological mechanisms of heat and cold effects and by body adaptation and short-term acclimatization to extreme temperatures, but statistic research goals are to only detect any statistic regularities, and not to explain them. Therefore an expert in biological statistics who studies death predictors (air temperature, for example) confines him or herself to such a correct conclusion as "we revealed a correlation between air temperature and mortality". In this case air temperature is considered to be a risk factor, and this factor can be a reason or just a marker of an effect.

If we take only one specific wave, than our null hypothesis (H0) can be stated as follows: mortality which occurred during a period of the wave has no statistical discrepancies from mortality expected under other conditions being equal in case the wave was absent. The same hypothesis is apparently generalized for research on an ensemble (a certain set) of waves during a long-term research period. Individual waves in this ensemble are different both in terms of their duration and intensity (amplitude). Depending on research goals, experts can examine dependence of ultimate health indexes on these parameters by comparing corresponding wave ensembles. The simplest models, especially in case of short time series, give a possibility to examine an ensemble of all the identified waves; thus it is possible to calculate only additional mortality risk which is averaged as per this ensemble. Defined exactly, a risk is a ratio of mortality expected during the examined wave ensemble to mortality expected during the same days but when there is no extreme heat.

A possible time lag between a temperature wave and a response in mortality makes null hypothesis statement more complicated as it requires additional assumptions on a delayed effect and corresponding mathematical tools.

A usual research object is a population of just one city. Population number determines a mathematical expectation of daily mortality as a random variable and a dispersion of this parameter which, in their turn, have their influence on sensitivity of a statistical test applied to verify H0.

Time series analysis. Regression analysis with Gaussian and Poisson's generalized linear models is the most widely spread technique applied to examine long time series of daily mortality [11]. An assumption stating that outcomes are independent leads to Poisson distribution of daily mortality. But in reality the basic property of Poisson distribution (mathematical expectation of daily outcomes number λ is equal to dispersion) holds only approximately for daily mortality. As λ grows, an excessive dispersion occurs, and daily mortality distribution itself becomes Gaussian when λ values are high. Apparently, one of the reasons for the phenomenon is that an assumption on independence of outcomes is false.

If a dependent variable complies with Poisson distribution, than when we apply a natural logarithm as a functional correlation in a regression models, regression remains will be distributed as per the normal law. But if a dependent variable is distributed as per the normal law, then it is correct to apply a linear functional correlation (Gaussian regression). For example, linear regression can be applied in Moscow where $\lambda \approx 300$. However, we don't "win" much by doing this: if Poisson model is applied in Moscow, we can obtain risk assessment results which are quite comparable in terms of their statistic significance.

Model specification. Let us consider a Poisson model for daily mortality Mi. As a time series Mi is a random function of a number of a day i, then a dependent variable in regression equation is an expected daily mortality value $E(Mi) \equiv \mu i$. It is convenient to divide all the predictors into those which apparently depend on time t and all the remaining regressors of daily resolution x1, x2, … xP, including ecological ones, i.e. regressors which describe influences exerted by the environment (meteorological factors and contamination) and mediate the effect [12]:

$$\log[E(M_i)] = \alpha + \sum_{j=1}^{P} g_j(x_{ij}) + f(t_i) + \beta\ DOW. \quad (1)$$

Generalized linear regression has an advantage of being flexible in selecting functional dependences gj on continuous regressors and possibility to include discrete regressors into the model without loss of generality. A good example is the last summand in the model (1) which is a vector consisting of seven categorial variables labeling days of week (DOW) with corresponding regression coefficients β.

An apparent dependence of daily mortality on time includes seasonality, a long-term trend, dependence on a day of week, holidays, flu epidemics etc. If a researcher wants to focus on seasonal changes in mortality, then the function f(t) can contain a periodical summand with a period being equal to 1 year. In general cases, allowance for smooth time dependences on various scales is achieved via including splines S(t) with a preset number of degrees of freedom (or nodes) over the whole examined period into the model.

Heat waves risk assessment. If we concentrate only on general effects exerted by heat waves on mortality, then our regression model will not include temperature explicitly. It will be quite sufficient to apply a binary variable which labels all the days included into an examined heat waves ensemble (with a preset time lag in days). Regression coefficient for this variable βheat (its exponent, to be exact) will give a numeric characteristics for mortality increase on average for this waves ensemble adjusted as per all the other factors which influence mortality and are included into the model (1).

