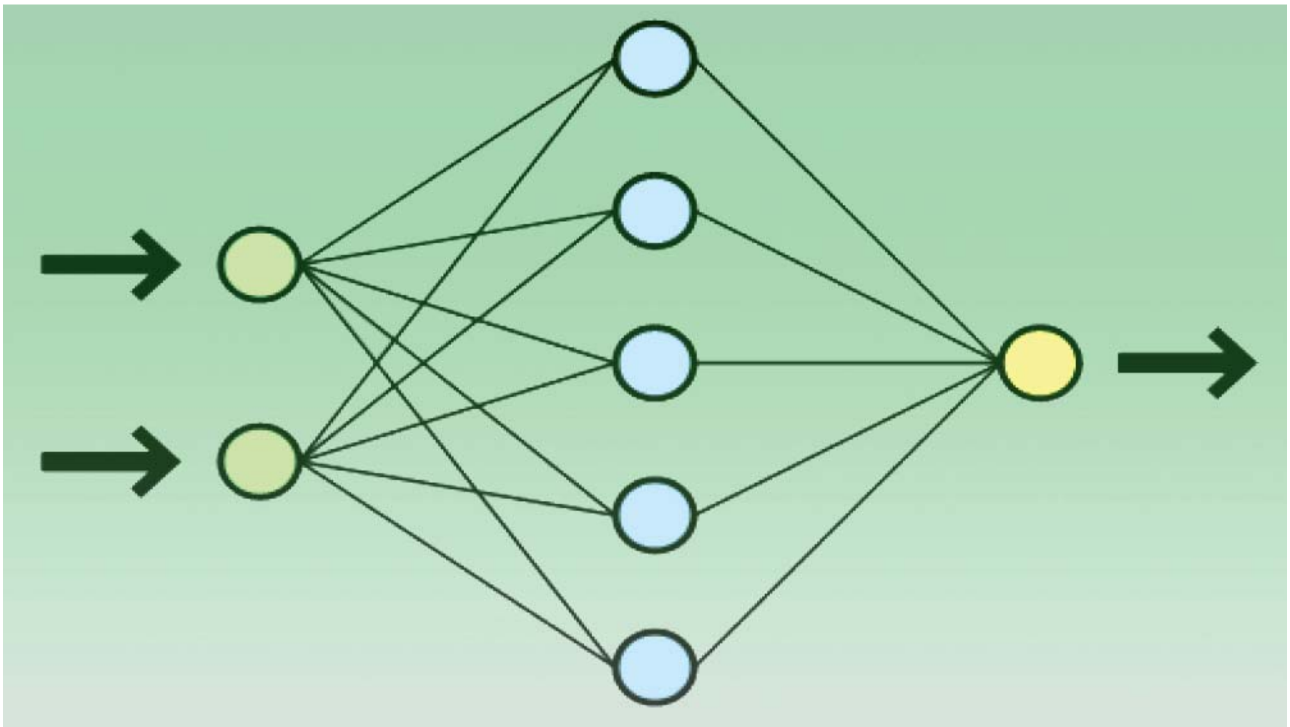
ALP science 2006, No. 498

QUANTITATIVE FORECAST OF LISTERIOSIS - FORECAST OF SWISS LISTERIOSIS INCIDENCE BASED ON FOOD CATEGORIES-RELATIONSHIP BY ARIMA AND ARTIFICIAL NEURONAL NETWORK MODELS

Technical-scientific information



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ALP science

Title
Quantitative Forecast of Listeriosis -
forecast of Swiss Listeriosis incidence
based on Food Categories-Relationship
by ARIMA and Artificial Neuronal Network Models

First edition

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Figure on frontpage
Neuralnetwork.png (17KB, MIME type: image/png)
From Wikipedia, the free encyclopedia

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Layout
Helena Hemmi

Publication frequency
Several times yearly at irregular intervals

ISBN 3-905667-39-8
ISSN 1660-7856 (online)

