euroMOMO

European monitoring of excess mortality for public health action

Work Package 7 Report

A European algorithm for a common monitoring of mortality across Europe.

Bernadette Gergonne (bernadette.gergonne@epilife.eu, WP7 leader), Anne Mazick, Joan O'Donnell, Ajay Oza , Bianca Cox, Françoise Wuillaume, Zalman Kaufman, Mikko Virtanen, Helen Green, Pia Hardelid, Nick Andrews, Richard Pebody, Martin Holmberg, Marios Detsis, Costas Danis, Helmut Uphoff, Loic Josseran, Anne Fouillet, Baltazar Nunes, Paulo Nogueira, Christoph Junker, Liselotte van Asten, Tessa van Klooster Fernando Simon,Victor Manuel Flores, Sonja Tomsic, Gianfranco Spiteri, Jens Nielsen, Kåre Mølbak.

STATENS SERUM INSTITUT - 5, Artillerivej - DK-2300 Copenhagen S

European Commission

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Affiliations of WP7 partners

Bernadette Gergonne
National Board of Health and Welfare, Sweden
Staten Serum Institute, Denmark

Anne Mazick, Jens Nielsen, Kåre Mølbak
Staten Serum Institute, Denmark

Joan O'Donnell, Ajay Oza
Health Protection Surveillance Centre, Ireland

Françoise Willaume, Bianca Cox
Public Health Institute, Belgium

Zalman Kaufman
Israel Center for Disease Control, Ministry of Health, Israel.

Mikko Virtanen
National Institute for Health and Welfare, Finland

Nick Andrews, Helen Green, Pia Hardelid, Richard Pebody
Health Protection Agency, Centre for Infections, United Kingdom

Anne Fouillet, Loic Josseran
Institut de Veille Sanitaire, France

Martin Holmberg
National Board of Health and Welfare, Stockholm, Sweden

Marios Detsis
Hellenic Centre for Disease Control and Prevention, Greece

Helmut Uphoff
State Health Office, Hesse, Germany

Paulo Nogueira, Baltazar Nunes
National Health Institute, Portugal

Christoph Junker
Federal Statistical Office, Switzerland

Liselotte van Asten, Tessa van Klooster
National Institute for Public Health and the Environment, The Netherlands

Victor Manuel Flores, Fernando Simon
National Health Institute, Spain

Sonja Tomsic
Public Health Institute, Slovenia

Gianfranco Spiteri
Infectious disease prevention and control unit, Malta

Contents

Summary

INTRODUCTION

Most of the European Countries collect individual mortality data in order to annually monitor the impact of chronic diseases, plan and evaluate public health interventions. The EuroMOMO project was implemented to promote and implement at European level the weekly monitoring of mortality related to possible public health threats such as major epidemics, extreme temperatures, deliberate or accidental release of biological or chemical agents.

METHODS

To be generalised and applicable at European level, a statistical algorithm has been designed to fit the requirements proposed by the institutes' partners of the project. Every week, the EuroMOMO algorithm is run individually by each partner institute on individual mortality data. The algorithm correct for the delay observed in data collection and data processing in each countries. A Serfling – like model is computed on the weekly number of deaths in order to define the baseline mortality. Mortality variation around the baseline is computed in order to detect and measure possible excess mortality, and data are standardised using Z-score in order to enable comparison between age groups or other population subgroups. Data are then transmitted to the EuroMOMO coordination team, compiled and released on a dedicated website accessible to the project national and international partners. The standardization enables an easy comparison between countries and a European bulletin is publicly released every week.

RESULTS

The EuroMOMO algorithm was gradually implemented in partner institutes from June 2009, following the outbreak of pandemic influenza A/H1N1 in Europe. It could correct for delays in notification with a good accuracy in countries with a stable flow of information. Standardization of mortality and excess mortality enable an easy comparison between countries and between age groups, including countries with various population distributions. European compilation of national results is displayed weekly on the

Euromomo dedicated website. During the 2009 A/N1N1 pandemic of influenza, 9 countries were monitoring weekly their mortality using the Euromomo algorithm and could observe on real time that the pandemic had not a large impact on elderly and adult population. Only small sustained shift could be observed in children 5-14 years of age. Winter and summer increase could also be studied on real time and retrospectively. Similarities and discrepancies between countries helped to describe the distribution of severe health threats with impact on mortality across Europe, possibly related to heat waves and cold snaps, generate hypothesis and design more in depth studies.

CONCLUSION

The Euro-MOMO pilot project demonstrated the feasibility and usefulness of a weekly mortality monitoring at National and European level. The value of the monitoring was particularly evident during the 2009 A/H1N1 influenza pandemic. Real time monitoring of all cause mortality should become part of the routine epidemiological surveillance to complement information already provided by disease specific and environmental surveillance. Alike disease surveillance, routine mortality monitoring requires adequate funding as well as dedicated and trained human resources. The Euro-MOMO pilot project is now ready to be implemented at a larger scale and become an integral part of routine epidemiological surveillance across all of Europe.

Introduction

Mortality indicators are considered to be basic but robust measurements of the general health status of populations. This is fundamental for evidence-based public health planning, implementation and evaluation of actions [1, 2]. For that purpose, all European countries collect individual mortality data in their own populations and produce with a certain delay at least annual statistics [3, 4]. In addition to annual indicators the ability to conduct early analysis of mortality trends across different population groups could provide crucial information, not only to monitor of influenza through the monitoring of pneumonia and influenza death as performed in the United States in a sample of cities [5] but also for other public health crisis (other large epidemics, extreme weather conditions, release of hazardous biological or chemical agents) in order to assess magnitude and rapidly target, implement and evaluate interventions. Information on the impact on mortality of severe public health crises should be shared between countries for a better national and European response and contribute to already existing European surveillance, early warning and reponse tools [6, 7]. However, only few European countries can monitor mortality on a frequent regular basis and comparability of indicators produced are limited [8]. For that purpose, alike morbidity surveillance, a standardized European approach is needed, in order to produce in a timely manner indicators comparable between countries, facilitate the exchange of information and produce global European indicators.

In that context, the Euro-MOMO (European monitoring of excess mortality for public health action) was funded by the European Union Health Program and implemented in 2008 under the coordination of the department of epidemiology at the Statens Serum Institut (SSI) in Copenhagen [9]. The Euro-MOMO project involves numerous national and international stakeholders including the European Centre for infectious Disease prevention and control (ECDC) and the WHO regional Office for Europe. Its aim is to develop and operate a coordinated mortality monitoring across European countries in order to contribute to National and European risk assessment associated with major health threats. More specifically, technical objectives includes the delivery to participating European countries of a statistical computer program (called Euro-MOMO algorithm) designed for the near real time detection, measurement and comparison of all cause excess mortality indicators, in various population groups. Objectives of the Euro-MOMO coordination center also includes the centralization of indicators produced regularly in participating countries, their compilation and release on a dedicated website accessible to the partners to the project in order to detect at European level temporal or geographical shifts in various population age groups. The Euro-MOMO pilot project is committed to respect the autonomy of countries who are the originators and authors of the data. Any national data or indicators shared at European level must first comply with the legal framework of that country, as some countries do not authorize the early publication of raw indicators. The project also keeps to the limitations that may be set by partners with respect to what type of data can be released to the general public.

The implementation of the Euro-MOMO faced various challenges. Most European countries collect individual data from death certificates established and registered at the peripheral level [10]. This information is subsequently transmitted to the national central office. Causes of death are coded usually using the international classification of diseases (ICD) and statistics are published every year, once it is considered that nearly 100% of the death certificates have been collected, compiled and analyzed [11]. These common procedures may not always be adapted to an efficient real time monitoring of mortality trends. In a number of European countries, coding the causes of death takes years to be completed and only all-cause mortality indicators based on demographic data (age, sex , place of death) can be generated in a near real time basis. Delays in data transmission from the peripheral offices to the central level do occur as a result of logistical, technical or even legal reasons, and could between countries vary from a few hours to several weeks. As a consequence, at a specific date, only a proportion of the number of deaths that occurred during the previous days or weeks is known. Delays of more than 2 weeks can seriously challenge a real-time mortality monitoring in a rapidly developing public health threat situation. Finally, type and format of data collected and indicators produced may vary between countries, also challenging comparability of mortality indicators at European level.

A consensus between partners was necessary to build a uniform and consistent approach and efficiently monitor mortality at European level. Comparability between countries and European use of information relies on standardized data collection (common frequency, common definitions and common format) and on standardized analysis (common definition of expected mortality, common definition of shifts or excess to detect, common definition of age groups to analyze and indicators to produce).

