Dynamic Modeling in Health Research as a framework for developing statistical applications free of misuse of statistics

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Abstract

We introduce a novel framework for developing statistical applications in health research, based on dynamic modeling of the investigated processes. We formulate the principles of dynamic modeling in health research, which are coherent to those in other fields of research. Dynamic models explicitly describe causal relations which are to be adequately accounted in statistical methods, making them free of misuse of statistics and statistical fallacy.

We propose the Dynamic Model of Population Health describing temporal changes in health indicators, having nature of state variables. The Dynamic Regression Method was developed as statistical method for the identification of the model. This method evaluates cohort trends for state variables at each age and calendar year. The method is illustrated by evaluating cohort trends for the Body Mass Index for men, using survey data collected in the years 1982, 1987, 1992, in North Karelia, Finland.

Key words: Cohort trends; Dynamic Model of Population; Dynamic Regression Method; Principles of Dynamic Modeling; Secular trends; State Variables.

1 Introduction.

Misuse of statistics and statistical fallacy are issues of concern in many fields, including medical research. The detailed classification of misuse and recommendations of how to avoid statistical fallacy could be found in books (Jaffe and Spirer, 1987), (Campbell, 1974). One category of misuse, "lack of knowledge on subject matter" (Jaffe and Spirer, 1987), could well be interpreted as addressing causality among other things.

Recently, it was acknowledged that a large proportion of published medical research contains statistical errors and shortcomings . "The problem is a serious one, as the inappropriate use of statistical analysis may lead to incorrect conclusions, artificial research results and a waste of valuable resources" (Strasak et al., 2007). Interestingly, the authors believe that one of the reason for misuse is lack of statistical literacy: "Medical researchers have to be encouraged to learn more about statistics, as various studies point to a lack of statistical knowledge among medical residents" and "statisticians should be involved early in study design"

In disagreement with this, we consider the case of statistical misuse, which occurs when a formally correct statistical method is used, however, causality is missing. These are the methods of evaluating secular trends in health indicators using data from a set of independent cross-sectional surveys (review on these methods is presented in section 2). The linear secular trends are also used as a tool for interecensal estimates of population size (review of this could be found in (Moltchanov et al., 1999). We use term "secular trends" to refer to all these methods.

Formally, methods evaluating secular trends look correct: data, linear model and assumptions on data properties, in combination lead to evaluation of the model's parameters and testing hypotheses. In this schema, the wrong element is assumptions on data, usually suggesting smooth-line type of dependency of estimated means.

Note that Hill's criteria for causation (see, for example, http://en.wikipedia.org/wiki/Bradford-Hill_criteria), though sound reasonable, provide only circumstantial evidence for causality, and leave plenty of room for subjective judgments.

To our view, the data on population size shown on Figure 1 provide a very strong evidence that secular trends do not exist in nature. Rather there are smooth evolution of population size along birth cohort. However, some of the statisticians and field researcher may disagree with this statement.

To address properly and unambiguously causality in a real world process, first of all, knowledge and skill on dynamic modeling should be applied. Only at the next stage, statistical tools are to be considered to evaluate parameters of the dynamic model.

Our practical task (target task) is to evaluate temporal changes in health on population level, using data from a set of independent cross-sectional population surveys. Traditionally, this task is approached by evaluating secular trends, which appeared to be a statistical fallacy. To build up an alternative approach, we develop Dynamic Model of Population Health (DMPH) and statistical method for its identification, the Dynamic Regression Method(DRM), producing time trends for health-related indicators within birth cohorts (Cohort trends, or C-trends for short).

In turn, to build up a dynamic model, first we derive some principles, which we call the Principles of Dynamic Modeling in Health Research. These Principles are independent of the target task, so they could be applied to any other task, for example, to follow-up analysis with end-points.

The aims of this paper are as follows:

- to derive the Principles of Dynamic Modeling In Health Research
- to develop the Dynamic Model of Population Health
- to build up the Dynamic Regression Method and algorithm
- to run the illustrative analysis

Note that each of the four parts above is worth of more detailed, separate presentation.

Therefore, the challenge was to provide concise and logically completed descriptions of all parts, clearly outlining logical interrelations between them.

The earlier version of the Dynamic Regression Method was developed and presented by (Moltchanov and Mik'halskii, 2008), where C - trends were suggested as an alternative to circular trends, used so far. Historically, the method developed in MONICA for checking consistency of the reported demographic data ((Moltchanov et al., 1999)) served as the prototype for the method developed by (Moltchanov and Mik'halskii, 2008). Some general aspects, such as criteria for commonly used health indicators to serve as system State Variables, have been considered earlier by (Moltchanov, 1993).

Section 2 contains historical review of time-trend analysis. Section 3 presents history and key properties of Dynamic Modeling. Section 4 describes Dynamic Model paradigm being applied to health research on Individual and Population Level. In Section 5 we present the analytical model for the case of continuous, normally distributed one parameter. The example of application, employing the data of real study, is given in section 6. Section 7 contains conclusion and discussion.

2 History of Time-Trend Analysis in Health Research

Time-trend analysis of health indicators has been widely used so far in health research. One motivation for this comes from the fact that running a cross-sectional survey is the cost-effective way to collect the data for such an analysis (Mann, 2003).

So far, this problem has been approached by assessing trends over time for means and other statistics (for example, percentiles) of the age-specific distributions of parameters of interest, such as traditional risk factor indicators (for example, systolic and diastolic blood pressure, cholesterol, body mass index), and their categorical derivatives (such as prevalence of high blood pressure, prevalence of high cholesterol, prevalence of obesity).

Various terms are used in literature for such trends: "trends", "secular trends", "time trends". Here we will use the term "secular trends" for all of them.

Among approaches used for trend analysis, the first one, "trends by linear regression", was the key element of the analysis in the WHO MONICA Project (Tunstall-Pedoe et al., 2003). Its steps include, first, calculating the age-group specific trends using linear regression, then, aggregation using direct age standardization with fixed weights. This method has been applied to risk factors only (Dobson et al., 1998a; Dobson et al., 1998b), or to both, risk factors and rates (Kuulasmaa et al., 2000). In the last case, the aggregated trends were subject to correlation analysis in order to test MONICA hypotheses. Some indication of problems in this approach come when the time plots of the age-group and survey-specific mean values of data items exhibit clear non-linearity of time plots and diversity of these plots over age groups (see, for example, (Tolonen et al., 2000), POL-TARa, BMI).

A different modification uses the multiple logistic regression procedure applied to the whole set of data (Gregg et al., 2005). As a result, the marginal characteristics were obtained directly from the procedure. This is equivalent to direct standardization, with weights corresponding to the analyzed population.

In examples above the method was applied to the samples having wide age range (40 years and more) while spans between consecutive surveys were 3-10 years. Some studies of adolescents deal with samples of age range 5-8 years, being sampled every year or every other year. In that case, the trends were first examined visually by age , since, as it was acknowledged, "they exhibit a wide diversity of age-specific patterns" (Kautiainen et al., 2002; Chen et al., 2003).

One commonly used approach to cope with such a diversity subdivides the overall time period into several segments and the overall age range into several age categories, for which the corresponding plots suggest linear trends. Alternatively, trends are evaluated for aggregated (age-standardized) parameters (Kautiainen et al., 2002).

Summing up, we may conclude that methods used so far for the analysis of the changes of health-related indicators, though being the best available ones at that time, suffered from one principal drawback: lack of causality. In turn, this is due to the fact that comparison is made between different entities, or, in terms of Dynamic Model, between different objects (see section 3).

3 Dynamic Modeling: History and Inventory of General Principles

In order to apply adequately the dynamic model paradigm to population health, we have to summarize the key notions and principles of this paradigm. We will start our inventory with the Newton's second law, which historically is the very first dynamic model. We will end up this section with formulation of the main principles of Dynamic Modeling in form of definitions, labeled **P1 - P4**.

3.1 Newton's Second Law of Motion

The following stuff is quoting from the English translation by Motte (Newton and Motte., 1995) of the Isaac Newton's formulation in Latin in Principia, 1687.

"Law II (in English): The alteration of motion is ever proportional to the motive force impress'd; and is made in the direction of the right line in which that force is impress'd."

We would like to use the structure of the above law's formulation as golden standard for general definition. In this view, the following comments are essential.

- The above law was expressed verbally. The mathematical expression for it, for example in modern form
$$m\frac{d\mathbf{v}}{dt} = \mathbf{F} \tag{1}$$
is not fully equivalent to the original verbal form, since it does not specify what is cause and what is effect.
- The law is not a kind of assumption to be used later in calculation, rather this is property of real world, derived by Newton from observation and logical inference.
- The law postulates causality clearly: the cause is (motive) force, while the effect produced by this cause is the alteration of motion.

3.2 Definition of Dynamic Model in General Case

Mathematical forms of dynamic models, often being considered as a complex of several interlinked dynamic models, are subject to special mathematical discipline - theory of dynamic (dynamical)systems (see, for example, (Luenberger, 1979)). It is important to stress, that our prime interest is in dynamic models, not in dynamic systems.