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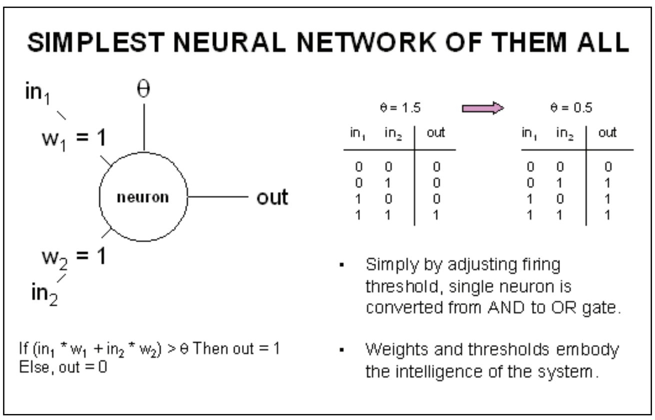
Keywords: Forecasting
Monte Carlo simulation
ARIMA
Artificial Neuronal Network

Abstract

The aim of the present study was to forecast Swiss listeriosis incidence based on food categories contamination. Health authorities might use forecasting as early alert system and become aware of potential health threats in time. Preventive control measures might be implemented before the expected onset of an epidemic.

Technically, the cases of listeriosis were forecasted with Artificial Neuronal Network and ARIMA models from static (relative distribution of contamination within food categories is assumed to remain constant) distributions of contamination within four food categories: dairy, meat, fish and other products. However, in reality distributions of contamination are not constant trough time and space. Therefore, the forecasted figures were subsequently simulated in connection to the dynamic relative distributions of contamination within food categories generated by means of Monte Carlo simulation (@Risk software, Palisade Corp.) from Beta distributions. The confidence interval of listeriosis cases related to each food category and age group will depend on their relative distributions from Beta distribution. Results showed that the Swiss population enters a decreasing phase of listeriosis cases 2004 (-30%) and 2005 (-9%) at the basis of 2003. Consumption of food of categories others and dairy products represents the highest and lowest risk, respectively. Population groups at high risk (reference is the age group population) are elderly people and perinatals (0 year old). At most, negligible risk might mathematically be related to the consumption of Swiss hard cheese.



1 Introduction

Listeria monocytogenes causes illness (listeriosis) by penetrating the lining of the gastrointestinal tract and infecting sterile body sites (29). The infection will depend on the number of ingested organisms and the incriminated strains of *Listeria monocytogenes.* Listeriosis is clinically manifested, if the microorganism is isolated from blood, cerebrospinal fluid, or an otherwise sterile site (30). Manifestations of listeriosis include meningoencephalitis, miscarriage, septicemia, meningitis, encephalitis, and intrauterine or cervical infections in pregnant women. Subpopulations at increased risk include pregnant women and perinatals, immunocompromised adults and elderly people (5, 13, 31). The ingestion of high numbers of *listeria monocytogenes* poses a significant health risk for sub-populations at increased risk. Since the 1980s, food-borne listeriosis was positively linked to food (16, 18, 28). Annual incidence was 1-8 cases per million at international level and associated with mortality rates >20% (7, 31). Frequently associated food categories are deli-meats/paté, salads/vegetables, seafood and milk/dairy products (28). For that reason, it was of interest to know and forecast the listeriosis-distribution within the age groups of the Swiss population according to the contamination of incriminated food categories.

The contribution of likely incriminated food categories was estimated by Monte Carlo simulation on basis of the corresponding dynamic relative distributions of contamination (if a variable x follows Beta distribution with parameters α and β, the probability density function is given by

$$P(x) = \frac{(1-x)^{(\beta-1)} x^{(\alpha-1)}}{B(\alpha;\beta)} = \frac{\Gamma(\alpha+\beta)}{\Gamma(\alpha)\Gamma(\beta)} (1-x)^{(\beta-1)} x^{(\alpha-1)})$$

with $\Gamma(a) = \int_0^\infty t^{(a-1)} e^{-t} dt$, which is a gamma function (20). ARIMA(1,1,1) and Artificial Neuronal Network models were used for forecasting the number of listeriosis-cases in Switzerland. The procedure first forecasted the number of listeriosis-cases from 2004 to 2007 by ARIMA(1,1,1) and Artificial Neuronal Network. Thereafter the listeriosis cases related to each food category and age group were analysed taking into account their relative contaminations deduced from Beta distribution (20).