Overall effects by heat waves can be divided into two summands. The first summand is called "a basic temperature effect" as it depends on average daily air temperatures. The second summand is a "wave addition" which occurs only under long-term exposure to heat and is a function of a number of a day in a continuous consequence of hot days. As A. Gasparrini revealed, the basic effect is several times greater than the wave addition for waves which are usual in their duration (5-10 days) [13]. However, we observed a rather opposite ratio during abnormal heat in Moscow in summer 2010 [14].

Experts have long known that the basic temperature effect is not "instant"; it is distributed over time in a complicated way, that is, it influences mortality during all days which follow the reference one. Various ways were suggested to examine delayed dependences allowing for a time lag between exposure and effects [15, 16]. Statistical functions describing non-linear models with distributed lag were integrated into the software environment R and are now freely accessible in CRAN (Comprehensive R Archive Network) [17].

Mixing factors. According to a "ventilation hypothesis", atmospheric air contamination has different influence on health during hot days and days when temperature is moderate. On hot days people keep their window open in order to ventilate their homes and spend more time outdoors; therefore, they are exposed to greater doses of air contaminants [18]. If this hypothesis is true than a certain part of high temperature risks is actually caused by contaminants concentrations in the atmospheric air (first of all PM_{10}) and greater exposure to such pollutants. As for surface ozone, here there is also a functional correlation with temperature as speeds of multiple photochemical reactions depend on air temperature. Therefore, air contamination can also be considered a heat effect mediator, and allowance for average daily levels of PM_{10}, NO_2, and ozone in the model (1) is a good practice (provided we have sufficient data on contamination).

Air pressure fluctuations also influence daily mortality [19]. If contamination is usually included into regression model as linear members (according to a hypothesis on non-threshold effects), then to describe air pressure effects correctly, we need more flexible representation. Both high and low pressure, as well as drastic pressure fall statistically cause greater mortality. It is convenient to apply cubic splines to describe non-monotony dependences; such splines should have "natural" boundary conditions (the second variable at splining range boundaries is equal to zero).

Influence exerted by population number on validity of results. Difficulties in examining small samples. We examined influences exerted by temperature waves on mortality in 9 cities in Russia with different population number. Our research results can be applied to assess how probable it is to obtain statistically significant results in assessing risks caused by temperature waves at different values of λ (average daily mortality). The model which is described below should help other researchers to plan their examinations on small samples when there is a question: what minimal population number is required to obtain significant results in assessing risks caused by temperature waves? In this case we examine a binary significance sign at 95% level of regression coefficient β_{heat} in the model (1), therefore, it is only reasonable to assume there will be an increase (and not a fall) in additional mortality when a stress-factor occurs and to apply a one-sided z-test. Modeling a probability of obtaining or not obtaining a significant result depending on population number is quite similar to drawing up a demand curve in econometrics (whether a buyer agrees or doesn't' agree to buy a product depending on its price).

Initial data are taken from our own works accomplished according to comparable procedures in 9 cities and during comparable examination periods being equal to 10 years on average. In this research we calculated mortality risks during wave ensembles (for heat and cold separately) which lasted 5 and more days and which were identified in the examined period in this or that city. Data on daily mortality were obtained from the Federal State Statistic Service databases; data on air temperature and other meteorological variables were taken from the Rosgidromet web-site (http://cliware.meteo.ru/meteo/). Mortality risks caused by climatically dependent reasons should be more significant than for overall mortality. According to our experience, infarctions (coded I20-I25 as per ICD-10) and strokes (I60-I69) are the most climatically dependent death causes. For example, when there was extremely intense and long heat wave in Moscow from June 6 to August 18 2010, we estimated additional mortality due to all causes to be equal to 11,040 cases, 5,045 out of them were death cases caused by infarctions (46%), and 3,712, by strokes (34%) [14]. Therefore, cardio-vascular reasons accounted for up to 80% of all the additional mortality in Moscow during that period.

To obtain sufficient initial data to model how probable it was to obtain significant results in assessing heat and cold waves risks depending on λ, we calculated risks separately for "average" and "old" age groups: death cases at the age of 30-64, and death cases at the age older than 65. Such division into two different age groups is quite conventional in world practice as 65 years is an age when people retire in many countries, and, accordingly, age group of 30-64 comprises population who are able to work. Quantity of deaths among those younger than 30 is negligible. A lot of medical and statistical parameters are usually reported for these two groups separately in order to reveal any age-related discrepancies. Therefore, we examined four different mortality parameters in each city: death cases caused by infarctions and strokes separately in two age groups. We assumed that probability to obtain statistically significant results of risk assessment at a preset value of λ was approximately the same for these four parameters. Otherwise, we wouldn't be able to combine risk assessment results for all four of them into one sample. This assumption holds in the case when the risks themselves for the examined mortality parameters are comparable. To verify validity of our assumptions, we included not only the binary variable (0 means risk is not significant, 1 means risk is significant) into the Table, but also estimates of relative increases in mortality during heat or cold waves. But by no means was the Table drawn up to compare absolute values of previously obtained risk assessments between cold and heat, or north and south.