Usually, there were no problems in application of dynamic models in engineering and economy, as well as in interpretations of the results obtained. The need for re-inventory of the notion of dynamic model, has been encountered, however, when applying it in biology.

The following definition was given by (Ellner and Guckenheimer, 2006) : "Dynamic models are simplified representations of some real-world entity, in equations or computer code. They are intended to mimic some essential features of the study system while leaving out inessentials. The models are called dynamic because they describe how system properties change over time."

We formulate the following definition:

P1: Definition of Dynamic Models: Dynamic models are simplified representations of process of change (over time) of some real-world entity, in verbal and mathematical form. They are intended to mimic some essential features of the study object in process of change, while leaving out inessentials. The models are called dynamic because they describe changes of object properties over time, cased by driving forces. (from Greek dynamikos "powerful", dynamis "power") ;

Thus, dynamic model operates with object, characterized by set of properties, and Driving Force, acting at object and causing changes of the object's essential properties.

Definition **P1** differs from one cited above in the following elements:

- **P1** defines that dynamic model represents process of change of real-world entity, rather than real-world entity itself.
- In **P1** "computer code" is excluded, since computer code may be an image of any process, possibly violating physical laws. While we are concerned with exploration of real world.
- The models are "dynamic" not at all because of properties are changing. Rather because of the cause is postulated, generating these changes, - Driving Force.

P2: Definition of Object: The real-world object is physical entity, traceable in time, which means that it could be observed over some time interval, possibly small enough, being virtually the same in common sense, and carrying the set of properties.

P3: Definition of State Variables: An object is associated with a set of potentially measurable characteristics - State Variables. These characteristics are assumed to be essential properties of the object. For each such variable, the rate of change is proportional to the variable-specific net driving force, acting upon the object. Hence - State Variables are continuous and right-differentiable function of time.

P4: Definition of Controls: The model (1) could be extended by adding position vector and written in "Dynamic Systems" format:

$$\frac{d\mathbf{x_1}}{dt} = \mathbf{x_2}, \quad \frac{d\mathbf{x_2}}{dt} = \frac{1}{m}\mathbf{u(t)}, \tag{2}$$

where $\mathbf{x_1}$ is position vector, $\mathbf{x_2}$ - velocity vector, $u(t)$ - represents driving force F , underlying the fact, that it could be non-continuous function of time.

Note that in (2) Driving Force for State Variable vector $\mathbf{x_1}$ is State Variable vector $\mathbf{x_2}$, thus being continuous, while Driving Force for State Variable vector $\mathbf{x_2}$ is external force defined by (vector) function $\mathbf{u(t)}$. We will use term "Controls" to call such an external Driving Forces.

For a body moving in gravitational field of a planet, State Variables position and velocity "predict" further behavior of this object, such as ability to "escape" the gravity of the planet without additional propulsion. In this respect State Variables differ from controls: the last ones modify State Variables rates of change, however they can not serve as predictors.

Using dot notation for differentiation and combining vectors $\mathbf{x_1}$ and $\mathbf{x_2}$ into common vector $\mathbf{x}$, equations (2) could be rewritten as:

$$\dot{\mathbf{x}} = \mathcal{F}(\mathbf{x}, \mathbf{u(t)}) \tag{3}$$

In verbal form, it postulates that rate of change of State Variables is a function of State Variables and controls.

For any real-world object, a dynamic model is built-up to facilitate the following three main practical tasks pertaining to this object:

Task1: Analysis: Ultimately, design of function $\mathcal{F}$ is made by a researcher, dealing with a real-word object and its dynamics, depending on his/her intuition, experience and skill. The known prototypes play also important role. After design is made, the functional form is known up to a set of still unknown parameters. The simplest case is linear form with coefficients to be set up. To evaluate these parameters, the measurements on State Variables and controls should be used, collected during some time period. We will use term "Analysis" for this task.

Task2: Prognosis: If function $\mathcal{F}$ is identified and State Variables are known for a moment t_0 and functions $\mathbf{u(t)}$ are defined on interval $[t_o, T]$ then State Variables could be calculated for this interval, thus making prognosis of future behavior of the object.

Task3: Control: If criteria are set up, identifying the favorable future behavior of the object, and options are given for possible choice of controls as functions of time, then the task of control is to find out such a functions that optimize the given criteria.

4 Dynamic Modeling in Health Research

4.1 Health Research, Individual Level

In the following example we consider a human-being whose weight change over time is subject of some study. Let $\mathbf{x(t)}$ be a weight of the subject measured in standard way at moment t. Due to measurements error it has a nature of random variable. In addition, the theoretical plot of this function over time will expose daily cycles, which are not of the study primary interest. Rather we would like to operate with some smoothed characteristics of weight. We assume that according to study protocol, weight is measured every day at the same time in the morning, after "emptying body tanks" before eating. So, we may think of sequence of measurement time moments t_i, where i is sequence number of day since the beginning of the study.

We introduce function $v(t)$ defined as follows:

$$\begin{aligned} v(t_i) &= E(x(t_i)), \quad t = t_i, \\ v(t) &= v(t_i) + (v(t_{i+1}) - v(t_i)) \cdot \frac{t - t_i}{t_{i+1} - t_i}, \quad t_i \le t \le t_{i+1} \end{aligned} \tag{4}$$

This function satisfies all the requirements for the State Variable: it is continuous and right-differentiable function of time. The current knowledge on weight changes in adults could be summarized as follows. Weight change in adult is, in fact, change in amount of body fat, which is determined by balance of calories taken with meal and burned throughout the body activity in over a certain time period. Thus, we can introduce function $u(t)$ representing daily balance of calories, expressed in weight units (see, for example, http://www.weightlossforall.com/calories-per-pound.htm "One pound of body fat equals roughly 3,500 calories."). This function plays role of control for $v(t)$ and we may postulate simple model for weight change:

$$\dot{v} = u(t) \tag{5}$$

We consider a hypothetical study testing some technique for weight reduction (it may include education, dietary recommendation, advice on physical activity etc.). Assume that measurements of weight are available before and after the beginning of intervention, moment t_0.

To highlight principal conceptual aspects, we make the following additional simplifying assumption: $u(t) = u_1$, if $t \le t_0$, $u(t) = u_2$, if $t > t_0$, where u_1, u_2 are scalars. In practice, estimates for u_1 and u_2 could be obtained as slopes in linear regression models applied to measurements $x(t)$ for $t \le t_0$ and $t > t_0$ correspondingly.

Condition $u_2 > u_1$ indicates that tested technique is better than previous one (in practice, value α could be added having sense of "practical significance", so that condition will look like $u_2 > u_1 + \alpha$). Note, that "success" is derived from comparison of time trends for weight, not from the fact of decreasing weight for $t > t_0$. Theoretically, positive u_2 may indicate success, if the weight growth has diminished, and negative u_2 is not a success, if u_1 also was negative and approximately the same in value.

It is convenient to call all the data items, available in the study database and pertaining to a subject at certain moment of time, measurements.

In dynamic model view, most of the measurements fall into three categories:

1: State Variables: for example, age, weight, height, schooling years. Recall, that measurements for State Variables are not State Variables. They refer to each other as $x(t)$ and $v(t)$ in the described above example.

2: Modifiers: for example, smoking status (smoking now, ex-smoker, or never-smoker), current physical activity, current dietary habits (including 24 hours food consumption recall)

3: Class indicators: for example, sex, race, community, other characteristics, which are categorical and believed to be constant during the study time span.

Outside of the above categories are multi-item outcomes of different questionnaires and tests. Some of them could result in one summary item (for example, current physical activity level, which then could be classified as control). Questionnaire on smoking history may result in total amount of tobacco smoked so far. This indicator has a nature of State Variable. We leave further consideration of this issue for future publications.

Similar to models in mechanics, Modifiers in health research modify status of body in terms of State Variables, however they can not serve as predictors, for example, as predictor of instantaneous failure. Thus, current Hazard can not depend, for example, on smoking or physical activity. This simple rule of dynamic model philosophy is widely violated in practice of methods used so far in health research.

Observe that continuous function of any number of State Variables is itself a State Variable, and the same function applied to the measurements of corresponding variables serve as measurement for resulting variable. The expression (5) remains valid for this variable after control $u(t)$ is properly scaled.

In our future example we will deal with such a variable, The Body Mass Index, defined as

$$BMI = \frac{weight(kg)}{height(m)^2} \tag{6}$$

Here we pay tribute to tradition, using term weight instead of scholastically more correct term "mass".

4.2 Dynamic Model of Population: Heuristic Approach

We may think of population as a collection of subjects identified for each calendar date by a certain rule. For example, for population of an urban district such a rule may identify all permanent citizens having home address within unambiguously defined administrative boundaries. The rule must be the same throughout the calendar period for which the population is supposed to be analyzed.

Health-related and other population characteristics, if available, has a form of age-distributed profiles, specific for calendar years, rather than individual-specific measurements for all current subjects of population.

Measurements on population level are performed for random samples (stratified or not), taken, for example, every 5 year.

Thus, the challenge is how to adopt for population level the dynamic model paradigm described so far for individual level.