2 Materials and methods

Data sources and assumptions

From 1988 to 1989, Swiss Listeria National Reference Centre (Centre National de Référence des Listérias, CNRL) tested 3220 samples where 1927 were from the food categories dairy, meat, poultry, fish, shellfish, and other products (15). An other set of analysis concerning *Listeria monocytogenes* food contamination has been realized by the Institute of Microbiology and Immunology, St. Gallen, during epidemic outbreaks of listeriosis over several years. Here, 1999 food samples were analysed (10). The statistical problem was that data was not randomly sampled but obtained with the objective of *Listeria monocytogenes* strain identification. The analysis of contamination within food categories would result biased. So, it was decided to apply Germany's nationwide food survey data concerning *Listeria monocytogenes* (Table 1, 33) to Switzerland.

Contamination of food categories were ranged in the three levels $<10^2$ cfug^{-1} (low), 10^2-10^4 cfug^{-1} (medium), and $>10^4$ cfug^{-1} (high). High loads of *Listeria monocytogenes* are thought to be more likely to cause foodborne listeriosis. For that reason, only high-level contamination $>10^4$ cfug^{-1} was selected for modelling. Switzerland was assumed to present similar relative distributions of contamination within the four main food categories dairy, meat, fish and other products. Nevertheless, our research station (Swiss Federal Research Station for Animal Production and Dairy Research, ALP) collected interesting data on milk products and cheese 1990-99 (U. Spahr, unpublished data). Relative distribution of *Listeria monocytogenes*-contamination in Swiss hard, semihard and soft cheese between 1990 - 1999 was 0%, 89%, 11% (edible parts, 27). Moreover, the Swiss canton's chemist food control collected interesting data on dairy products 1990-97 (*32*). These data sets allowed an estimation of the likely proportion of listeriosis related to cheese consumption. For listeriosis time-series (forecast) and distribution of listeriosis cases by age groups, data provided by the Swiss Federal Office of Public Health (http://www.bag.admin.ch/infreporting/mv/f/index.htm, acc. 18.06.2004 and http://www.bag.admin.ch/k_m_meldesystem/00733/00804/index.html ?lang=de?webgrab_path=http://www.bag-anw.admin.ch/infreporting/mv/ d/../../tab/tc13.htm, accessed 14. 06. 2006) was used.

Artificial Neuronal Networks modelling

Artificial Neuronal networks (19) models are mathematical computational models inspired by the neuron cell structure of the biological nervous system. They are based on two simple concepts, the topology of *nodes* and *connections* between them, and *transfer functions* which relate the input and output of each node. A node receives input data through its input connections, performs an operation on the data (weighted sum and some kind of threshold function), and passes the results to its output connection(s) either as a final output or for further use in other node(s).

Each node takes different inputs simultaneously and sums them, then produces a response dependent on the level of inputs received. If the sum of inputs is high, the node produces a strong response; if the sum of inputs is low, the response is "triggered" i.e., the activation function adds weight to high-value patterns and ignores the low-values. Roughly, the information processing performed in this way may be summarised as follows. Signals (action potentials) appear at the nodes' inputs (synapses). The effect each signal has may be approximated by multiplying the signal by some number (weight) to indicate the strength of the synapse. The weighted signals are summed to produce an overall unit *activation*. If this activation exceeds a certain threshold the node produces an output response.