The current report describes the method and achievements of the common Euro-MOMO algorithm in order to increase the understanding of the process, the confidence in the system and facilitate the analysis of the results.

Methods

The methods that were used for this project will be reported in sequential order to reflect the work that was involved. The sections will describe briefly the following procedures:

- Requirements
- General principles
- Input data
- Correction for delay
  + Assumptions
  + Delay distribution
- Studying mortality variation
  + Modeling the expected number of deaths (baseline mortality)
  + Analysis of the characteristics of mortality time series and assessment of the model fit.
  + Measurement of weekly mortality variation
  + Standardized measurement of weekly mortality variation
  + Detection of sustained shifts and Cumulative Sum Control (CUSUM) charts
  + Indicators computed for specific periods of time

- Transmission of data at Euro-MOMO Hub for European analysis and the European bulletin

Requirements

Several consensus meetings were held early in the project between the Euro-MOMO coordinating team, the participating national public health partners and other international counterparts. The purpose of these meetings was to define the minimal technical requirements needed for the monitoring of mortality across Europe. It was agreed that the partner institutes from each country would used their own "all-cause mortality" data when running the common Euro-MOMO algorithm to compute the agreed indicators. Aggregated weekly results would be sent to the coordinating team at SSI. The latter would be responsible for compiling all country indicators and uploading results on a dedicated website such that the information could be shared with all the national partners.

The Euro-MOMO algorithm would be used as the common tool for producing weekly indicators, including:

- the Observed Number of Deaths
- the Expected Number of Deaths (Expected Baseline)
- the deviation from the baseline (difference between observed and expected number of death)
- the Number of Deaths corrected for delay in data transmission

The algorithm would derive the expected baseline according to the mortality pattern of the last 3 to 5 years, according to the availability of data in each country, and remove the effect of any previous unexpected peaks during that period. These crude indicators would be reported by "Total Population" and by "Age Group"(<5 years, 5 - 14, 15 - 64, >=65), reflecting the same age groups that are used by the European Influenza Surveillance Network (EISN). It was also agreed that partner institutes using the algorithm would also have the possibly to define and study other population subgroups (e.g. by sex, by sub-national level) and that the algorithm would be able to accommodate various type of mortality patterns and a variable range of data, as it was expected that there would be marked differences in the total number of reported deaths that would occur between larger and smaller countries and also between the very young and the older age groups. The algorithm would also estimate a corrected number of deaths in order to compensate for incomplete data caused by delays in the data transmission.

The algorithm would also compute various additional indicators to enable easy comparisons between countries and population subgroups. Due to the lack of precise population data in some European countries, it was agreed that during the pilot phase of Euro-MOMO, demographic information would not be used and mortality rates not calculated. Finally, the algorithm would facilitate the rapid detection of excess deaths every single week and during longer time periods. It would also help to detect very small increase of mortality, sustained over several weeks (sustained shifts).

To comply with the requirements, the Euro-MOMO algorithm was computed using the Stata 10 statistical package and was delivered to the participating countries. For the countries where the Stata package was not available, the Euro-MOMO algorithm was run for the country by the coordination team and national results then sent back to the partner institute.

General principles

Every week, each partner institute updates the data files containing individual mortality records reported during the past 3 to 5 years according to the new information received, and run the algorithm on the updated file. Weekly time series of the number of deaths are compiled for each of the predefined population subgroups. The corrected numbers of deaths is computed in order to compensate for the delay in notification and transmission of mortality data. The expected baseline mortality is then calculated using historical data and is forecasted for the most recent weeks. The observed and the corrected weekly numbers of deaths are then compared to the expected baseline and the agreed indicators are computed. The partner institute sends the results every week to the coordinating team at the SSI who compiles country indicators and produces the European MOMO output, displayed on the website.

Input data

The individual input data included the:

- Date of death
- Date of data reception.
- Age of the deceased

The date of data reception is defined as the date at which a specific death becomes known to the corresponding Euro-MOMO national partner institute. This date is needed in order to study and model the pattern of the delay in data transmission. Weeks are numbered using the ISO standards [12].

Correction for delay

Assumptions

When calculating the corrected number of deaths, a number of simple assumptions are made. These assumptions are kept simple to remain valid in all countries and be easy to model.

Between the week of a death occurrence (Week of Death, WoD) and the week the information about that specific death is received at the partner institutes (Week of Reception, WoR), a delay of i weeks can be observed (Figure 1). As a consequence, only a proportion (p_i) of the real number of deaths (N) that occurs during a certain week of death (WoD) will be received by the partner institute at the end of a period of i weeks.

It is also assumed that p_i depends on the number of deaths (N) that occurred in that week and on the number of days (d_i) the administration offices were open for the registration of the death and for the transmission of the data , during the i weeks.

The delay i can vary between 0 (when deaths occurred and information is received at the partner institute in the same week) and n_w, the number of weeks needed to obtain the information on 100% of the deaths that occurred during a specific week. Therefore, when working in real-time, *i* also represents the period requiring a correction for delay when studying the most recent weeks of the mortality time series. Finally, it is assumed that N can be predicted using n_i, p_i and d_i.

Delay distribution

In order to correct for the delay in data transmission, the distribution of the delay *i* is studied and computed by the Euro-MOMO algorithm on a weekly basis, using the valid and complete historical period of the latest updated national data. For each individual, date of death and date of reception are converted into week of death (WoD) and week of reception (WoR) . The delay *i*, in weeks, between WoD and WoR is computed. On the same day every week, each partner institute compiles the most recent update of mortality data. The Euro-MOMO algorithm first computes the time series of the weekly number of deaths for the population subgroups chosen. For the most recent weeks, only a proportion of the total number of deaths is known (Figure 2) and that proportion increases with time. For each week in the valid historical period, the algorithm computes the part n_i of the total number of deaths N transmitted to the partner institute *i* weeks after the death occurrence (Figure 2a), with *i* varying from 0 to the number of weeks requiring a correction for notification delay. A binomial regression is used in order to model the proportion $p_i = n_i / N$ according to d_i, (the number of days the administration offices were open for the registration and the data transmission). The model P_i of the proportion p_i is forecasted during the period to correct according to d_i. In a second step, the real number of deaths N is modeled according to n_i, P_i and a trend using a generalized linear model (GLM) of the Poisson family. This model will predict the “corrected number of deaths” for each week *i* requiring a correction for delay (Figures 2a and 2b).

Studying mortality variation

Modeling the expected number of deaths (Expected Baseline Mortality)

Only the valid and complete part of the historical data with correct dates of death is used to model the expected baseline mortality. The modeling method used in this project is based on the following assumptions:

- A mortality time series is one realization of a stochastic underlying process composed by a trend, a sine-like cyclical seasonality of a one year period, and random variations [13, 14].
- The underlying process of weekly mortality and its variability can be modeled on a part (a sample) of the data set, using independent variables depending only on time (for trend and seasonality) [15].The resulting model can be considered as the Expected Baseline Mortality and can be forecast to parts of the time series not used to fit the model.
- In addition to the underlying process, the weekly mortality can be affected, generally increased, by external non cyclical factors, in particular during winter and summer, mainly (but not only) related to winter respiratory infections such as influenza [16-18], and to waves of extreme temperatures (heat waves and cold snaps) [19]. As these events do not occur with the same regularity or intensity every year, they are not considered as being cyclical in nature or being part of the underlying process of the expected baseline mortality. Thus winter and summer should be removed from the historical data set before modeling the expected baseline mortality.
- Parts of spring and autumn are less likely to be influenced by additional external factors leading to an excess deaths e.g. from influenza outbreaks or extreme temperatures. In the absence of specific indicators or agreement on the definitions for an influenza epidemic or extreme temperatures, the underlying process of the mortality variation can be modeled using only those part of the year, in the spring and autumn seasons, which are most likely to be free from these additional events. After an extensive review of different series from a number of European countries it was decided to set week 16 to 25 in spring and week 37 to 44 in autumn as the two

periods which are least likely to affected by additional external factors. However, this default option can be changed if needed.