To describe population history, it is convenient to use plane (y, a), where y is real-valued calendar time in years, vertical axis, a is real-valued age in years, horizontal axis. Such a set up for axes anticipates further use of matrices with indexes y, a, when the first index is row number (vertical coordinate). For consistent setup, we have to specify an observational frame in terms of ranges $[y_{min}, y_{max}]$ for y and $[a_{min}, a_{max}]$ for a.

Each subject may enter this population due to birth (if $a_{min} = 0$), or crossing left-low boundaries, or migration in. Each subject may leave this population due to death, migration out or crossing the right-upper boundaries. If a subject with coordinates (y_0, a_0) is within the population during time t , at that time it has coordinates $(y_0 + t, a_0 + t)$. Thus we may say, it is moving along cohort line.

Consider all subjects having coordinates on half-open interval $((y_0, a_0 - \Delta a), (y_0, a_0)]$ at time $t = 0$. At time Δt all those left in population will arrive at $((y_0 + \Delta t, a_0 - \Delta a + \Delta t), (y_0 + \Delta t - \Delta a, a_0 + \Delta t]$. In other words, the birth cohort of width Δa moves from (y_0, a_0) to $(y_0 + \Delta t, a_0 + \Delta t)$. We may think of such a cohort as of a container moving on plane (y, a). The contents of each container in process of movement is changed due to migration and death. If the rate of contents update is negligible (say, less than 1% per year), we may ignore it in our analysis. If not, the analysis has to take this into account.

Each container fits the definition of the dynamic model object, if we regard the corresponding State Variable as mean of State Variables for currently available subjects. The dynamic equation then could be obtained from ones for each subject, having form (5), by taking means of both sides:

$$\dot{\overline{v}} = \overline{u}(t) \tag{7}$$

Since the whole selected observational frame could be covered by collection of non-overlapping cohorts of selected width, we may conclude that, in case of population, the overall dynamic model is a collection of dynamic models specific for each cohort.

4.3 Dynamic Model of Population: Axiomatic Setup

The theoretical abstraction for birth cohort is one of infinitesimal age range, characterized by multidimensional distribution of the parameters of interest, not by physical subjects.

Let $\mathcal{C}$ be a 2-dimensional real compact:

$$\mathcal{C} = \{(y, a) : y \in [y_{min}, y_{max}], a \in [a_{min}, a_{max}]\},$$

where y is calendar time in years and a is age in years.

Consider a population defined on this compact, which suggests that there potentially exists a set of random variables (r.v.) X_i, $i = 1...k$ representing the corresponding set of measurable indicators of interest (State Variables) defined at each point (y, a) of compact $\mathcal{C}$. In this paper we restrict ourselves to the case of one indicator, so that subscript of X will be omitted. To make the following description more illustrative let us keep in mind the Body Mass Index (BMI) as an example of the indicator in question.

We introduce the following notation

$$v(y, a) = E(X(y, a)).$$

For the sake of simplicity while describing the core dynamic model, we assume,

$$X(y,a) = v(y,a) + \epsilon, \text{where } \mathrm{E}(\epsilon) = 0,\ \mathrm{D}(\epsilon) = \sigma^2,\ \forall(\mathrm{y,a}) : (\mathrm{y,a}) \in \mathcal{C} \tag{8}$$

The dynamic equations describe changes of the distribution of r.v. X for a birth cohort taken at point (y,a) over time interval dt:

$$v(y + \mathrm{d}t, a + \mathrm{d}t) = v(y,a) + u(y,a)\mathrm{d}t + o(\mathrm{d}t), \text{where } \frac{\mathrm{o(dt)}}{\mathrm{dt}} \ \rightarrow\ 0, \text{as dt } \rightarrow\ 0. \tag{9}$$

On one hand, function $u(y,a)$ represents the rate and direction of change of the State Variable due to the driving force generated by the environment. On the other hand, it is the driving force (control) itself, properly scaled.

The driving force at (y,a) does not depend on the properties of the cohort passing at the time y the age a. Moreover, theoretically, the very fact of its existence doesn't depend on whether or not there is a non-empty cohort passing at the time y the age a.

For the sake of convenience we will use terms "Mean levels" or "levels" for the values of function $v(y,a)$, and "cohort trends" or "C-trends" for the values of function $u(y,a)$.

In the advanced model the function $u(y,a)$ represents sum of the environmental force and the force due to current state of the cohort. This will lead to replacement of $u(y,a)$ in (9) by $u(y,a) + bv(y,a)$, where b is a model parameter.

Let $v_0(y,a)$ be the value of $v(y,a)$ at low-left boundary of the compact $\mathcal{C}$ for a (birth) cohort crossing the point (y,a):

$$v_0(y,a) = v(y-\delta, a-\delta), \qquad \text{where } \delta = \min(\mathrm{y} - \mathrm{y_{min}}, \mathrm{a} - \mathrm{a_{min}}). \tag{10}$$

Then $v(y,a)$ can be expressed as

$$v(y,a) = v_0(y,a) + \int_0^\delta u(y-t, a-t)\mathrm{d}t$$

Thus, if the values of $v_0(y,a)$ at low-left boundary and $u(y,a)$ on $\mathcal{C}$ are known, then the function $v(y,a)$ could be evaluated for each point on $\mathcal{C}$.

The generalization of the model (8), (9) for the case of multidimensional distribution and state-dependent dynamics is straightforward, by treating functions $v(y,a)$ and $u(y,a)$ as vector functions, by replacing $D(\epsilon) = \sigma^2$ in (8) by $Cov(\epsilon) = \Sigma$ and by replacement of $u(y,a)$ in (9) by $u(y,a) + bv(y,a)$, treating b as a matrix.

5 Dynamic Model of Population: Analytical Form

5.1 General Formulation of the Task

Suppose that a set of measurements is available (x_k, y_k, a_k), $k = 1, \ldots, K$, for subjects selected in a set of the independent cross-sectional surveys. We assume that for each survey the stratified by gender and age group random sample scheme was used. The age group stratification could be different in different surveys, however, for standard case, we assume that overall age range is the same in all surveys.

The general formulation of the task is to estimate the functions $v_0(y,a)$ and $u(y,a)$ on $\mathcal{C}$, using the available measurements (x_k, y_k, a_k), $k = 1, \ldots, K$.

To solve this problem one option would be to formulate the optimization problem in functional space: to minimize the functional I:

$$I(u, v_0) = \left(\sum \left(x_k - v(y_k, a_k) \right) \right)^2, \quad (11)$$

applying some additional requirements on functions $u(.,.)$ and $v_0(.,.)$, such as continuity (piece-wise continuity), and /or restricted variation.

However, it seems more convenient to transform the above problem into the discrete - scale analogue and to take the advantage of the simplicity of the analysis and adaptation of the numerical methods available in the standard statistical packages.

5.2 Discrete-Scale Model

Let i and j be an integer value of time in years and an integer value of age in years correspondingly. Our intention is to build up the integer-values proxies of the equations (8 - 11).

Let $P(i, j)$ be a parallelogram-shaped element (convex hull) defined by its angle points:

$$\{(i, j-1),\ (i, j),\ (i+1, j+1),\ (i+1, j)\}$$

excluding its left and upper boundaries, which could be written as

$$P(i, j) \doteq \{(a, y) : y \in [i, i+1),\ a \in ((j-1) + (y-i),\ j + (y-i)]\} \quad (12)$$

We impose for function $u(.,.)$ the conditions of being constant on each $P(i, j)$ and for functions $v(.,.)$ being constant on a and linear on y with constant slope $u(i, j)$.

Formally this could be expressed as follows:

$$u(y, a) = u(i, j),\ \forall i, j, y, a :\ (y, a) \in P(i, j) \quad (13)$$

$$v(y, a) = u(i, j) \cdot (y - i) + v(i, j),\ \forall i, j, y, a :\ (y, a) \in P(i, j) \quad (14)$$

We derive minimal and maximal values for i and j from the correspondent values for y and a using definition (12):

$$\begin{array}{c} (i_{min}, j_{min}) : (y_{min}, a_{min}) \in P(i_{min}, j_{min}), \\ (i_{max}, j_{max}) : (y_{max}, a_{max}) \in P(i_{max}, j_{max}) \end{array} \quad (15)$$

For convenience, from now on we will use relative scale for age and time, defined by transformation

$$i - i_{min} \to i,\ \mathrm{j} - \mathrm{j_{min}} \to \mathrm{j}$$

Consider functions $u(i, j)$ and $v(i, j)$ defined on integer-valued two dimensional domains

$$\begin{array}{rcl} \mathcal{U} & = & \{(i, j) : i \in [0, I],\ j \in [0, J]\}, \\ \mathcal{V} & = & \{(i, j) : i \in [0, I+1],\ j \in [0, J+1]\}, \end{array} \quad (16)$$

correspondingly, where

$$I = i_{max} - i_{min},\ \mathrm{J} = \mathrm{j_{max}} - \mathrm{j_{min}}$$

Now the main dynamic equation (9) could be rewritten as

$$v(i+1, j+1) = v(i, j) + u(i, j),\ \forall (i, j) \in \mathcal{U} \quad (17)$$

Let $v_0(i,j)$ be the value of $v(.,.)$ at low-left boundary of the domain $\mathcal{V}$ corresponding to a (birth) cohort crossing the point (i,j):

$$v_0(i,j) = v(i-\delta, j-\delta), \text{where } \delta = \min(\mathrm{i},\mathrm{j}). \tag{18}$$

Combining (17) and (18), we rewrite equation (10) as:

$$v(i,j) = v_0(i,j) + \sum_{m=1}^{\delta} u(i-m, j-m) \tag{19}$$

From (19) it follows that if $v(i,j)$ is set up on the low-left boundary of $\mathcal{V}$ and $u(i,j)$ is set up on the whole $\mathcal{U}$ then $v(i,j)$ could be calculated for the whole $\mathcal{V}$.