A single artificial neuron is the basic element of the Neuronal Network. It comprises several inputs ($x_1, x_2, ..x_n$) and one output y that can be written as follows:

$$y = f(x_i . w_i) \tag{1}$$

where w_i are the function parameter weights of the function. Equation (1) is called activation function. This activation function may be linear or non-linear.

Estimation and forecasting

For computer procedure (35), the "Alyuda forecaster" (http://www.alyuda.com/downloads/forecaster_xl.zip, accessed 18.06.2004) software was used. It is described as follows:

$$y_{k+1} = f(y_k, y_{k-1}, ...y_{k-p}; \varepsilon_k, \varepsilon_{k-1}, ...\varepsilon_{k-m}) \tag{2}$$

where y_i is the time series or processed time series, and $\varepsilon_k, ...\varepsilon_{k-d}$ are residuals. The computed output is compared to known observations. In order to reach close correspondence, the weights of the activation function are adjusted. This process is continued for the time-series, until the Artificial Neuronal Network correctly reproduces the output of the given input. That means, a future value is derived from past values with some inherent errors. The processing of the input data (y) and errors (ε) are needed to determine the performance of the "Alyuda forecaster". This performance is measured in terms of Mean Absolute Percentage Error (MAPE), meaning that the same positive and negative errors are considered differently:

$$MAPE = \frac{1}{n-1} \sum_{i=2}^{n} (y_i - y_{i-1}) / y_i \tag{3}$$

ARIMA *(AutoRegressive Integrated Moving-Average)* describes a stochastic process, i.e. a statistical process involving a number of random variables depending on a variable parameter (usually time). The method was developed by Box and Jenkins in 1976 and popularised (9) in 1994. It represents a systematic methodology for identifying and estimating parameters and is widely used as a powerful and flexible class of models. ARIMA models allowed to forecast time series in many scientific domains.

The autoregressive (AR) model is a common approach for modelling univariate time series, i.e. historical data (one dimension)

$$y_t = \mu + \gamma_1 y_{t-1} + \gamma_2 y_{t-2} + \gamma_3 y_{t-3} + ... + \gamma_p y_p + \varepsilon_t \tag{4}$$

where μ is a constant (intercept), $\gamma_1, \gamma_2, ..\gamma_p$ are the autoregressive model parameters and *p* is the order of the AR model. An AR process represents a linear regression of the current value of the series against one or more prior values of the series. This means, that each observation is made up of a random error component (named random shock or white noise, ε) and a linear combination of prior observations. The relationship of equation (4) becomes possible in case of stationarity (statistical properties, i.e. mean value, variance, autocorrelation do not change over time) of the time series. So, an AR(1) process is only stable (stationary and invertible) if the parameters are within the interval of -1 < γ < 1. Otherwise, past effects would accumulate and the values of successive y_t would move towards infinity, meaning that the series would not be stationary (9).

The model of the MA process is

$$y_t = \mu + \varepsilon_t - \phi_1 \varepsilon_{t-1} - \phi_{t-2}\varepsilon_{t-2} - \phi_3 \varepsilon_{t-3} - ....\phi_{t-q} \tag{5}$$

where μ is a constant and $\phi_1, \phi_2, ...\phi_{t-q}$ are parameters of the moving average model.

MA represents a linear regression of current value of the series against random shocks of one or more prior values of the series. The random shocks at each point are assumed to come from the same distribution, typically a normal distribution, with location at zero and constant scale. The distinction in this model is that these random shocks are propagated to future values of the time series. MA(q) models never have problems of stationarity and methods for detecting stationarity are available, e.g. the "Test for Unit Root" (9,11).