Based on these assumptions, the expected weekly number of deaths in a particular population sub-group is modeled using a GLM of the Poisson family, accounting for over-dispersion, using a trend and 2 sine components of a 52.18 week period (one year), with a different phase, in order to fit a one year sine-type cyclical seasonality with the appropriate phase and amplitude [14, 20]. The model is fitted on the valid historical period with a minimum of 3 years and a maximum of 5 years, and excluding:

- The period to correct for the delay in data transmission (as defined by user)
- The weeks when the likelihood of increased mortality due to influenza outbreaks and waves of extreme temperature is expected to be high (weeks 1 to 16, weeks 26 to 36, and weeks 44 to 52/53).
- The data after week 34 in the year 2009, in order to exclude any possible influence of the 2009 A-H1N1 pandemic. This condition was modified in autumn 2010 once it was established that the H1N1 pandemic did not greatly affect all cause mortality

The model represents the Expected Baseline Mortality when the occurrence of events increasing mortality is low (Figure 3a). The standard deviation of the residuals during the same period represents the expected average variation of mortality around the baseline when the occurrence external events affecting mortality is low and can be used to compute prediction intervals. It is an indicator of the random part of the underlying process.

The model is then used to predict the expected baseline during the periods previously excluded in order to provide an expected number of deaths during the whole historical period. It is also forecast to provide a real time estimation of the expected number of death during the most recents weeks studied.

As the GLM Poisson model is applicable to series that can be either normally or Poisson distributed, it can be used for both high or low counts time series. A 2/3 power transformation is used to normalize the series before the computation of prediction intervals [21].

In the Euro-MOMO algorithm, models by default are suggested and composed by a linear trend and no sine term for the age groups 0 to 4 years and 5 to 14 years, and by a linear trend and one sine component for the age groups above 15 years and for the total population as a whole. Small modifications of the model can be made by the user according to the characteristics of the mortality time series to study. The user can define whether a linear trend is appropriate or if a set of 3 linear spline variables with knots equally spaced on the historical period better fit small variation of historical trends. The user can also define whether a sine-like seasonality is needed or not to fit the particular data sets studied.

Analysis of the characteristics of mortality time series and assessment of the model fit.

In order to select the best components to use in the model, various diagrams are systematically generated in order to visually assess the characteristics of the series and the model fit. The data plots, the baseline, the residual and the standardized mortality against time are used to assess the visual fit and the stability of the residuals over time. The plot of the residuals against the baseline reflects on the homoscedasticity and the periodogram verifies the presence of cyclical seasonality in the series and in the residuals. The plot of auto-correlation and partial auto-correlation are also used to assess seasonality and the importance of the remaining autocorrelation in the residuals that could be related to the occurrence of unexpected events still affecting mortality during the period used to fit the model [14].

Measurement of weekly mortality variation

The Euro-MOMO project does not define what constitutes excessive mortality. Each participating country has the choice to define its own alert threshold and to investigate or not. The Euro-MOMO algorithm however computes several indicators intended to facilitate decision making and comparisons between population subgroups at both the country and at the European level. Every week, the algorithm computes the crude variations of the number of deaths around the expected baseline. The observed number of deaths is replaced by the corrected number of deaths during the period requiring a correction for delay in notification. This provides near real-time weekly estimates of mortality variations around the expected baseline (Figure 3b).

Standardized measurement of weekly mortality variation

Variations around the expected baseline mortality are standardized using standard deviation scores (Z-score) in order to compare results between population subgroups with different mortality means and standard deviations. Z-score standardization also facilitates the quick estimation of the probability of a particular weekly measurement to occur and help users to define alert thresholds according to their needs (Figure 3 c).

In the Euro-MOMO algorithm, the Z-score is derived from the computation of the prediction interval normalised using a 2/3 power transformation [21].

The Z-score of mortality therefore varies around 0 and the amplitude of the variation is expressed as a number of expected standard deviation.

Detection of sustained shifts and Cumulative Sum Control (CUSUM) charts

A sustained shift occurs when the mean of consecutive measurements is consistently and significantly above the expected baseline, although the probability of each individual measurement may not be significantly different from the baseline for a chosen alpha risk. This can be interpreted as a significant cumulative excess or a small but significant change in trends. To detect such changes in the mortality series, CUSUM methods were applied on the data after Z-score standardization [22]. To detect sustained shifts with a high sensitivity, the CUSUM parameters have currently been chosen and computed as follows:

$CUSUM = \max(0, CUSUM_{t-1} + Zscore - k)$, where k is the reference value (or allowance parameter). In the Euro-MOMO algorithm, k was set at 0.25, in order to enable the detection of a shift of 1.5 Standard Deviations or more over 3 weeks. Considering an acceptable level of 5 % of false alarms, the “in control Average- Run Length” (ARL0) would be 20 weeks. The decision limit h is a function of ARL0. This means that, in the absence of any external event affecting the underlying process of mortality variation (represented by the expected baseline and expected standard variation), the CUSUM will on average cross the decision limit h and generate a "false" alert once every 20 weeks due to random variation. In the current Euro-MOMO algorithm, the user can define when the detection of sustained shift is initiated. Every week the CUSUM is computed and compared to the reference limit, a variable “alert” is set to 1 if the CUSUM crosses the decision limit. In addition to the CUSUM chart, plots of crude and standardized series, we include the plot of crude and standardized cumulative sums in order to have an additional visual assessment of the magnitude of the shift.

Indicators computed for specific periods of time

The Euro-MOMO algorithm also computes indicators over set periods of time in order to facilitate comparisons of specific time periods every year. Total and Expected number of deaths, Crude and Z-score standardized variations around the baseline are computed by year (week 1 to week 52/53), by season (week 27 to week 26 of the following year, thus effectively centering on winter and the influenza season), by winter (defined as week 40 to week 20 of the following year, the peak period for influenza) and by summer (defined as week 21 to week 39, the period when heat waves can be expected). User defined periods can also be studied. For a period of several weeks, the Z-score standardized mortality is computed as the sum of the individual Z-scores during the period under consideration, divided by the square root of the number of weeks during that period. Thus the standardized mortality can be compared between different years and population subgroups having different age group distributions, different mortality means and different standard deviations.

Transmission of data at Euro-MOMO Hub for a European analysis and the European bulletin

Every week, participating countries sent a standardized selection of updated aggregated data to the Euro-MOMO Hub in Copenhagen where all the European data are compiled. The crude and the Z-score standardized weekly number of deaths is represented as charts with the results of all participating countries plotted on the same time axis. From these charts the time occurrence and the amplitude of any peaks in mortality between countries could be easily compared. The data of participating countries are also pooled every week and the Euro-MOMO algorithm used on pooled data to obtain a single estimation of the crude number of deaths and expected baseline for all partner institutes participating in that specific week. The European bulletin is updated with results every week and uploaded on the Euro-MOMO website. The results of the participating countries and pooled analysis is accessible to all the partner institutes and European international public health counterparts. In accordance with country requests, only pooled results is released for public viewing.

Results

Design and implementation of the Euro-MOMO algorithm

The design of the algorithm was expected to meet the requirements agreed during the consensus meeting with the partner institutes and was initially planned to be completed by the end of 2009. The emergence of the A/H1N1 influenza pandemic in the same year speeded up the process and the first version of the algorithm was completed by June 2009. Four partner public health institutes in Denmark, Belgium, Ireland and also Israel took part in the preliminary testing by running the algorithm on a weekly basis during the summer months. As a result, the algorithm was regularly refined to better respond to the needs of users at both the national and the European level. By September 2009, other partner institutes were gradually recruited and started to send their results to the Euro-MOMO hub. The results were uploaded on the Euro-MOMO website but access was restricted to only national and international partner institutes. By October 2009 (week 40), at the time when the A/H1N1 influenza pandemic had reached continental Europe, a total of 10 countries were already monitoring and reporting mortality (for total population and by age group) by using the Euro-MOMO algorithm. This increased the capacity to monitor to the impact of the A/H1N1 influenza pandemic on mortality in the populations of these countries. By the end of 2010, the number of recruited partners had increased to 15 and all started to monitor weekly mortality in their country or state (Note: only one state could participate in Germany, and data are received only from a part of the country in Greece).

In order to satisfy the wishes of participating countries this report will only include country data that is already in the public domain and any detailed individual mortality analysis data will be displayed anonymously.

Characteristics of the study population

The study population was not homogeneous and showed interesting differences [23]. The total population estimates of countries which were implementing the Euro-MOMO algorithm varied significantly, from less than half a million (Malta) to over 65 millions (France). The age sub groups also varied markedly: the population under 15 years ranged from 14.0% (Slovenia) to 21.4 % (Ireland) while the population older than 64 years ranged from 11.3% (Ireland) to 18.9% (Greece). Eurostat data between 2007 and 2009 also revealed differences in the age distribution of the deceased in the European Countries: The proportional mortality of children under 15 years of age ranged from 0.3 % (Slovenia) to 1.3 % (Ireland); the proportion mortality of adults older than 64 years ranged from 77.6 % (Ireland) to 86.3 % (Sweden) (Table 1).