Finally, assembling (8), 19) and (14) for each available observation (x_k, y_k, a_k), $k = 1, \dots, K$, we obtain:

$$x_k = v_0(i,j) + \sum_{m=1}^{\delta} u(i-m, j-m) + (y_k - i) \cdot u(i,j) + \epsilon_k,$$
$$\text{where } \mathrm{Var}(\epsilon_\mathrm{k}) = \sigma^2, \ \mathrm{Cov}(\epsilon_\mathrm{k}, \epsilon_\mathrm{l}) = 0, \ \text{if } \mathrm{k} \neq \mathrm{l} \tag{20}$$

Let $\mathbf{z}$ be a vector with components $v_0(i,j)$ and $u(i,j)$ ordered in the following way:

$$\begin{aligned} \mathbf{v}_0 &= \big(v(I+1,0), \dots, v(0,0), \dots, v(0,J+1)\big)^T \\ \mathbf{u} &= \big(u(0,0), \dots, u(0,J), \dots, u(I,0), \dots, u(I,J)\big)^T \\ \mathbf{z} &= \big(\mathbf{v}_0^T \ \big| \ \mathbf{u}^T\big)^T \end{aligned} \tag{21}$$

Using vector $\mathbf{z}$ and introducing vector of coefficients $\mathbf{b}_k$, we can rewrite (20) in the form

$$x_k = (\mathbf{b}_k, \mathbf{z}) + \epsilon_k, \ \text{where } \mathrm{Var}(\epsilon_\mathrm{k}) = \sigma^2, \ \mathrm{Cov}(\epsilon_\mathrm{k}, \epsilon_\mathrm{l}) = 0, \ \text{if } \mathrm{k} \neq \mathrm{l} \tag{22}$$

This form represents a particular case of Gauss-Markov Setup for the Least Squares Linear Estimation problem (Rao, 1973).

Let $\mathbf{B_0}$ be a matrix composed of row vectors $\mathbf{b}_k^T$ in (22), $\mathbf{z}$ and $\mathbf{x}_0$ stand for column vectors of the parameters z_j and the variables x_k correspondingly, and S_0 be a scalar function defined as

$$S_0(\mathbf{z}) = (\mathbf{B_0}\mathbf{z} - \mathbf{x}_0)^T (\mathbf{B_0}\mathbf{z} - \mathbf{x}_0)$$

Note that if $rank(\mathbf{B_0}) = dim(\mathbf{z})$, then estimates obtained by unconditional minimizing of function $S_0(\mathbf{z})$ are unique ones. Such a case takes place only if the observations cover all the elements $P(i,j)$ when surveys cover the whole analysis period without gaps.

In practical cases, minimizing of S_0 results in singular or ill-posed Inverse Problem, and so-called regularization techniques are needed to obtain meaningful solution estimates. Most of these techniques employ the idea of smoothing of some function having clear physical interpretation (Neumaier, 1999).

Here we suggest one such technique for smoothing.

5.3 Smoothing

We define the following indicator of smoothness of function $v(.,.)$

$$S_1(\mathbf{z}) = \sum_{i=0}^{I+1}\sum_{j=1}^{J}\Big(v(i,j-1)-2v(i,j)+v(i,j+1)\Big)^2 + \sum_{j=0}^{J+1}\sum_{i=1}^{I}\Big(v(i-1,j)-2v(i,j)+v(i+1,j)\Big)^2 \quad (23)$$

Each term in this sum represents the square for a proxy of the second derivative of function $v(.,.)$ with respect to age or with respect to calendar time at point (i,j).

Replacing $v(.,.)$ by $v_0(.,.)$ and $u(.,.)$ using (19), and the last ones by vector $\mathbf{z}$, we will transform the previous expression to the following form:

$$S_1(\mathbf{z}) = (\mathbf{B_1 z} - 0)^T(\mathbf{B_1 z} - 0) \quad (24)$$

Similarly, we define indicator of smoothness of function $u(.,.)$

$$S_2(\mathbf{z}) = \sum_{i=0}^{I}\sum_{j=1}^{J-1}\Big(u(i,j-1)-2u(i,j)+u(i,j+1)\Big)^2 + \sum_{j=0}^{J}\sum_{i=1}^{I-1}\Big(u(i-1,j)-2u(i,j)+u(i+1,j)\Big)^2$$

allowing form

$$S_2(\mathbf{z}) = (\mathbf{B_2 z} - 0)^T(\mathbf{B_2 z} - 0) \quad (25)$$

Now we can add one or both constraints $S_k(\mathbf{z}) \le \alpha_k$ with some selected $\alpha_k \ge 0$, $k = 1,2$, to the model (22). Observe that indicators S_0, S_1, S_2 are quadratic functions in finite vector space E_n with elements (vectors) $\mathbf{z}$ and $n = dim(\mathbf{z})$. The optimization problem for point estimation for our case, could be formulated as

$$\min_{\mathbf{x}\in \mathrm{E}_n} S_0(\mathbf{x}), \text{ subject to } S_k(\mathbf{x}) \le \alpha_k, \text{ with given } \alpha_k > 0,\ k = 1,2. \quad (26)$$

Let n_0 , n_1 and n_2 be numbers of rows in matrices $\mathbf{B}_0$, $\mathbf{B}_1$ and $\mathbf{B}_2$ correspondingly. Let λ_1, λ_2 be some non-negative scalars. Introducing matrices and vectors

$$\mathbf{B} = \begin{pmatrix} \mathbf{B}_0 \\ \hline \mathbf{B}_1 \\ \hline \mathbf{B}_2 \end{pmatrix}, \quad \mathbf{x} = \begin{pmatrix} \mathbf{x}_0 \\ \hline \mathbf{0} \\ \hline \mathbf{0} \end{pmatrix}, \quad \mathbf{W} = \left(\begin{array}{c|c|c} \mathbf{I}_0 & 0 & 0 \\ \hline 0 & \lambda_1 \mathbf{I}_1 & 0 \\ \hline 0 & 0 & \lambda_2 \mathbf{I}_2 \end{array}\right) \quad (27)$$

where $\mathbf{I}_0$, $\mathbf{I}_1$ and $\mathbf{I}_2$ are identity matrices of rank n_0 , n_1 and n_2 correspondingly, we can formulate the problem of least squares estimation in the following form (a modification of Gauss-Markov setup which fits form of Aitken setup (Rao, 1973)

$$\mathbf{x} = \mathbf{Bz} + \epsilon, \quad E(\epsilon) = \mathbf{0}, \quad D(\epsilon) = \sigma^2 \mathbf{W}^{-1} \quad (28)$$

for which the point estimation problem is

$$\min_{\mathbf{z}\in \mathrm{E}_n} S(\mathbf{z}), \text{ where} S(\mathbf{z}) = (\mathbf{Bz} - \mathbf{x})^T \mathbf{W} (\mathbf{Bz} - \mathbf{x}) = S_0(\mathbf{z}) + \lambda_1 S_1(\mathbf{z}) + \lambda_2 S_2(\mathbf{z}) \quad (29)$$

(Moltchanov and Mik'halskii, 2008) have shown that problems (26) and (29) are equivalent: problem (26) with given α_1, α_2 possesses the same solution as problem (29) with some λ_1, λ_2, and vice versa, or both don't possess any solution.

Since part of its components are set to zero, the data vector $\mathbf{x}$ in (27) could not be treated as a "true" data vector if the problem is considered from the classical frequentist prospective. The last one is based on retrospective evaluation of the procedure used to estimate parameters over the distribution of possible data values conditional on the true unknown values of parameters (Gelman et al., 1995), p.7. The logically consistent treatment of the problem is based on Bayesian paradigm, where statistical conclusions about unknown parameters are made in terms of probability statements, conditional on observed data. As noted in (Gelman et al., 1995), p.7, in despite this difference , it will be seen that in many simple analyses, superficially similar conclusions result from the two approaches to statistical inference. In particular, this concerns Bayesian analysis of the classical regression model: under a standard noninformative prior distribution, the Bayesian estimates and standard errors coincide with the classical results (Gelman et al., 1995), p.235. The last statement justifies use of classical formulas and numerical procedures for our "non-classical" case.

The question of primary practical importance is the existence of a unique solution for the problem (29).