If an ARMA process (AR process combined with MA process) does not reveal stationarity of data, integration of the process may be a possible solution. Considering a random walk, i.e. a stochastic process consisting of a sequence of changes each characterised - as magnitude or direction- by chance, with a drift,

$$y_t = \mu + y_{t-1} + \varepsilon_t \tag{6}$$

substitution yields

$$y_t = \sum_{i=0}^{\infty} (\mu + \varepsilon_{t-i}) \tag{7}$$

which is a sum of infinite numbers of random variables. In this case, the random walk is clearly not stationary. But a first differencing (d) of y_t results in

$$\Delta^d y_t = y_t - y_{t-1} = \mu + \varepsilon_t \tag{8}$$

which is stationary again. The series y_t is named *"integrated of order one"* and denoted I (1). A time series needing (d) differencing steps to reach stationarity is named "*integrated of order d*" denoted I(d). A process which is autoregressive and moving average is called ARMA(p,q) process

$$y_t = \{\mu + \gamma_1 y_{t-1} + \gamma_2 y_{t-2} + \gamma_3 y_{t-3} + ... + \gamma_p y_p\} + (\varepsilon_t - \phi_1 \varepsilon_{t-1} - \phi_{t-2}\varepsilon_{t-2} - \phi_3 \varepsilon_{t-3} - ....\phi_{t-q}) \tag{9}$$

d differencing(s) of the process yields

$$\Delta^d y_t = \{\mu + \gamma_1 \Delta^d y_{t-1} + \gamma_2 \Delta^d y_{t-2} + \gamma_3 \Delta^d y_{t-3} + ... + \gamma_p \Delta^d y_p\} + (\varepsilon_t - \phi_1 \varepsilon_{t-1} - \phi_{t-2}\varepsilon_{t-2} - \phi_3 \varepsilon_{t-3} - ...\phi_{t-q}) \tag{10}$$

where $\Delta^d y_t = y_t - y_{t-1}$, which is an ARIMA (p, d, q) model.

S-plus software (http://elms03.e-academy.com/splus/, accessed at 28.06.2004) was used for estimation and forecasting. The parameters were estimated with ARIMA(1,1,1) by using non-linear functions of minimization procedures, where the sum of squared residuals is minimized (22, 23). The algorithm used the likelihood which is computed by forming the Choleski decomposition (1,6) of the covariance matrix of the process. In presence of missing values, the likelihood is computed using the Kalman filter (*34*) applied to a state space representation of the likelihood. Autoregressive and moving average parameters are transformed to ensure stationarity and invertibility (21).

For simplification, the 2 vectors of forecasted listeriosis-cases from ARIMA and Artificial Neuronal Network are supposed to be constant, therefore their distribution represent joint density of 4 Beta functions. This assumption is helpful because it can be tiresome to calculate the joint distribution of vectors composed by variables from ARIMA or Artificial Neuronal Network and Beta distribution.

Finally, Monte Carlo simulation (24) in @Risk software (http://www.palisade.com, accessed at 28.06.2004) was applied on these vectors and dynamic relative distributions of contamination within food categories were obtained. The same procedure was applied for cheese and age groups.

Forecasting by considering food categories

Here, information about relative distribution of contamination within the four food categories was included. Denoting $p(i)$ = probability of being contaminated by *Listeria monocytogenes* for i food category generated by Beta distribution, therefore the relative contamination for i food category = $p(i)/\sum_{j=1}^{4} p(j)$.

$z_{(4\times1)}$: column vector of forecasted listeriosis-cases from 2004-2007 (by ARIMA model)

$y_{(4\times1)}$: column vector of food categories relative distribution deduced from Beta distribution

$I_{(4\times1)}$: an identity column vector, i.e. a vector composed by 1 as value (easy way for multiplication between matrix of different sizes)

$\Psi_{(4\times1)}$: column vector of forecasted listeriosis-cases by incriminated food category.

results in $\Psi = y^T.I.z^T$

where y^T, z^T are transposed vectors of y, z (for transposition of a matrix or a vector turn each column into a row and vice versa).

Then, Monte Carlo simulation on Ψ and on the distributions of contamination of the food categories was performed. The same proceeding was applied for the Swiss dairy products and cheese by first calculating the relative distribution of contamination (deduced from Beta distribution) within dairy products and cheese.