Delay distribution

In each participating country, logistical, administrative and legal issues influenced the flow of information. Most of the partner institutes received well over 98% of the data within 5 weeks but in a few countries this delay can be up to 25 weeks. (Figure 1).

National outputs

A number of graphs, tables and data sets are produced every week at national levels but only key examples are presented with this report. For each population subgroup tested, (by total population, by 4 age group and by other groups as defined by users), a single graph combines the mortality series, the expected baseline and the values corresponding to the baseline with + 2, +4, +6 expected standard deviations (Z-score) in order to facilitate the visual assessment of the relative amplitude of a measurement, and second graph, plot the Z-score standardized series on the same time axis which allows easy comparisons to be made of any possible excess deaths over time and between population subgroups. Partner institutes at the national level could also study different population subgroups and for instance study events occurring at sub-national level. One example is included and represents results obtained in the county of Gothenburg, Sweden (Figure 5). All results were provided as graphs and as data sets. Results computed over specific period of time are also provided as summary data files in order to facilitate the rapid compilation of tables (Figure 2) that enables comparison of mortality indicators across season and across age groups.

European output

The results of participating countries are weekly uploaded online on the web-based Euro-MOMO bulletin in the form of maps and graphs. The correction for delays enables a faster analysis, for the first near real-time monitoring of mortality in Europe. By November 2010 (week 47), 13 countries or states had sent in their results to the Euro-MOMO hub (Map 1). Graphs of crude and Z-score standardized mortality are available for each country by age group, but only a sample of the most significant results is included in this report. The country results are included in a single a graph (Figure 6) which facilitated the comparison of time occurrence and amplitude of mortality peaks possibly related to similar specific events. The algorithm can be applied to a very small number of deaths (Figure 6a). Crude numbers displayed together with their baseline facilitate the comparison of the crude amplitude of expected and observed mortality (Figure 6 a,b). The Z-score standardized mortality enables the comparison of the severity of specific events between countries (Figure 6 c). A global overview of all the participating countries is made possible by the analysis of pooled data (Figure 7).

Monitoring of mortality during the 2009 A/H1N1 Influenza pandemic

During the 2009 influenza pandemic, 9 countries were able to send data regularly to the Euro-MOMO hub and their results were made available to all partners. From this active monitoring it was evident that in spite of the dramatic increase in the number of medical consultations for influenza like illnesses and laboratory confirmation for A/H1N1 virus strain (week 40 to 50) in many European countries, in reality the virus was not causing any marked excess mortality. The elderly and adult populations were in general being spared. Cumulative data suggested a slight increased mortality among the 5 to 14 years age group, identified by examining cumulative deviations [24].

Other findings

Once standardized, the 2008-2009 winter mortality increase almost similar in amplitude and pattern across European countries (Figure 6 and 7). Timing of occurrence was also very similar and no consistent geographical East to West spread pattern could be observed. Slight increases in mortality also occurred in some countries during the summer months of 2009 and during the first weeks of 2010, but the pattern, time of occurrence and amplitude varied between countries.

Discussion

Summary

The Euro-MOMO pilot project demonstrated that it is feasible to implement and manage a common European-wide monitoring of mortality in near real-time. The Euro-MOMO algorithm, purposely designed to measure mortality variation on a weekly basis and facilitate detection and quantification of excess of deaths, is now being routinely used by 15 states across Europe. Weekly mortality reporting has become an integral part of epidemiological surveillance by several public health institutions in Europe.

Real-time mortality monitoring increases the capacity of countries to initiate a rapid alert and response to major public health threats, contributing to early evidence- based decision making for targeted interventions and prioritizing resources. The added benefit from real-time monitoring was clearly demonstrated during the A/ H1N1 influenza pandemic which reached Europe in 2009, when 9 countries, representing around 30% of the EU population and with a good geographical representation, had already started running the algorithm.

The project has also served as a channel for communication and exchange of information between participating national centres and international bodies which include the European Centre for Disease Prevention and Control (ECDC) and the Regional Office for Europe of the WHO (WHO-EURO). All the results from this project were release in real-time as weekly updates and are available on a dedicated website which can be accessed by all participating centres.

The Algorithm

Limitations of the algorithm

The algorithm fulfilled the requirements that were defined by the partners in the project. It is currently only available in one statistical package (Stata 9 to 11) which is a limitation for the institutes that do not have a specific license for using this software. Adaptation to other software packages may be needed but was difficult during the pilot phase because of the frequent modifications that were made to improve the system and gradually adapt it to common needs or situations in countries. It is anticipated that once European mortality monitoring becomes part of a routine European-wide surveillance network, a stable statistical program can be “translated” into various statistical packages which would suit all partner institutes.

Correcting the observed number of deaths to account for delay in data transmission requires individual data sets with a known date of reception for at least one year of historical records. This initially restricted the use of the algorithm in some countries that had joined the project, but this situation improved rapidly and this information is now being collected in all participating countries. The correction for delay will perform well if the transmission of data is smooth and regular, even if the reporting delay is very long. In cases where there is batch reporting and irregular data transmission, the system will perform less well as it is likely to predict a mean mortality rather than existing variations. For countries that cannot access weekly to individual data because of practical or legal reasons, a similar algorithm can also be used but correction for delay cannot be computed. Various graphs are available to help evaluate the regularity of information flow and the performance of the correction for delay. However, during the pilot phase, performances could only be evaluated in a retrospective manner (the model based on the whole data set and comparison with the real data on the same data set), because in most participating countries, times series were not long enough to enable evaluation of the model in a prospective manner (model based on 3 to 4 years of historical data, iterative weekly forecast one week ahead for at least a year and comparison with the real number of deaths). With 2 years of pilot monitoring, enough data have now been collected in various countries to enable prospective evaluation.

The model chosen to compute the expected number of deaths, when no excess is anticipated, is simple and is based on simple assumptions. The sine pattern is widely accepted as a simple but robust model of the expected mortality. Different assumptions about the pattern and what is considered as the "expected mortality" could be made and more complicated models can be designed to better fit the mortality patterns in each specific country. This could however decrease the comparability of the results across countries. Although some countries can use their own models and may obtain similar or slightly different results [25, 26], it was agreed from the beginning of the project that one common algorithm would be used and similar indicators reported. This requirement was made in order to ensure that meaningful comparisons between populations could be made.

The examination of the model residuals suggests that the model chosen seems to perform well for removing trend and seasonality in the numerous mortality time series. Z -score standardized mortality, newly used in mortality monitoring is an useful method to study and compare possible excess deaths between various populations and sub groups.

Comparing deviations from the expected baseline mortality between countries and between different populations.

One of the aims of the Euro-MOMO project is to monitor the possible impact of public health threats on mortality and compare any resultant increases between countries. The Euro-MOMO algorithm is not designed to compare the overall level of mortality as calculated for instance for the health reports of the World Health Organization [27] or for Eurostat [23].

The amplitude of a positive deviation from the baseline mortality above the expected variations could possibly be interpreted as an excess of death. Furthermore, in a specific population, excess deaths are mainly related to the severity of a particular health threat. Thus, monitoring and comparing the amplitude of weekly deviations between countries contributes to assess any geographical and temporal differences as well as compare the severity of the impact from severe public health threats. The ability to measure and study mortality variation on a weekly basis can thus provide crucial information for risk assessment and decision making in such situations.

Weekly mortality can be considered as a stochastic process composed of a predictable baseline (mean), expected random variation around that baseline (standard deviation) and in addition, the occurrence of unexpected positive (or possibly negative) deviations from the baseline that can be associated with external events. The level of the baseline and the amplitude of expected deviations will depend on the population size and the expected risk of dying in that population. That risk is related to factors such as the age distribution, the health status and the access to health care.

It seems reasonable to assume that a geographically widespread public heath threat (such as an outbreak of influenza) will increase the risk of dying in a multiplicative manner (contrarily to a large single accident that will increase the risk of dying in an additive manner). The amplitude of an unexpected positive deviation from the baseline can be related to the inherent vulnerability of the population to a particular threat. For instance, the vulnerability of a population might be increased by a higher virulence of a specific pathogen (e.g. the 2008-2009 H3N2 seasonal influenza epidemic), a possible increased susceptibility of a specific population to a new microorganism (e.g. influenza pandemics and young age groups) or a difference in behaviour regarding extreme climatic events (e.g. similar levels of cold weather do not have the same effect in Northern and Southern Europe).