Data sources are:

- for Arkhangelsk, Murmansk, Yakutsk, and Magadan, [8];

- for Volgograd, Rostov, Astrakhan, and Krasnodar, [6,7];

- for Krasnoyarsk, [5].

Results of assessing temperature waves risks in 9 cities

City*	Cause and age of death	λ	RR_{heat}	Significance (RR_{heat})	RR_{cold}	Significance (RR_{cold})
Arkhangelsk (350 thousand)	Infarction 30-64	1,4	0,94	0	1,18	1
	Infarction ≥65	2,1	0,93	0	1,22	1
	Stroke 30-64	0,62	1,01	0	1,13	0
	Stroke ≥65	2,5	1,30	1	1,19	1
Murmansk (325 thousand)	Infarction 30-64	1,7	1,03	0	1,18	1
	Infarction ≥65	1,7	0,76	0	1,09	0
	Stroke 30-64	0,65	0,88	0	1,07	0
	Stroke ≥65	1,7	1,25	1	1,14	0
Yakutsk (236 thousand)	Infarction 30-64	0,42	1,15	0	1,38	1
	Infarction ≥65	0,55	0,90	0	1,41	1
	Stroke 30-64	0,23	0,91	0	0,8	0
	Stroke ≥65	0,32	1,61	1	1,69	1
Magadan (100 thousand)	Infarction 30-64	0,31	1,44	0	1,01	0
	Infarction ≥65	0,31	1,23	0	1,39	1
	Stroke 30-64	0,19	1,57	0	1,37	0
	Stroke ≥65	0,25	1,23	0	1,66	1
Volgograd (989 thousand)	Infarction 30-64	3,5	1,25	1	1,12	1
	Infarction ≥65	7,6	1,39	1	1,10	1
	Stroke 30-64	1,5	1,36	1	1,29	1
	Stroke ≥65	10,7	1,55	1	1,08	1
Rostov (1053 thousand)	Infarction 30-64	2,1	1,20	1	1,16	1
	Infarction ≥65	7,0	1,39	1	1,12	1
	Stroke 30-64	1,4	1,51	1	1,23	1
	Stroke ≥65	9,7	1,75	1	1,15	1
Astrakhan (500 thousand)	Infarction 30-64	1,7	1,42	1	1,23	1
	Infarction ≥65	4,2	1,58	1	1,14	1
	Stroke 30-64	0,72	1,40	1	1,04	0
	Stroke ≥65	3,4	1,57	1	1,28	1
Krasnodar (710 thousand)	Infarction 30-64	1,4	1,24	1	1,14	0
	Infarction ≥65	5,6	1,37	1	1,17	1
	Stroke 30-64	0,93	1,50	1	1,33	1
	Stroke ≥65	6,4	1,76	1	1,08	1
Krasnoyarsk (932 thousand)	Infarction 30-64	2,2	1,10	0	1,17	1
	Infarction ≥65	5,3	1,14	1	1,04	0
	Stroke 30-64	0,96	1,19	0	1,24	1
	Stroke ≥65	4,6	1,44	1	1,11	1

Note: * – Population number is given in thousands in the middle of an examination period; λ is average mortality during an examination period, number of death cases a day; RRcold и RRheat are relative mortality risks during heat and cold waves; significance: 1 means risk is significant at 95% level; 0 means risk is not significant at 95% level.

These sources contain detailed description of Poisson models which were applied by the authors to assess risks.

Probability to obtain authentic risks assessment results at this value of λ is the most probable under the following condition: it is necessary to find such function $\pi(\lambda) \in \{0;1\}$, when

$$\mu = E\,(y|\,\lambda) = P\,(y = 1|\,\lambda) \equiv \pi\,(\lambda), \quad (2)$$

where λ is a predictor; E in an expected value; P is probability; $y \in \{0;\ 1\}$ is a binary sign or response. If we assume reasonable boundary conditions for such a task, than probability of event y_i=1 depending on λ_i is conventionally approximated with binary logistic regression:

$$\pi(\lambda) = \frac{exp(\beta_0 + \beta_1\lambda)}{1 + exp(\beta_0 + \beta_1\lambda)}, \quad (3)$$

where β_0 and β_1 are estimated values of regression coefficients which are calculated linear regression of reverse conversion:

$$\ln(\frac{\pi}{1-\pi}) = \beta_0 + \beta_1\lambda + \varepsilon. \quad (4)$$

Regression coefficient β0 characterizes probability of obtaining significant results of risk assessment when population number is equal to zero, and β1 is a marginal effect at various values of λ.