Forecasting by age group

At the beginning, it was necessary to calculate the mean number of listeriosis-cases by age groups from historical data. Then, Monte Carlo simulations from Beta distribution of each age group followed according to the corresponding proportion of Swiss population and the relative distribution of listeriosis cases was deduced. The forecasted listeriosis cases by age group were simulated by multiplying four matrices (17).

Defining

$x_{(6\times1)}$: column vector of age groups. The vector has 6 rows related to the 6 age groups with their relative distributions of listeriosis cases (deduced from Beta distributions generated from the reported values within the age groups of the Swiss population)

$\Omega_{(6\times4)}$: matrix of forecasted listeriosis cases by age group (produces 4 years forecasting figures for the 6 age groups)

$$\Omega = x.y^T.I.z^T$$

Monte Carlo simulation on Ω yields relative distribution of listeriosis-cases by each age group.

3 Results

Forecasted cases of listeriosis

According to the cyclical data on the basis of historical data (1973-2003) of the Swiss Federal Office of Public Health, forecasted figures from Artificial Neuronal Network model show that the Swiss population entered in a decreasing phase of listeriosis-cases 2004 followed by an increasing phase 2005 (Fig. 2). ARIMA forecasting confirms the decreasing phase 2004 but shows delayed onset of the increasing phase which will start 2006 (Table 2). Concerning the short-term (e.g. <4 years) forecasting of listeriosis cases both, ARIMA and Artificial Neuronal Network models, lay close together (Fig. 2). However, in the long-term forecasting, the two models show different evolution of values over the years and forecasting is not conclusive.

Forecasted listeriosis risk by age group

The proportion of risk is based on the weight of the age group population (27). In the Swiss population, 0 year old (set perinatals including foetuses and neonates) and elderly people (>65 years old) were found to represent subpopulations at high relative listeriosis risk (weight of 23 of 37 cases in 2004). Nevertheless, Table 3 shows high standard deviation for both groups. The relative listeriosis risk was on a mean level for the population group aged 20-39 years (weight of 2 of 37 cases) and at lowest level for infants and young adults 1-19 years (e.g. weight of 0 of 37 cases).

Forecasted cases of listeriosis by incriminated food categories

According to the simulation results in Table 4 the food category others (including pastries, salades, etc.) represents the highest risk to consumer health (min. 6, mean 10, and max. 15 forecasted listeriosis cases). Meat (including sausages, meat, poultry, etc.) and fish products show decreased risk range (min. 4, mean 7, and max. 11 forecasted listeriosis cases). In comparison, dairy products (including butter, raw & pasteurised milk, etc.) (min. 3, mean 4 and max. 7 forecasted listeriosis cases) represent a relatively low risk. With regards to cheese, roughly 20% of listeriosis cases from dairy products might be expected to be caused by cheese, accounting for 0 listeriosis case (min., and mean) and 1 listeriosis case maximal. After the analysis of Swiss dairy sector's data, no sample of edible parts of Swiss hard cheese showed *Listeria monocytogenes* contamination (27) and at most negligible risk could mathematically be related to this traditional food (proportion of 0-1 listeriosis case per 7.2 million Swiss population and year) as well as an extremely low probability of listeriosis mortality because of the absence of high *Listeria monocytogenes* loads in edible parts of Swiss hard cheese.

4 Discussion

Statistical data modelling with either ARIMA or Artificial Neuronal Network was already successfully implemented for other diseases (4, 8, 14). Despite of differences between the two discussed forecasting models at least in long term forecast of numbers of foodborne illnesses, there is a demand for linking microbiological food contamination with adverse health effects (3, 12). Good forecasting of foodborne microbial diseases is dependent on data-availability especially concerning the relationship between the level of ingested number of bacteria of a foodborne pathogen – i.e. dependent of environmental conditions (25) - and the frequency of disease. Otherwise existing Swiss data sets allowed for preliminary estimates of the distribution of *Listeria monocytogenes* contamination within food categories. The not randomly sampled data revealed relative distributions of contamination of 23%, 61%, and 16% for dairy, meat and other products from 1999 samples taken during different epidemic listeriosis outbreaks over several years (10) and 21%, 45%, 22% and 11% for dairy, meat, fish and other products from 1927 samples analysed for strain identification (15). Both data-sets do not contain numbering of the micro-organisms. Thus, the selection of Germany's actively performed quantitative nationwide food survey (33) data as a basis for forecasting was justified and motivated by the geographical and structural "proximity" of the two neighbouring countries.