The amplitude of unexpected deviations expressed as a number of deaths cannot be compared between countries with different population size (Figure 6 a). However, “mortality deviation rates”, defined as the difference between the observed and the expected number of deaths reported to the population size of the group studied, could be calculated. Thus, comparison could be undertaken by age groups and direct or indirect age-standardization can be performed to compare overall populations, as the main factor influencing the risk of dying is the age. However, if a public health threat increases the risk of dying in a multiplicative manner in a particular population, then the deviation rate will also depend on the initial risk of dying of that population. Deviation rates (or excess rates) do not account for the expected baseline mortality and can be misleading when comparing populations of different sizes or different expected baseline mortality. To overcome this problem, some authors compute a deviation expressed as a percentage of the baseline. In that case, population data are not needed anymore as the rates in the numerator and denominator are computed on the same population. An increase that is expressed as a percentage of the baseline is easier to understand for users who are not familiar with statistics. However, the percentage of the baseline does not inform about the significance of a possible excess, nor does it enable comparisons between population subgroups with different baseline mortality or population size, because it does not account for the difference in the expected standard variation. For instance, the meaning of a 100 % excess (doubling mortality) is very different if the expected number of deaths is 5 or 1000, and it also depends on the expected random variation expected during a period when no particular threat is present.

To compare measurements in populations with different means (baseline) and standard deviations (expected variation), a Z-score standardization must be performed. Subtracting the baseline will remove trend and cyclical seasonality from the weekly mortality while dividing the remaining variations by the expected standard deviation actually computes an indicator (the Z-score) that can be compared in populations with different distributions. The Z-score will enable the comparison of an increased risk of dying between countries and also between age groups or other groups of population. Furthermore, it can be applied to detect small increases in group of population where the risk of dying is already very small (e.g.5 to 14 years), providing that the series have been normalised first.

Interpretation of the Z-scores

The Z-score indicates how many standard deviations an observation is above or below the mean and allows comparing observations from groups with different normal distributions. Using Z-score standardization to express weekly mortality (or mortality during a specific period) will help answering the following questions:

- Is an increased risk of dying being observed compared to the expected risk? => positive Z-score
- Is that increase statistically significant? => Z-score above 1.96 (corresponding to a 5% risk of concluding wrongly to a “statistical significance”). Public

health significance can be different from statistical significance, as it should account for various other aspects of the health event.

- Does a risk of dying increase more in one population compared to another? => Difference between the Z-scores not null, no overlapping of the confidence interval of each Z-scores

The Z-score can be easily used to define alert thresholds. During the Euro-MOMO project, partner institutes were willing to keep the option of defining themselves the level of the threshold that would be used to define an alert, according to the particular situation and constraints of each country. Therefore, it was decided that the project itself would not define the threshold alert level but would focus on providing the relevant data to the countries to assess their own situation.

Need for detection and interpretation of sustained shifts

Detecting an excess of mortality using thresholds based on the standard deviation of a mortality time series will show when a single measurement (mortality during a specific week) is unusually high. However, small but persistent increases of mortality (called sustained shifts) can be observed over several consecutive weeks even if single measurements do not cross a +2 standard deviation threshold. The CUSUM method detects these shifts. They can be interpreted either as an excess mortality, when the mean of the series comes back to the expected after some weeks, or as a change in trend, if the mean remains permanently above the expected mortality. In that case, the model computing the expected mortality should be adapted to the new trend and avoid overestimating any excess mortality.

The Euro-MOMO pilot project

Summary of unexpected variations of mortality detected and studied since the implementation of the monitoring system.

During the 2009 A/H1N1 influenza pandemic, the system could show that there was no particular excess mortality being observed and that the elderly population was not particularly at risk in country using EuroMOMO to monitor mortality. The number of deaths in the younger age groups did not significantly increase, although some individual deaths in previously healthy children were notified in some countries. This seemed contradictory to the results observed in the United States however results are available only for the time series for Pneumonia and Influenza (P&I) mortality based on the 122 cities surveillance and not general mortality [28]. It is possible that due to the heightened preparedness and activities related to the influenza pandemic, deaths were more frequently attributed to influenza and pneumonia during that period of time. Unfortunately, information about deaths attributed to P&I will not be available before several months in many European countries because of large delays in cause of death codification. The pandemic mortality data from the United States and from Europe cannot be currently compared as population studied are different (i.e. P&I versus “all causes” mortality).

Although no increase in mortality was observed during the 2009 A/H1N1 influenza pandemic, a substantial increase occurred during the previous winter (2008-2009) in most of the participating countries. That increase could be related to the seasonal influenza outbreak that was particularly important that winter [29]. EuroMOMO results suggest that the impact of the 2008-2009 seasonal influenza epidemic (and by extension its virulence and pathogenicity) was very similar among European countries, despite various discrepancies in population age structure, geographical distribution or influenza vaccine coverage. When studying the geographical spread and the public health impact of an influenza epidemic, comparing resultant mortality between countries or population subgroups might be more accurate than comparing the notifications or proportions of influenza like illnesses (ILI) consultations, or the number of laboratory confirmed influenza virus isolations. These two indicators depend a lot on the health system and the habit of doctors and patients in each countries or even counties (e.g. proportion patients consulting when having ILI or proportion of patient samples among ILI). They are useful for comparing trends in time, but are hardly comparable between countries. Mortality indicators are crucial to compare the impact of public health threats between countries.

Excess mortality during the summer months is likely to be related to heat waves and other concomitant climatic factors or air pollution. Summer peaks of mortality can differ substantially from one country to another. The 2009-2010 winter increase (around week 2009-50 to week 2010-5) occurred when the spread of the influenza virus in Europe was very limited but at that time a wave of unusually cold temperature was affecting European countries [30]. The link between the increased mortality and cold was statistically significant in a multivariable model developed in Sweden (data not shown but available in the Swedish report for work package 6). It is reasonable to suggest that cold could have been a triggering factor for the observed 2010 winter increase of mortality in Europe

The heat and cold related mortality differs between countries according to the occurrence, duration, intensity of the waves of extreme temperature and also according to the behaviours of affected populations. Climatic factors, influenza epidemics or other factors also possibly increasing mortality can occur during almost similar time periods each year, although presenting variations in their amplitude or exact time of occurrence. In that case, multivariable models are needed to disentangle their effect on mortality. Some of these models have been developed by EuroMOMO and are presented in the WP6 report. These model are currently easy to apply retrospectively. However, for a better interpretation of weekly mortality variation development of simple multivariable models could easily but used on a weekly or monthly basis, as in many countries, most of the data needed are weekly available.

Limitations and Challenges of the Euro-MOMO pilot project

The Euro-MOMO algorithm computes useful and simple indicators in a timely manner which can detect and measure possible excess mortality in near real-time. However the quality of mortality monitoring does not depend only on the usefulness and internal validity of the algorithm, but also on the whole chain of data collection, data transmission, data management, data analysis, and interpretation of results.

The type and coverage of population monitored may be unclear and may vary between countries. In some countries, only a part of the population is monitored weekly and it is not always clear at the hub level what part of the population was covered in terms of size and geographical representativity. In addition, some countries did not include data for children who are under one year as the age at the time of death was only recorded in years and these children could not be distinguished from still births in the data base of the partner institute. Death registration of citizens living abroad and death registration of foreigners dying in the country may not be recorded similarly across European countries. This could have some impact in countries observing large turistic migration.

Infant mortality is a special issue. The death of a baby is registered only if the birth has been recorded first. The legal definitions for spontaneous abortion and premature birth may differ between countries, especially for children born alive under 500g of weight. This can affect the homogeneity of infant populations being recorded and studied in mortality series.

A key challenge to the Euro-MOMO project has been a relative lack of human and financial resources. During the project it was not unusual for data not to be provided because key operators were unavailable. Several partner institutes can not receive weekly mortality data due to logistical constrains and could never participate to the Euro-MOMO weekly monitoring. In addition, once the end of influenza pandemic was declared by the WHO, the funding for influenza monitoring decreased substantially and some institutes could not afford to buy mortality data adapted to weekly monitoring. Only 15 countries could monitor weekly mortality using the Euro-MOMO algorithm. Lack of retrospective weekly data, availability and or high price of weekly updates are the main reasons why some public health partner institutes could not contribute to the pilot phase.