The following statement is proofed in (Moltchanov and Mik'halskii, 2008):

Corollary 1 For existence of a unique solution to problem (29) it is sufficient to have 4 data points such that the corresponding points (y, a) on plane y, a satisfy condition: no any 3 of them are located on a common straight line.

5.4 Outlines of the Algorithms. Setting up the Regularization Parameters

As soon as parameters λ_1, λ_2 are given in setup (27, 28), the following could be obtained routinely: $\hat{\mathbf{z}}$ - point estimate of vector $\mathbf{z}$, covariance matrix of this estimate $Cov(\hat{\mathbf{z}})$, and $\hat{\sigma^2}$ - estimate of σ^2.

Using functions $u(i,j)$ and $v(i,j)$ defined in (16), we can create matrices
$\mathbf{V} : v_{i,j} = v(i+1, j+1)$,
$\mathbf{U} : u_{i,j} = u(i+1, j+1)$,
and vectors
$\mathbf{v} = (Shape(\mathbf{V}, 1))^T$,
$\mathbf{u} = (Shape(\mathbf{U}, 1))^T$,
where Shape is matrix function reshaping the original matrix into resulting one with different number of rows and columns (available, for example, in SAS/IML (SAS Institute Inc., 2004b)). In our case, results are vectors with consequently concatenated rows of the original matrices.

Each element $v_{i,j}$ of matrix $\mathbf{V}$ corresponds to element v_k of vector $\mathbf{v}$ with

$$k = (i-1) \cdot ncol(\mathbf{V}) + j, \qquad (30)$$

where ncol(.) is matrix function returning number of columns. Similar rule could be applied for linking $\mathbf{U}$ and $\mathbf{u}$.

Definition of vector $\mathbf{u}$ in (21) and expression for functions $u(i,j)$ in (19) allow to construct matrices
$\mathbf{A_{z2v}} : \quad \hat{\mathbf{v}} = \mathbf{A_{z2v}}\hat{\mathbf{z}}$, and
$\mathbf{A_{z2u}} : \quad \hat{\mathbf{u}} = \mathbf{A_{z2u}}\hat{\mathbf{z}}$.
Hence, the covariance matrices could be derived as
$Cov(\hat{\mathbf{u}}) = \mathbf{A_{z2u}} Cov(\hat{\mathbf{z}}) \mathbf{A_{z2u}}^T$,
$Cov(\hat{\mathbf{v}}) = \mathbf{A_{z2v}} Cov(\hat{\mathbf{z}}) \mathbf{A_{z2v}}^T$,
from which the corresponding matrices of Pearson's correlation coefficients $\mathbf{R_v}$ and $\mathbf{R_u}$ could be routinely produced.

Consider two consecutive level estimates $\hat{v}(i,j)$, $\hat{v}(i,j+1)$ allocated along age axe (similar consideration could be applied to allocation along calendar years.

The coefficient of correlation for these estimates could be derived from $\mathbf{R_v}$ applying rule (30). Let denote it $r_{a,i,j}$. Similarly, coefficients of correlation $r_{y,i,j}$ could be derived for estimates $\hat{v}(i,j)$, $\hat{v}(i+1,j)$ allocated along years axe.

Consider task of predicting estimate $\hat{v}(i,j+1)$ using linear predictor based on $\hat{v}(i,j)$. The expression $1-r^2_{a,i,j}$ is proportion of "unexplained" part of variance of $\hat{v}(i,j+1)$, (see, for example, (Rao, 1973) p.266). This part could be interpreted as "new information", or "signal", while $r^2_{a,i,j}$ could be regarded as proportion of "Noise". The better smoothness is associated with lower signal-to-noise ratio. We combine all local indicators of smoothness into one common vector

$$\mathbf{f_v} = Shape(\mathbf{V_{sma}},1)\|Shape(\mathbf{V_{smy}},1), \quad where \quad v_{sma,i,j} = 1-r^2_{a,i,j}, \quad v_{smy,i,j} = 1-r^2_{y,i,j} \tag{31}$$

Vector $\mathbf{f_u}$ could be defined in similar way.

For practical use we have to select function, producing sample statistics for a vector-argument, such as mean, median, minimum or a value of one predefined component and a target value for this statistics, f_{sm}. Let $fstat$ be generic name for such a function. Then iterations are run by selecting λ_1 and λ_2 until the following condition is satisfied

$$max(abs(log(fstat_v(\mathbf{f_v}))-log(f_{smv})), abs(log(fstat_u(\mathbf{f_u}))-log(f_{smu})) \leq \delta, \tag{32}$$

where δ is predefined accuracy.

With increasing values of f_{smv}, f_{smu} the corresponding lines and surfaces visually become smoother. For level estimates, for example, if $f_{smv} \to 0$, then $\lambda_1 \to \infty$, and solution converges to 4-parametric surface ((Moltchanov and Mik'halskii, 2008)).

To measure difference in C-trends over age and calendar year, the pairwise comparison tests are performed for mean values of C-trends, evaluated for a set of age-year clusters, defined by cluster sizes, Δ_a and Δ_y.

Let $\mathbf{U_c}$ be matrix of such mean values, $\mathbf{u_c}$=$Shape(\mathbf{U_c},1)^T$ and matrix $\mathbf{A_{u2uc}}$ such that $\mathbf{u_c} = \mathbf{A_{u2uc}}\hat{\mathbf{u}}$. As soon as, matrix $\mathbf{A_{u2uc}}$ is created for given Δ_a, Δ_y, $\mathbf{U_c}$ could be calculated, as well as variance/covariance values for its elements in a format of

$\mathbf{C} = Cov(\hat{\mathbf{u_c}}) = \mathbf{A_{u2uc}}Cov(\hat{\mathbf{u}})\mathbf{A_{u2uc}}^T$.

For each cluster, statistics and corresponding probabilities are computed for pairwise comparison of mean C-trends for current cluster and for adjacent one for older age group, and for current one and for adjacent one for the next calendar years period (if the corresponding clusters exist). Using classical paradigm, this is done by testing linear hypotheses in form

$\mathbf{H}_0 : u_{ci} - u_{cj} = 0$.

General expression for F-value (see for, example, SAS/Stat manual, (SAS Institute Inc., 2004c)) in this case takes a simple form

$$F = \frac{(u_{ci}-u_{cj})^2}{c_{i,i}-2c_{i,j}+c_{j,j}}$$

Corresponding probability is computed using SAS function $probF$ (see (SAS Institute Inc., 2011)) as

$Pr = 1 - probF(F, 1, n-r)$

Note, that in Bayesian view, these probabilities should be referred to as tail-area probabilities for posterior predictive distributions ((Gelman et al., 1995) , p.169).

The algorithm, implementing the above outlines, is written in SAS code using SAS products ((SAS Institute Inc., 2011), citeSAS9.2PROC, (SAS Institute Inc., 2004b), (SAS Institute Inc., 2004c)

(SAS Institute Inc., 2004a)). Results of pairwise tests are presented graphically in figure, produced by PROC GCONTOUR, properly annotated (see Figure 5 in example of application).

For reference, we will call this algorithm DRM2(R), with prefix DRM2 to differentiate it from those developed in (Moltchanov and Mik'halskii, 2008). We have built up also the modification of this algorithm, processing aggregated data, DRM2(A), thus DRM2(R) for "oRiginal" data, and DRM2(A) - for "Aggregated" data.

Original individual data may be of quite big size, which reflects row number n_0 of matrix $\mathbf{B}_0$ in (27), and hence, the required memory and time for calculation.

Aggregation is applied to original measurements (x_k, y_k, a_k), $k = 1, \ldots, K$, producing summary statistics for $(age \cdot year)$ cells with size 1. As a result, arithmetic means are produced $(\overline{x}_c, \overline{y}_c)$, number of original measurements in each cell (n_c), and S_{CSSc} -Corrected Sum of Squares, where $c = 1, \ldots, C$ - collection of non-empty cells. Matrix $\mathbf{B_0}$ and vector $\mathbf{x}_0$ in (27) should be replaced by $\overline{\mathbf{B}}_\mathbf{0}$ and $\overline{\mathbf{x}}_0$, with cell-specific rows.

Let $\mathbf{n}_0$ be a frequency vector with components (n_c). The following expressions are essential elements of the DRM2(R) algorithm.

Contribution to cross-products $B \cdot x$ and $B \cdot B$:

EXPR1: $(\overline{\mathbf{B}}_\mathbf{0}{}^T \cdot Diag(\mathbf{n}_0) \cdot \overline{\mathbf{x}}_0)$

EXPR2: $(\overline{\mathbf{B}}_\mathbf{0}{}^T \cdot Diag(\mathbf{n}_0) \cdot \overline{\mathbf{x}}_0)$

Contribution to sum of squares of error terms,

$EXPR3: \quad (\overline{\mathbf{B}}_\mathbf{0}\hat{\mathbf{z}} - \overline{\mathbf{x}}_0)^T \cdot Diag(\mathbf{n}_0) \cdot (\overline{\mathbf{B}}_\mathbf{0}\hat{\mathbf{z}} - \overline{\mathbf{x}}_0) + \sum_{c=1}^{C} S_{CSSc}$

Note, that DRM2(A) and DRM2(R) will produce identical outputs if all y_k within cells are equal.