The choice of Artificial Neuronal Network was motivated by it's flexibility and simplicity. Data-analyses is performed differently to traditional statistical methods. This model type learns from experience and recognizes patterns that may appear within a given set of data. However, knowing an underlying relationship in the data makes model building with statistical methods easier. In the case of listeriosis for example, the historical data revealed a cyclical character with a mean length of seven years. This information indicated that statistical data modelling with ARIMA should lead to good predictions. According to the listeriosis cases reported until September, the ARIMA fore-casted cases seem to reflect closely the situation of the year 2004.

Monte Carlo simulation was performed imposing constant results of ARIMA and Artificial Neuronal Network. This condition was helpful because of the use of four different software packages. The rigorous and mathematical method would be an independent algorithm built in specialized software, e.g. Matlab, SAS. In addition, the existing data (1973-2003) yielded a cyclic period of 7 years to be used in the Artificial Neuronal Network model, too. However, the starting step of this model is often not known. As a consequence, some trials must be performed and the accuracy of the model repeatedly tested until a maximum of good forecasted values is found.

Artificial Neuronal Networks produce better and faster results than statistical methods in cases of unknown underlying data structure, complex problems or non-linearity, e.g. as in the Swiss listeriosis time-series. Moreover, this model-type is robust even in presence of incomplete data.

Forecasting by the mentioned methods could be a valuable tool for the direction of attention and risk minimisation efforts towards critical food categories and foodstuffs (2, 27). For public health authorities, forecasting might result useful for the planning of necessary future capacities and activities.

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Table 1 *Listeria monocytogenes* in German food categories (35)

Product category	No.of Samples	Contamination level			Proportion in percent		
		$<10^2$	10^2-10^4	**$>10^4$**	$>10^2$	10^2-10^4	**$>10^4$**
dairy	3889	180	11	**3**	4.6	0.3	**0.1**
meat	6381	512	90	**8**	8.0	1.4	**0.1**
fish	948	70	27	**16**	7.4	2.8	**1.7**
others	1655	178	30	**0**	10.8	1.8	**0.0**

Table 2 Forecasted listeriosis cases by Artificial Neuronal Network and ARIMA models

	Artificial Neuronal Network				**ARIMA**			
	Mean	Std Dev.	Min	Max	**Mean**	Std Dev.	Min	Max
2004	**31**	3	21	43	**37**	4	26	52
2005	**37**	3	26	53	**33**	3	22	48
2006	**29**	3	20	43	**36**	4	25	51
2007	**27**	3	18	41	**25**	3	15	39

Table 3 Forecasted proportion of listeriosis risk by age group (Switzerland, 2004-2007)