Conclusion

The Euro-MOMO pilot project has clearly shown the feasibility and usefulness of a weekly mortality monitoring at National and European level. The value of the monitoring was particularly evident during the 2009 A/H1N1 influenza pandemic. Real time monitoring of all cause mortality should become part of the routine epidemiological surveillance to complement information already provided by disease specific and environmental surveillance. Alike disease surveillance, routine mortality monitoring requires adequate funding as well as dedicated and trained human resources. The validation of alerts and interpretation of the results of weekly mortality monitoring necessitate some experience in time series analysis of mortality data.

The precision of the system can be increased if analysis at sub-national level is also included and this would provide a more detailed picture across the whole of Europe. The Euro-MOMO pilot project is now ready to enter into the next phase, that of wider dissemination and implementation and to become an integral part of routine epidemiological surveillance across all of Europe.

Tables and Graphs

Figure 1: Flow of information of mortality data from the death occurrence to the release of Euro-MOMO bulletin.

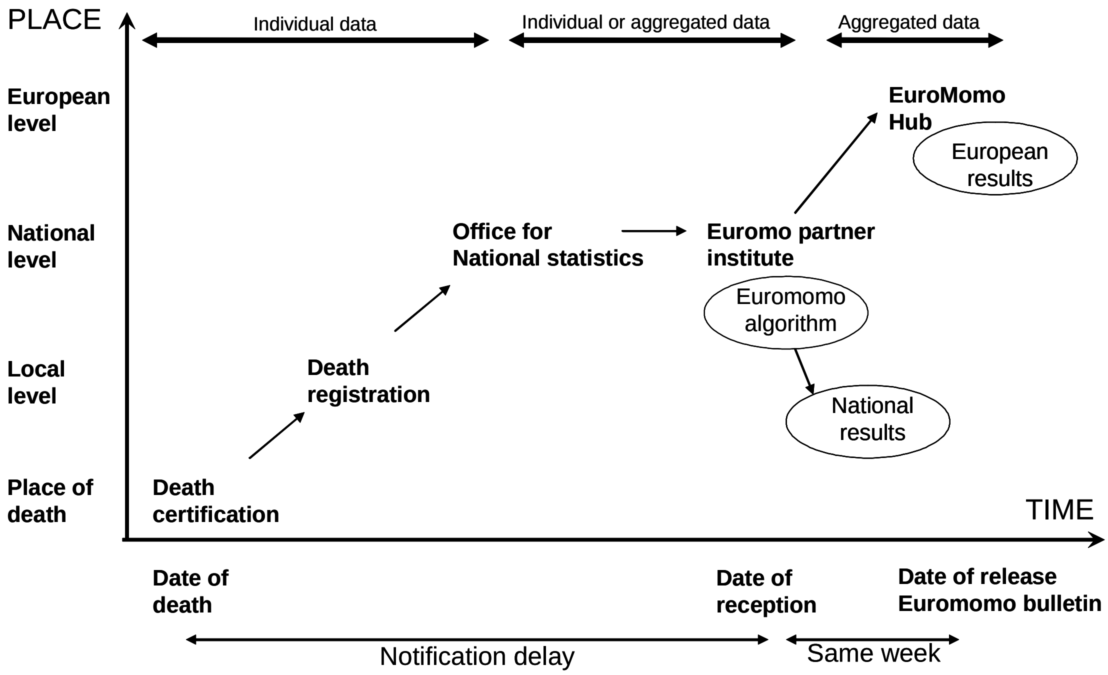


Figure 2: Principles of the computation of the corrected number of deaths according to the distribution of the delay in data transmission.

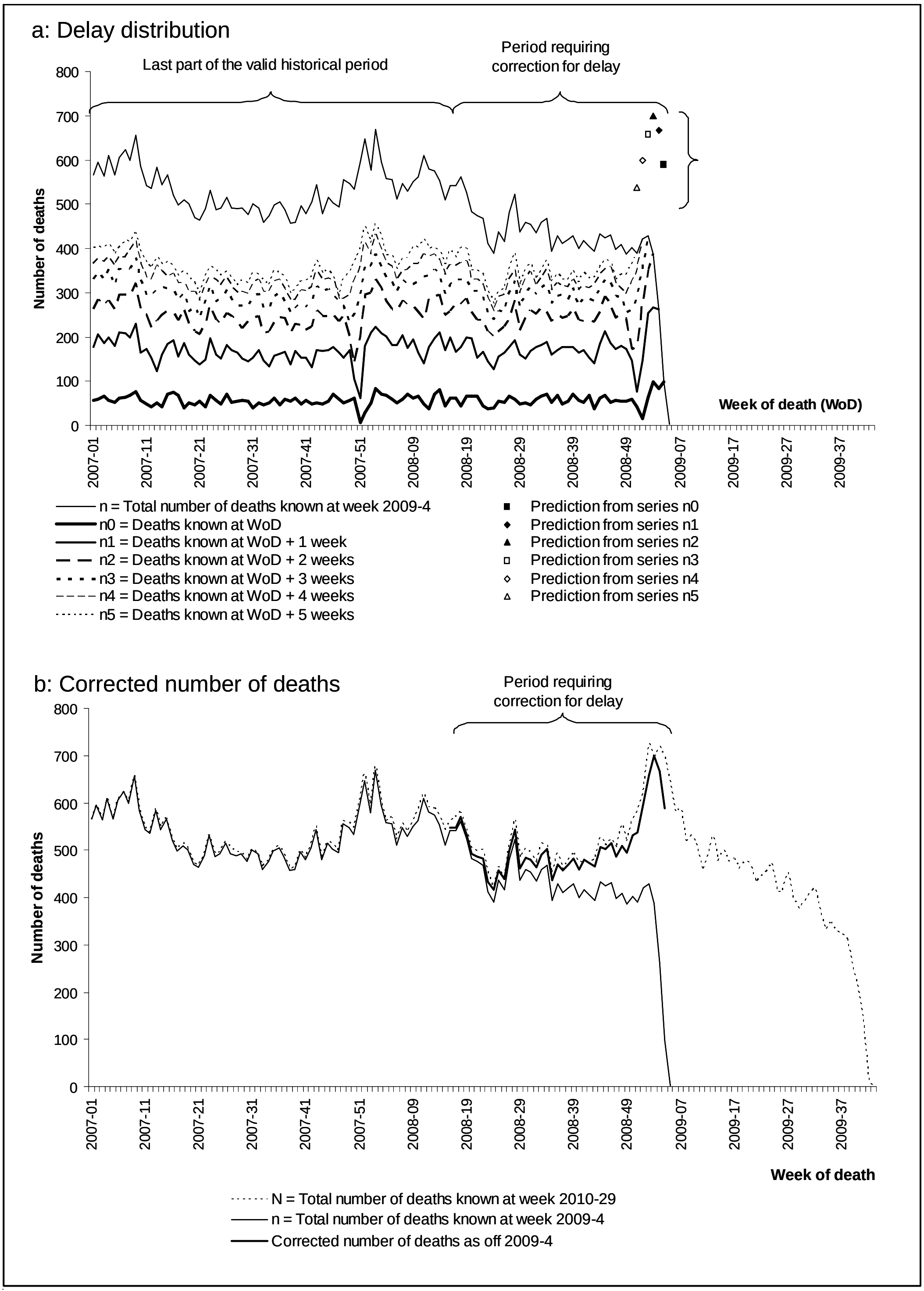


Figure 3: Principle of modelling of the expected baseline mortality and the measurement of mortality variation