6 Example of Application

6.1 Data

To illustrate the method and to demonstrate its performance, the data from three cross-sectional surveys, conducted in North Karelia, Finland, during the period 1982 -1992, will be used. Formally this set of data can be characterized as follows:

- Study population: North Karelia, Finland.
- Study period: 1982-1992;
- Source of data: cross sectional independent surveys conducted in years 1982, 1987, 1992
- Sampling frame for each survey: the stratified by 10-year age groups (25-34, 35-44, 45-54 and 55-64) and gender random sample.

The following specifications defines sub-sample of records and items selected for analysis.

Only data for men will be used; the number of examined men in years 1982, 1987, 1992 is equal to 1537, 1481 and 673, correspondingly.

Original measurements of interest are: gender, date of birth, date of examination, weight and height.

The analysis variables included in the model:

BMI - the Body Mass Index, defined as $weight(kg)/height(m)^2$.

AGE - age in full years, defined as year of examination minus year of birth.

YEAR - date of examination measured in years.

All surveys have started at the beginning of the year, surveys 1982 and 1987 have been completed in 4 months, survey 1992 - in three months period.

6.2 Analysis Setup

The algorithm modification DRM2(A) have been used, preprocessing original data into aggregated format. There were 120 aggregated observations, 40 for each survey year. The analysis was set up for the age range 25-64 and for the calendar year period 1982-1992. In rule, controlling iterations, (32), smoothing factors f_{smv}, f_{smu} were set to 0.2, accuracy level, δ was set to 0.05; cluster sizes, Δ_a, Δ_y, for producing comparison tests were set to 5.

We have found that for practical purposes it is enough to use one selected point, $(1,1)$ for $fstat_v$, and one selected point, $(int(ncol(\mathbf{U})/2), int(nrow(\mathbf{U})/2))$, for $fstat_u$.

6.3 Results

The results of the analysis are visualized by the set of 3-dimensional figures.

Figure 2 displays the values representing means of BMI calculated for each age and year, for which the survey data are available (number of cases in each cell exceeds 9). To visualize the along-cohort changes, the columns corresponding to the same birth cohorts in different surveys have similar shades of grey.

Figure 3 displays estimates for the mean levels of BMI for the whole domain, with study age range plus one year, and study period plus one year.

Figure 4 displays C-trends with 95% confidence intervals, shown at left and front boundaries only.

Figure 5 displays mean levels of C-trends for specified age-year clusters, with P-values for differences between clusters.

These figures illustrate the principle "one figure is better than one hundred tables", though all the underlying data are available and could be presented in a set of tables.

Figure 3 shows that mean BMI levels increase along cohort lines throughout the study period, although they are different for different birth cohort. Specific peaks and troughs follow cohort lines.

Recall that C-trends represent the net external Driving Force (Modifier) causing changes over time in cohorts. Therefore, changes in C-trends pattern over calendar years may indicate effect of preventive activities, while difference across age range may indicate both, age-specific uncontrolled changes and/or different susceptibility to prevention.

In our case, Figure 5 shows clear decrease of C-trends in the period 1987-1992 compared with the period 1982-1986 in the age range 35-40 ($p < 0.05$); No other significant differences between adjacent clusters were detected.

The further detailed analysis and final interpretation of the results may require a log of the events affecting the socio-economic and health care profiles of the study population during the study period. For example, a feasible explanation of the observed effect in C-trends in age range 35-40 could be associated with creating new working places in years 1987-1992, which have decreased population flow out of the area, taking place in years 1982-1986 in this age range and leading to negative health selection (subjects with low BMI were leaving the area in searching for job places).

Summing up, we can conclude that, in general, clustering of C-trends looks reasonable, so we can use the results of comparing C-trends levels in adjacent clusters for our analysis.

7 Conclusion and Discussion

In this paper we have presented a novel formulation of the key principles of dynamic modeling in general, and in application to health research, which justify the structure and interpretation of the core models dealing with C-trends. In particular, according to these principles, traditional risk factors' indicators fall into two categories, State Variables and Modifiers (see section 3), having different dynamical nature and, hence, playing different roles in the model and analysis.

As corollary of this, circular trends for State Variables have no sense at all. At the same time, only State Variables may determine instantaneous hazard rate of failure. In dynamic models, causality is postulated: changes are due to Driving Forces (Modifiers), existing in the real world. In case of consecutive survey data, C-trends are believed to be proxies for Driving Forces, providing the tool for three main practical tasks: analysis, prediction and control of health on population level (see section 3)

We have used these principles as a framework for developing the dynamic model of simulating the temporal changes in characteristics of a real-world object - population. In the course of this process, first, we have identified two interacting objects, population and its environment, on the top aggregation level. Further system analysis has led us to breaking down the study population into a set of potentially infinitesimally narrow birth cohorts, carrying over time health state profiles expressed in terms of health related indicators (State Variables).

The model employs the *health field* concept, suggesting existence of an influencing factors (Modifiers), generated by environment and acting on the population, specific for each calendar year and age, and causing within-cohort changes of the health indicator with rate of change corresponding to the strength of this factors.

For illustrative purposes we have selected one-parameter case with continuous, normally distributed parameter and with strength numerically equal to rate of change. While keeping model reasonably realistic, these simplifications help to highlight the key properties of the dynamic model of population health and method of its identification - the Dynamic Regression Method.

In the illustrative example, we have shown that the Dynamic Regression Method provides a sensible view on the BMI dynamics. It reveals clear difference between the levels of the parameter and its C-trends. From practical prospectives, it is C-trends, not levels, which primarily seem to be modifiable by preventive activities or involuntary changes affecting the population. It is worth noting that outcomes from the DRM analysis serve as data for the next-level analysis, involving other information and aiming at finding reasonable explanation of the observed dynamics (diagnostic property of DRM). One of the important complementary component for such an analysis is dynamics of the population size (we have developed a modification of the DRM for that type of data, this is a subject for one of the next publication). If there is significant migration "in" or "out" of the study population, the observed effects could be entirely or partially due to the population instability (health selective effect). The outcomes from the DRM analysis could be used straightforwardly for prediction of the age-specific profile of the State Variable, say, for 5 year period, by applying the C-trends at the last year of the study period to the estimates of the parameter's levels at that year. Such a projection will not cover the cohorts, not included in the study age range at the last study year.

Recall that this method has been developed as an alternative to the secular trends used so far. In this respect, it is worth noting that the model presented here is characterized by local cohort trends (C-trends), which have clear interpretation: changes in the State Variable of the same physical entity per time unit. If we will formally calculate a characteristics resembling age-specific secular trend, we will obtain a difference between two different physical entities (birth cohorts), caught occasionally at the moments of measurement. Hence, it may behave quite arbitrarily. In other words, in the view of the dynamic modeling approach, secular trends do not exist in nature. In one special case only, when all the age profiles of a State Variable are the same over calendar years (stationary case), formally calculated secular trends will be equal to zero at each age within the study age range. Only in that trivial case, secular trends possess both, predictive and diagnostic power.However, even in this case, secular trends are kind of statistical fallacy, since missing causality.

There are certain restrictions in using the current version of DRM methods, imposed by the size of the problem, due to using matrix operations. Transfer to the Bayesian Data Analysis and using Markov chain Monte Carlo simulation methods (Gelman et al., 1995) seems to be a solution for these problems.

The simplified dynamic equation used in the current model could be modified, accounting for the fact that rate of change may depend also on the current level of the State Variable.

Finally, the most comprehensive model needs to be developed, comprising multiple State Variables, and corresponding C-trends as a linear functions of current State Variables. Such a model could be a powerful practical tool for prediction of population health for about 5 year span.