	Artificial Neural Network				**ARIMA**			
Age group/ year	**Mean**	Std. dev.	Min	Max	**Mean**	Std. dev.	Min	Max
0 / 2004	**8**	5	0	26	**9**	6	0	32
0 / 2005	**9**	6	0	30	**8**	6	0	29
0 / 2006	**7**	5	0	24	**9**	6	0	31
0 / 2007	**7**	5	0	22	**6**	4	0	21
1-19 / 2004	**0**	0	0	3	**0**	0	0	3
1-19 / 2005	**0**	0	0	3	**0**	0	0	3
1-19 / 2006	**0**	0	0	3	**0**	0	0	3
1-19 / 2007	**0**	0	0	2	**0**	0	0	2
20-39 / 2004	**1**	1	0	7	**2**	1	0	8
20-39 / 2005	**2**	1	0	8	**1**	1	0	7
20-39 / 2006	**1**	1	0	6	**2**	1	0	7
20-39 / 2007	**1**	1	0	6	**1**	1	0	5
40-64 / 2004	**2**	1	0	8	**3**	1	0	11
40-64 / 2005	**3**	1	0	10	**2**	1	0	10
40-64 / 2006	**2**	1	0	8	**3**	1	0	10
40-64 / 2007	**2**	1	0	7	**2**	1	0	7
65-79 / 2004	**10**	3	2	23	**12**	4	1	28
65-79 / 2005	**12**	4	2	27	**11**	4	1	25
65-79 / 2006	**10**	3	2	22	**12**	4	1	28
65-79 / 2007	**9**	3	2	20	**8**	3	1	19
>=80 / 2004	**9**	4	1	24	**11**	5	1	27
>=80 / 2005	**11**	5	1	28	**10**	4	1	24
>=80 / 2006	**9**	4	1	22	**11**	4	1	26
>=80 / 2007	**8**	3	1	21	**7**	3	1	18

Table 4 Forecast of Swiss listeriosis cases by incriminated food categories

	year	**Mean**	Std.dev.	Min	Max
	2004	**4**	1	3	7
	2005	**6**	1	4	9
	2006	**6**	1	4	9
dairy products	2007	**5**	1	3	8
	2004	**0**	0	0	1
	2005	**1**	0	0	1
	2006	**1**	0	0	1
cheese	2007	**0**	0	0	1
	2004	**7**	1	5	11
	2005	**10**	1	7	15
	2006	**10**	1	7	15
meat	2007	**9**	1	6	13
	2004	**7**	1	4	11
	2005	**9**	1	6	14
	2006	**9**	1	5	15
fish	2007	**8**	1	5	13
	2004	**10**	1	6	15
	2005	**14**	1	9	19
	2006	**14**	1	9	20
others	2007	**12**	1	8	17

Figure 1 Listeriosis cases from historical data (Switzerland, 1976-2003)

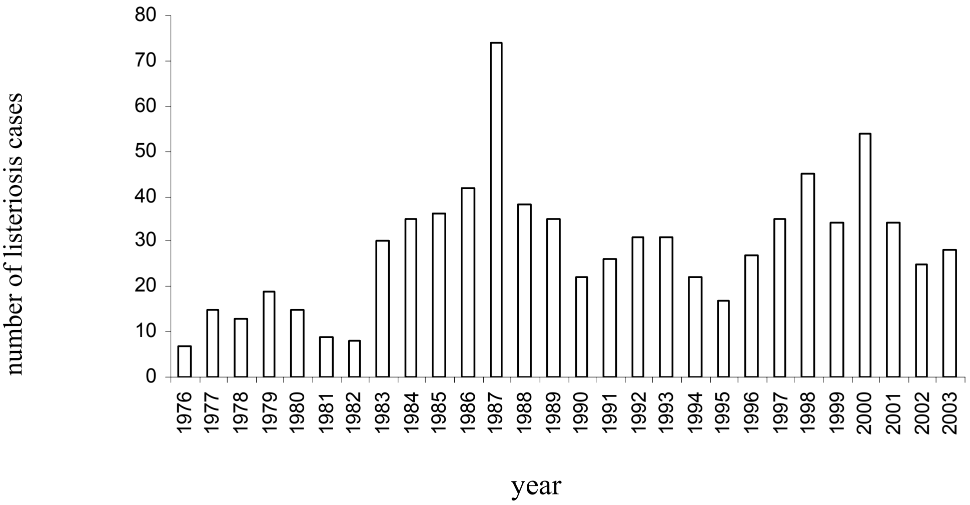

Figure 2 Long-term forecasting of listeriosis cases in (Switzerland, 1976-2003)