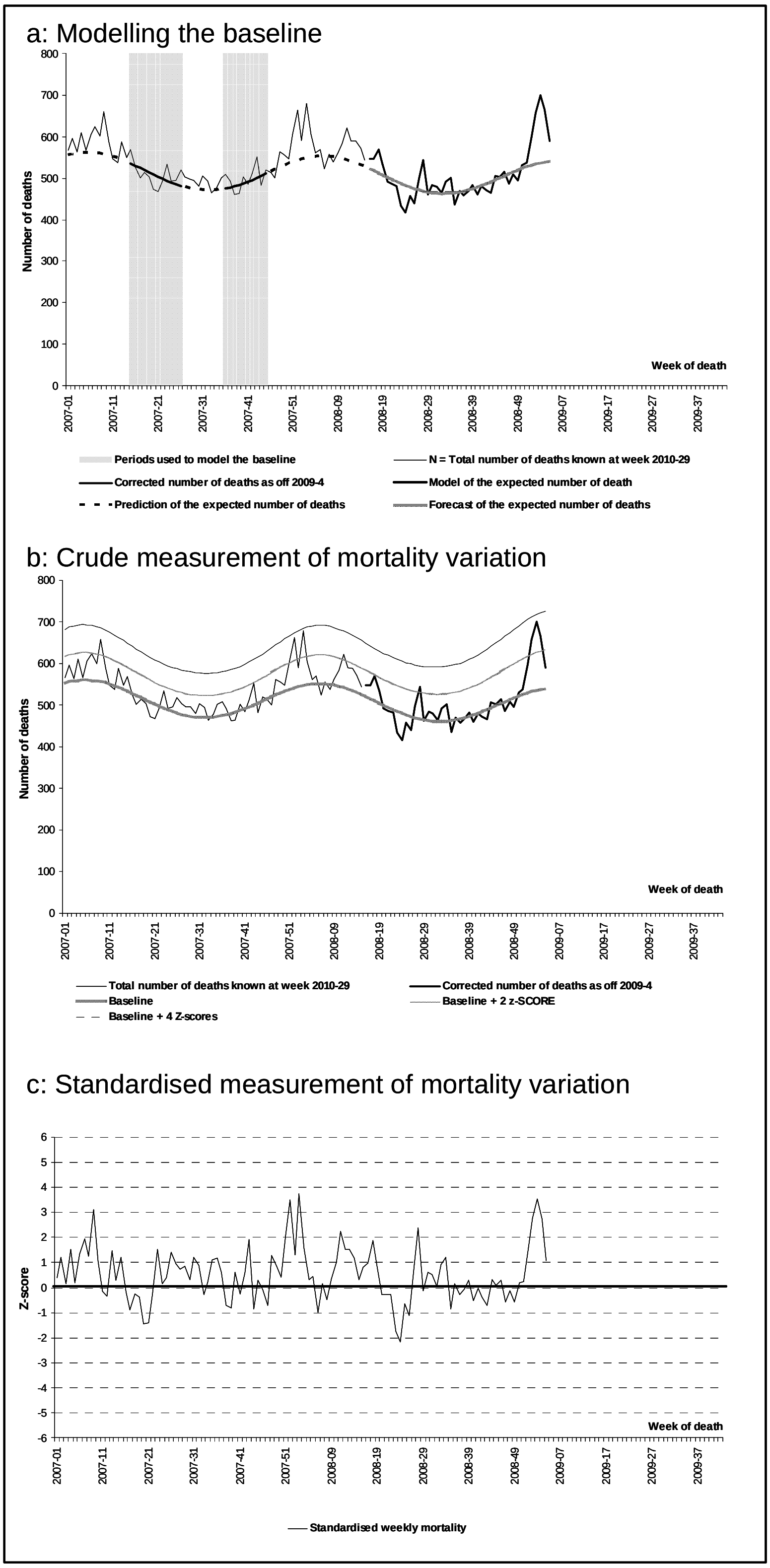


Table 1: Distribution by age group of population and mortality in the EuroMOMO Partner countries

	Population*					Number of deaths				
	Total	Proportion by age group (%)				Total**	Proportional mortality by age group (%) ***			
		< 5	5 to 14	15 to 64	>65		<5	5 to 14	15 to 64	>65
Belgium	10,753,080	5.7	11.1	66.0	17.1	104,509	0.5	0.1	17.8	81.5
Denmark	5,511,451	5.9	12.4	65.8	15.9	54,872	1	0.1	19.5	79.4
England and Wales §	54,809,100	6.1	11.4	66.1	16.4	491,348	0.8	0.1	16.5	82.6
Finland	5,326,314	5.5	11.2	66.5	16.7	49,883	0.4	0.1	21.7	77
France §§	64,369,147	6.2	12.3	65.0	16.5	548,689	0.9	0.2	20	78.9
Greece §§§	11,260,402	4.9	9.4	67.0	18.7	24,226	0.8	0.1	16.6	82.5
Hesse (Germany)	-	-	-	-	-	-	0.3	0.1	15.4	84.2
Ireland	4,450,030	7.6	13.3	68.0	11.0	28,898	1.1	0.2	21.3	77.6
Malta	413,609	4.9	11.0	70.1	14.1	3,221	0.8	0.2	18.2	80.9
Netherlands	16,485,787	5.7	12.1	67.3	15.0	134,235	0.6	0.1	17.5	81.8
Portugal	10,627,250	5.0	10.3	67.1	17.6	104,434	0.4	0.1	17.8	81.7
Slovenia	2,032,362	4.8	9.1	69.6	16.4	18,750	0.2	0.1	21.2	78.5
Spain	45,828,172	5.3	9.5	68.6	16.6	383,933	0.6	0.1	16.6	82.7
Sweden	9,256,347	5.8	10.9	65.6	17.8	90,080	0.4	0.1	13.2	86.3
Switzerland	7,701,856	4.9	10.4	68.1	16.6	62,476	0.6	0.1	15.3	83.9

* Source: Eurostat Populations 2009

** Source: Eurostat: http://appsso.eurostat.ec.europa.eu/nui/show .do?dataset=demo_magec&lang=en (update 04/05/2011)

*** Source: average proportions obtained on available Euromomo data, year 2007 to 2009.

§ England and Wales: Population data provided by Office for National Statistics http://w w w .statistics.gov.uk/statbase/Product.asp?vlnk=15106

§§ France: Population data and Total number of deaths are reported here for the w hole country, EuroMOMO is applied only 70% of the country, including overseas territories, w ith a homogeneous geographical coverage (Source InVS)

§§§ Greece: Total number of deaths and proportional mortality w as computed only for the eight participating counties (Athens, Keratsini, Pireas, Magnisia, Kerkira, Axaia, Kavala and Thessaloniki)

Figure 4: Proportion of national mortality data received every week in 12 of the EuroMOMO partner institutes, according to the delay for receiving the data.

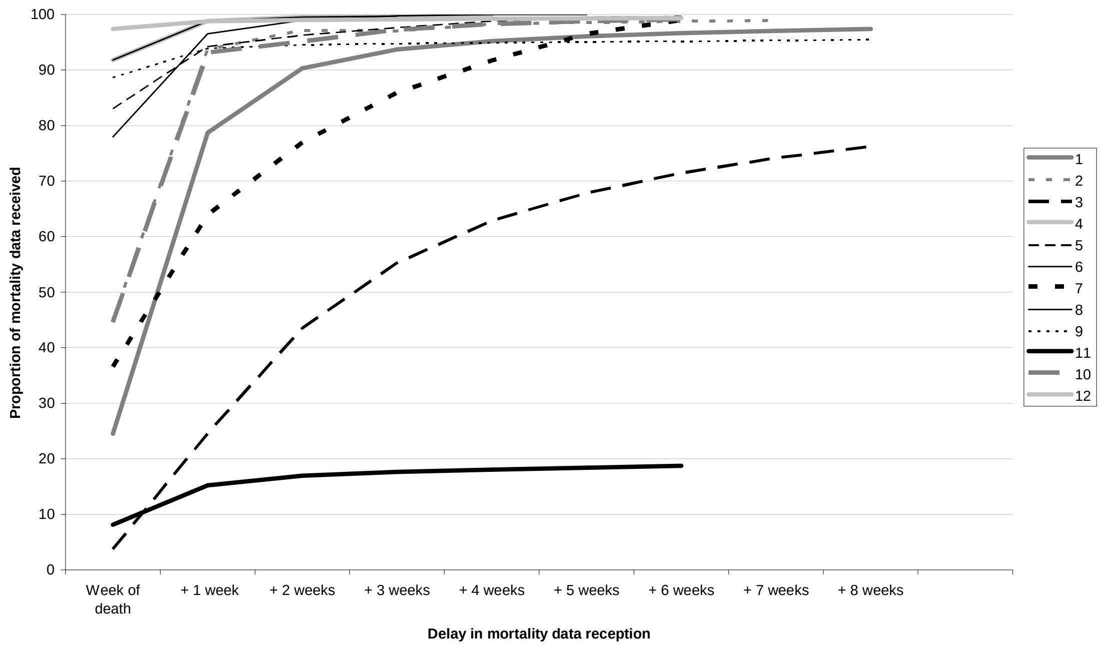


Figure 5: Graph of the mortality indicators computed each week by the EuroMOMO algorithm, example of output for Gothenburg county, Sweden as of 2010 week 38.