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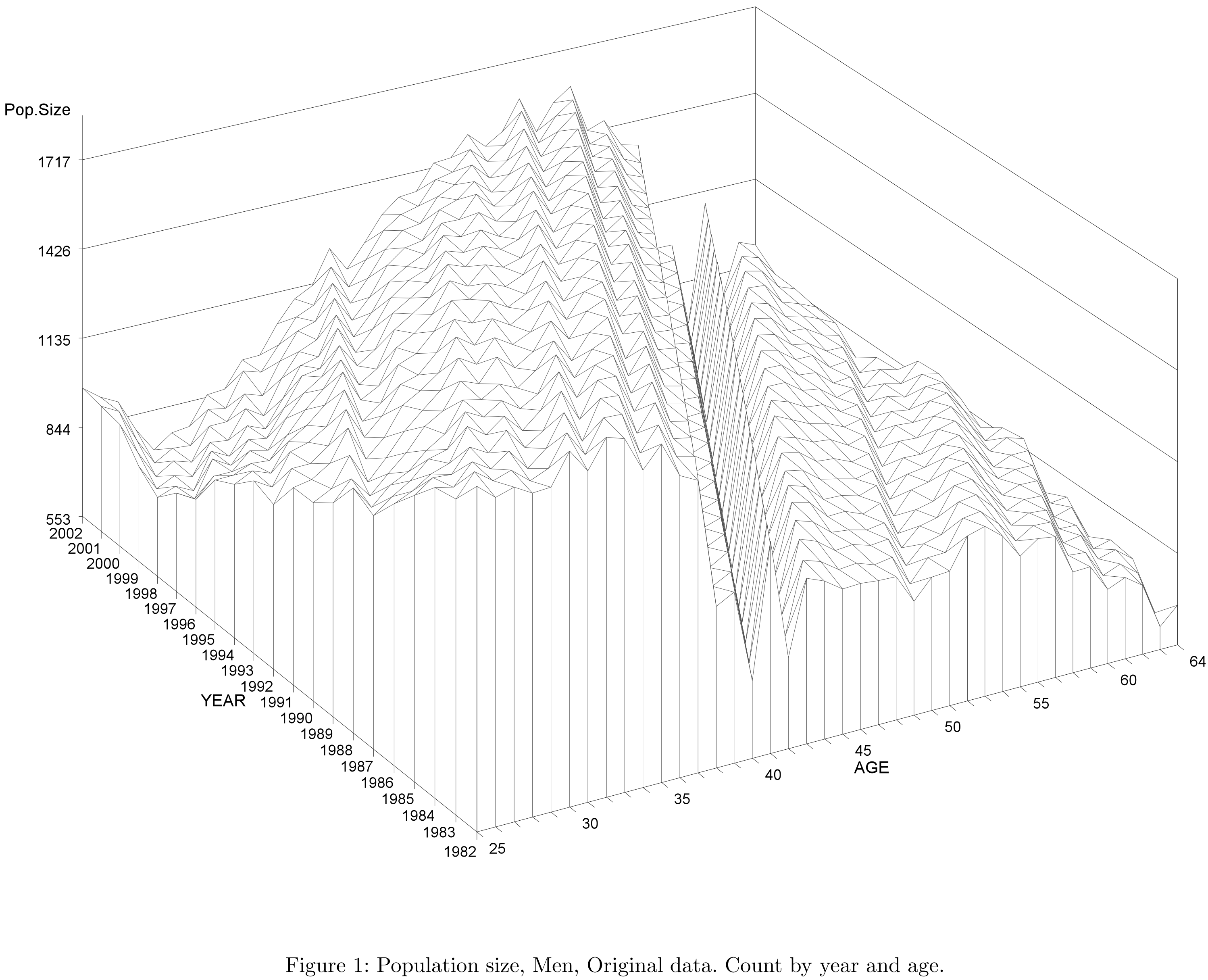

Figure 1: Population size, Men, Original data. Count by year and age.

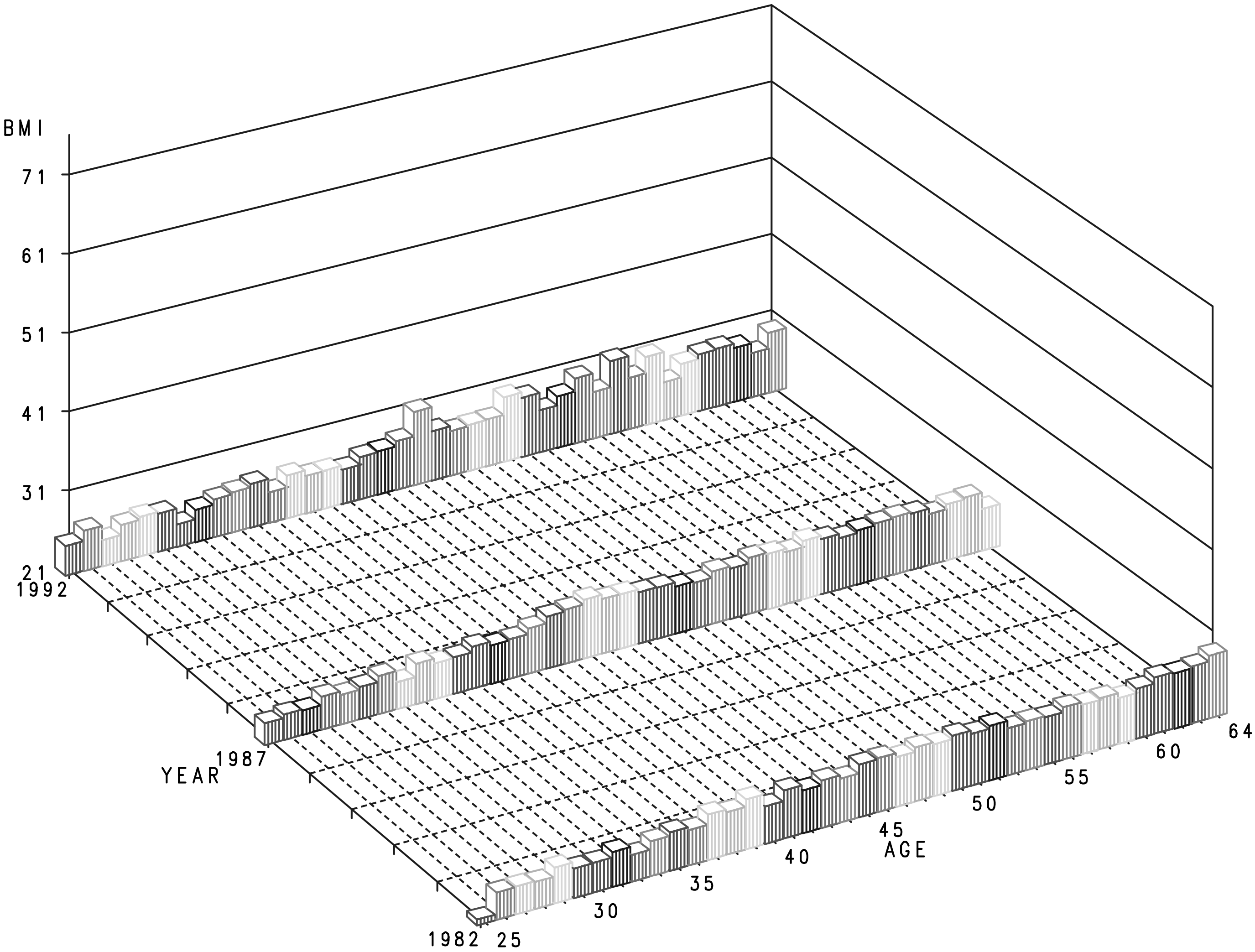

Figure 2: BMI, Men, Survey data. Means by year and age.

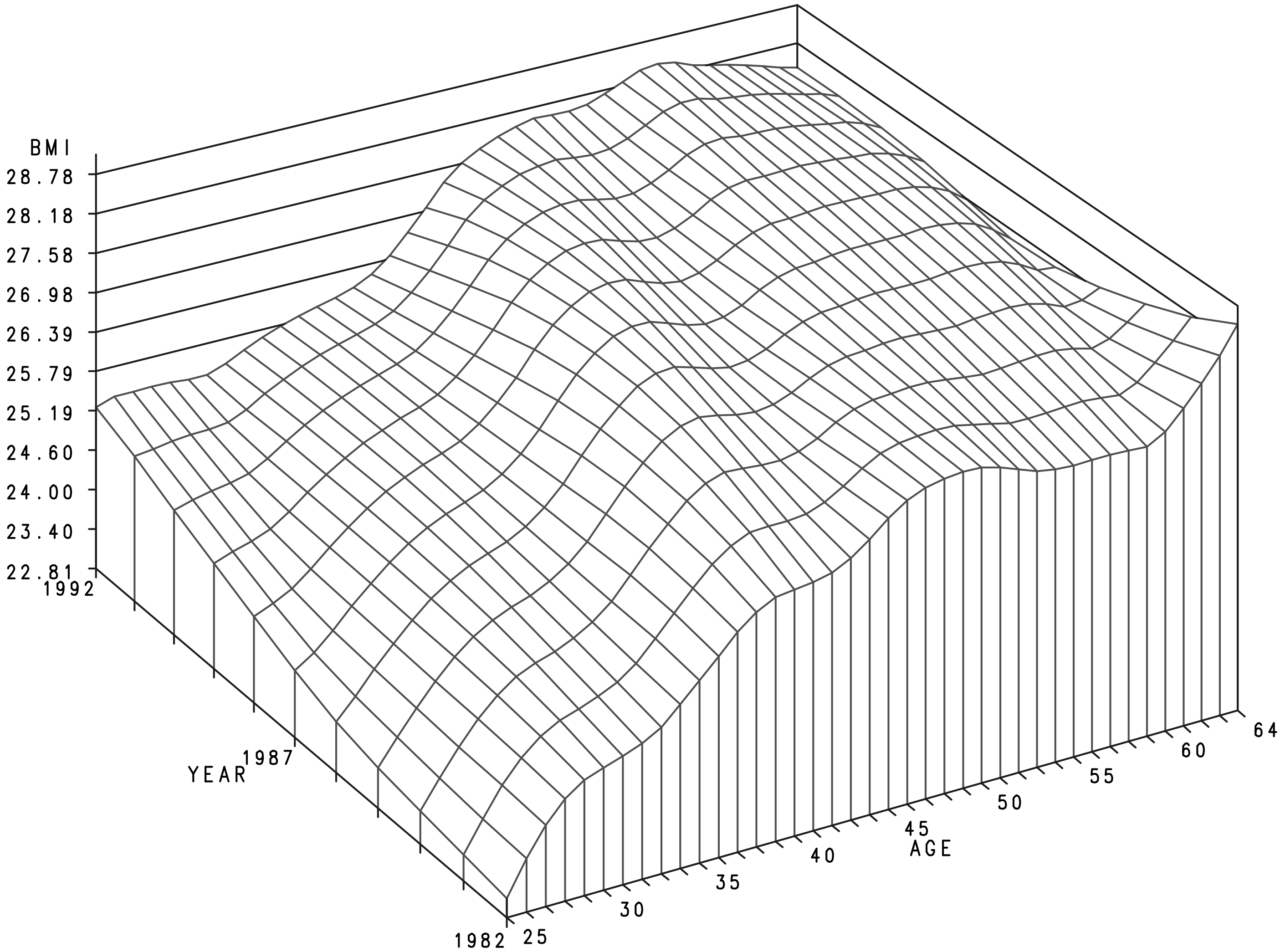

Figure 3: BMI, Men, Estimates of means by year and age.