You can see triangles on Figures 1 and 2 which show initial data for taken regression from the Table; you can also see logistic curves which approximate probability $\pi(\lambda)$ within $0{,}1<\lambda<5$ range. A broken line shows a standard regression error $\mu\pm\sigma$. Regression was accomplished with *logistic* command in Stata 14.0 program.

In case of heat waves (Figure 1) both regression coefficients β_0 and β_1 are statistically significant: β_0=-1.91±0.82, p=0.020; β_1=1.32±0.54, p=0.014. Therefore, a logistic curve allows to predict at what values of λ we can expect to obtain authentic risk assessment. The condition μ>1/2 (significant result is more probable than insignificant one) holds at λ>1.5 (this result is valid for examination periods which are equal to about 10 years). But what is population number which λ≈1.5 corresponds to?

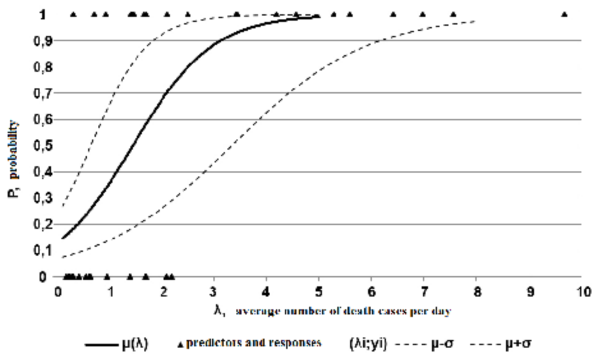

Figure 1. Probability of obtaining significant results in assessing heat waves risks

As we can see from the Table, stroke in the older age group prevails among four mortality parameters included into the model. Average daily mortality for this cause amounts to 40 cases per total population in 9 cities which is equal to 5.195 million. If we neglect a possible heterogeneity of ratios between mortality parameters in different climatic zones, we will see that 1.5 stroke cases a day correspond to the following population number: 5195×1,5/40=195 thousand people. This value is minimal population number which will allow us to obtain authentic heat wave risk assessment for at least one of the four selected mortality parameters.

In case of cold waves a logistic curve does not go lower than P=0.5 (Figure 2); therefore, we can't solve the task on minimal population number we are considering in the same manner which we described above. Most likely, it is due to a number of authentic cold waves risks assessment being overestimated in the sphere of small values of λ. Such overestimation can be caused by authors applying a great number of various lags (from one day to three weeks) in their search for the most probable lag between a cold wave and a response in mortality. Such searching for a lag makes a type II error more probable (that is, detection of discrepancies there where they don't actually exist). Selection procedure for heat waves is much stricter as only short lags with their duration being up to 5 days were included into the model

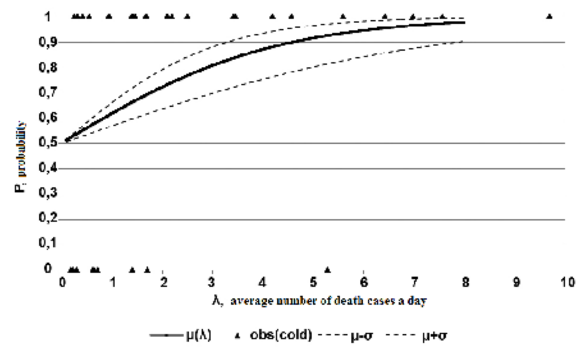

Figure 2. Probability of obtaining significant results in assessing cold waves risks

Conclusions. We recommend to apply percentiles of long-term distributions of average daily air temperatures as temperature thresholds for temperature waves identification. Such thresholds correspond to extreme temperature concepts (for this or that area) and give comparable results on expected number of waves in different climatic zones. Poisson's generalized linear model for daily mortality is the most widely spread technique applied to calculate risks caused by adverse environmental factors. We recommend to allow for an apparent dependence of mortality on time and air contamination in the regression model. One can allow for meteorological factors influencing heat balance (air humidity and wind speed) either by including them into the model explicitly or by bioclimatic indexes application; research in the sphere is going on at present. When calculating risks, it is necessary to allow for time lags between extreme temperatures waves and responses in mortality. When research is conducted in smaller cities and incorporates statistical data on daily mortality for periods equal to about 10 years, it is usually impossible to obtain authentic assessments of temperature waves risks when population is less than 200 thousand. In this work such a result was obtained for heat waves; however, it is most likely that it will be the case with cold waves as well.

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