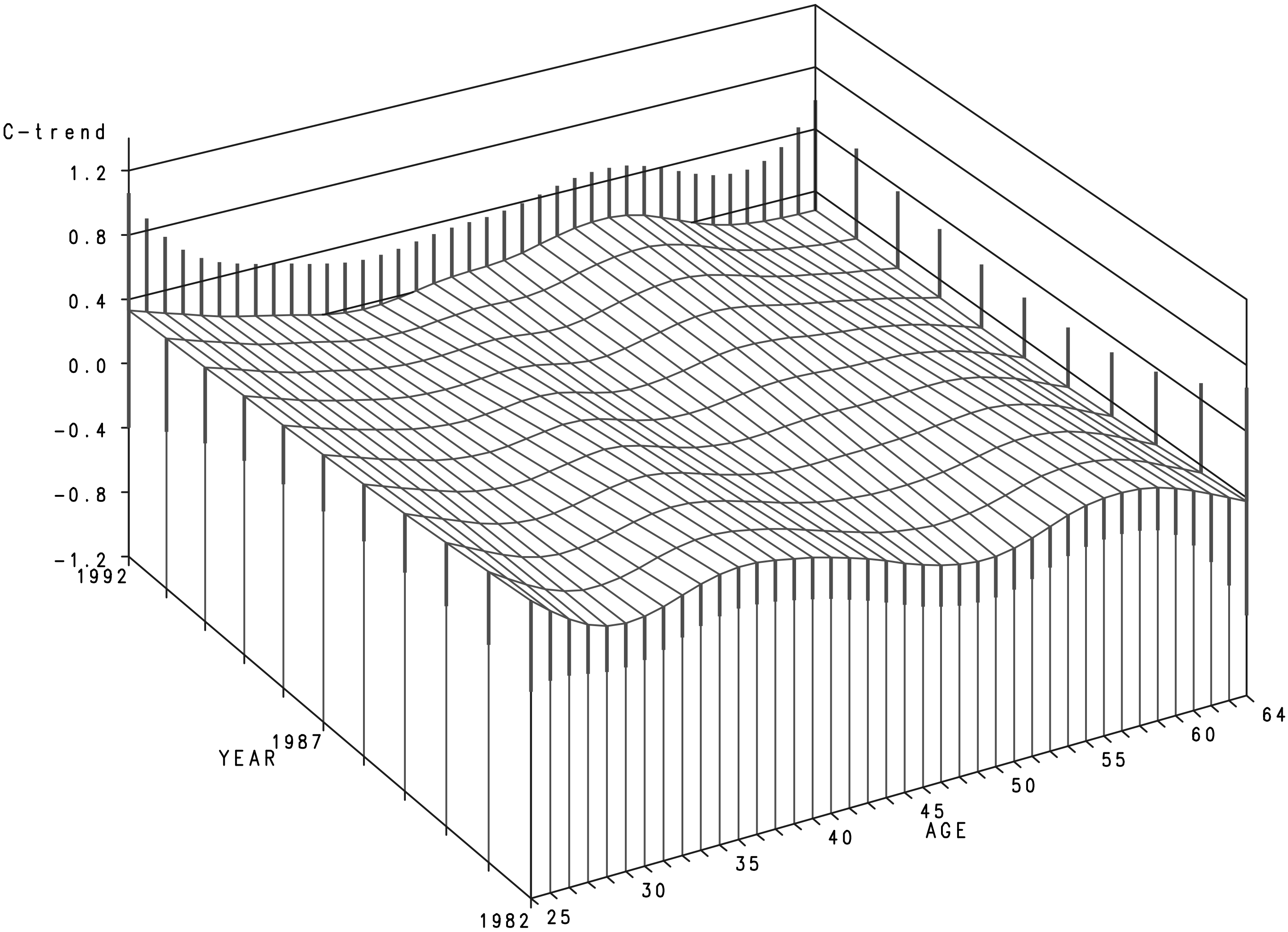

Figure 4: BMI, Men, Estimates of C-trends by year and age.

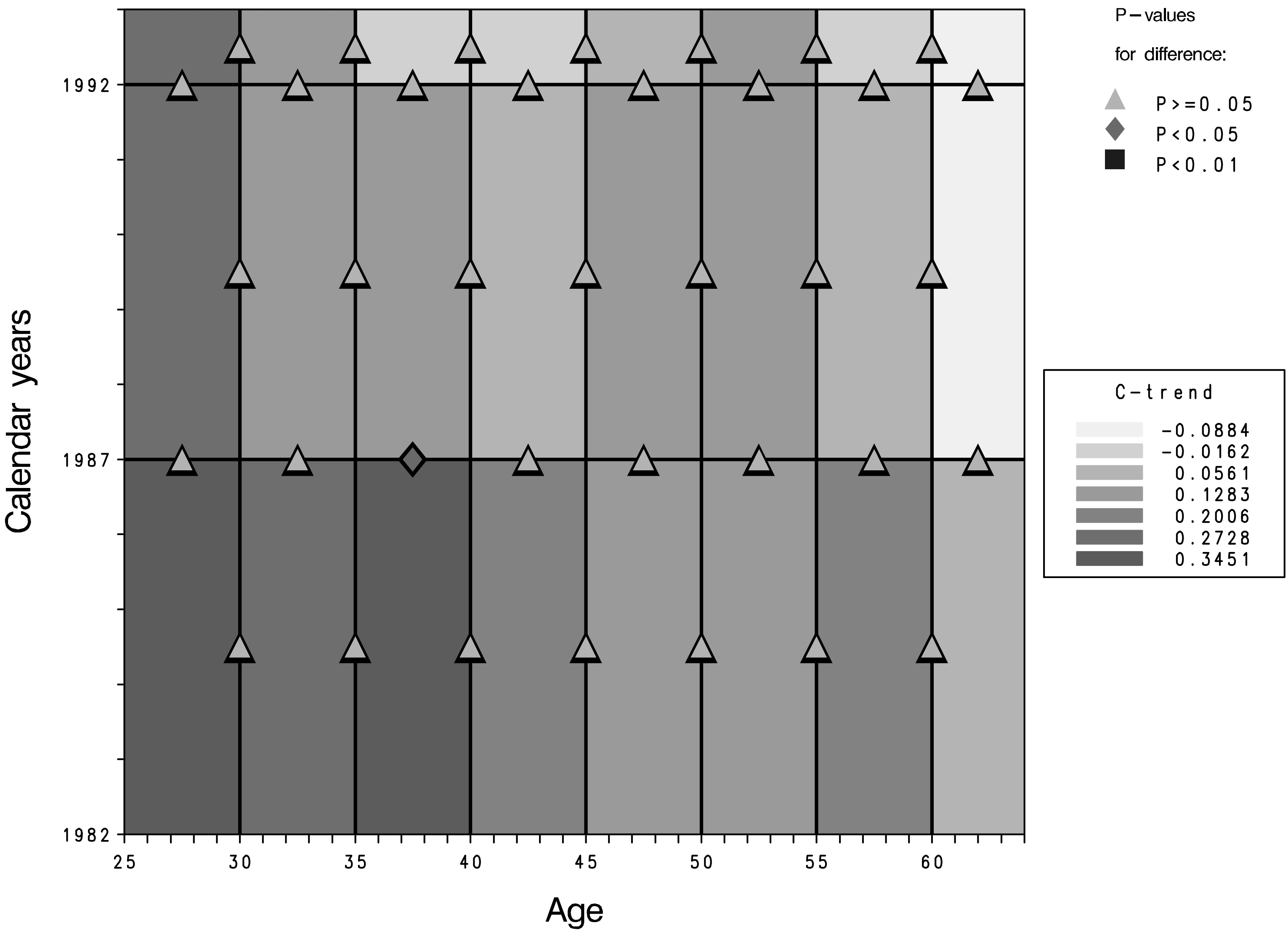

Figure 5: BMI, Comparison of C-trends by clusters of age and calendar years.