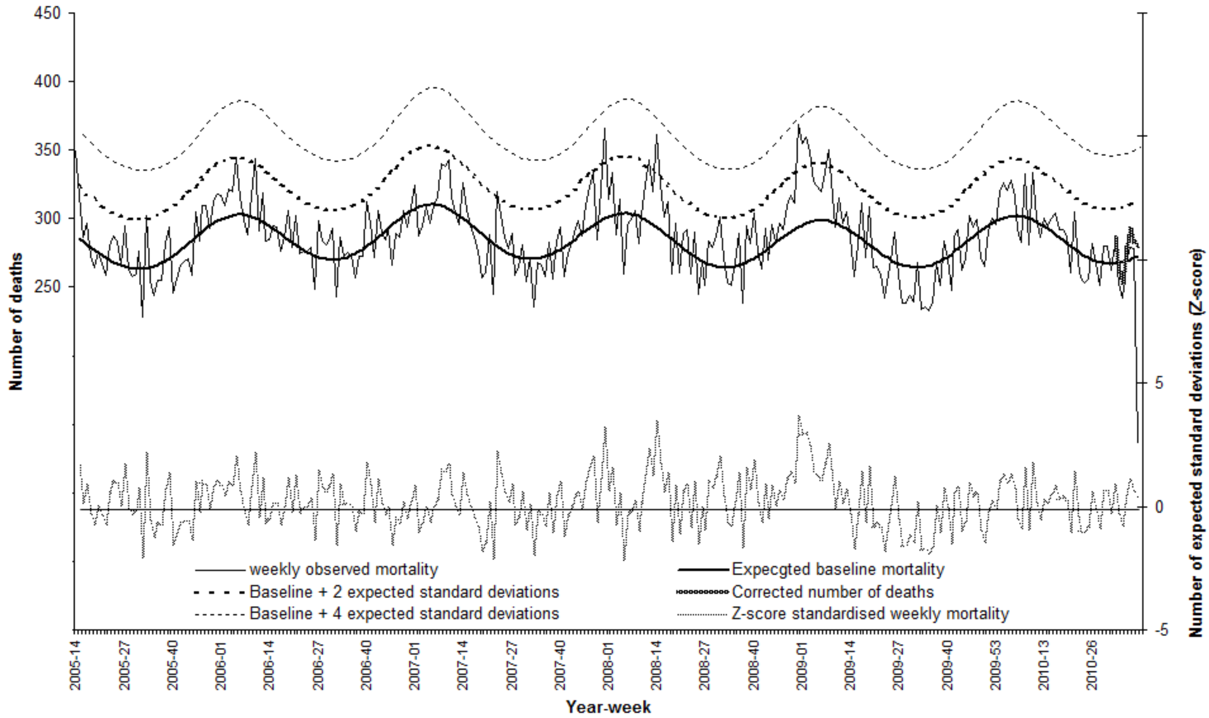
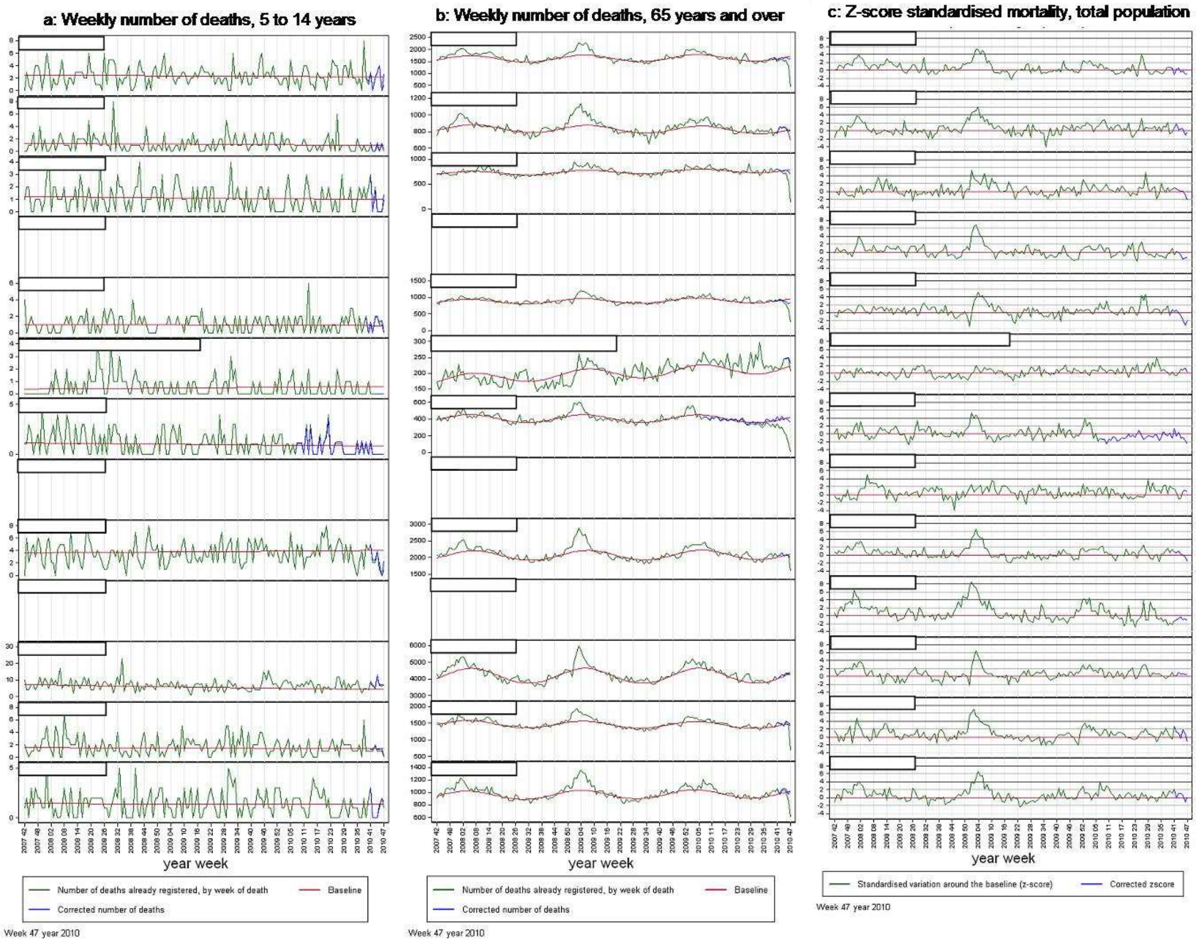


Table 2: Mortality indicators by age group, cumulated over the winter period (week 40 to week 20 each season), as computed and deliver weekly by EuroMOMO algorithm, example of Sweden.

		Period studied every winter (year-week to year-week)				
		2005-40 to 2006-20	2006-40 to 2007-20	2007-40 to 2008-20	2008-40 to 2009-20	2009-40 to 20010-20
	Duration of the Study Period	33	33	33	33	34*
0 to 4 years	**Total number of deaths**	254	211	204	232	255
	Expected number of deaths (baseline)	200	205	210	216	228
	Crude variation around the baseline	54	6	-6	16	27
	Z-score standardised mortality	2.9	0.04	-0.74	0.41	1.25
5 to 14 years	**Total number of deaths**	60	53	69	60	49
	Expected number of deaths (baseline)	56	53	51	49	48
	Crude variation around the baseline	4	0	18	11	1
	Z-score standardised mortality	-0.28	-1.16	1.09	0.58	-1.13
15 to 64 years	**Total number of deaths**	7841	7667	7857	7679	7827
	Expected number of deaths (baseline)	7623	7537	7452	7367	7507
	Crude variation around the baseline	218	130	405	312	320
	Z-score standardised mortality	2.04	1.11	3.83	2.95	3.03
65 years and over	**Total number of deaths**	49751	52081	51344	52350	51982
	Expected number of deaths (baseline)	49745	50453	50141	49694	50642
	Crude variation around the baseline	6	1628	1203	2656	1340
	Z-score standardised mortality	-0.31	5.54	4.25	8.83	4.56
Total	**Total number of deaths**	57906	60012	59474	60321	60113
	Expected number of deaths (baseline)	57626	58183	57906	57466	58356
	Crude variation around the baseline	280	1829	1568	2855	1757
	Z-score standardised mortality	0.63	5.68	5.06	8.74	5.52

* That period is longer in 2009 and 2010 because of the occurence of a week 53 in 2009.

Figure 6: Three examples of Euro-MOMO outputs at European level as displayed on the dedicated website. Comparison between country with crude mortality and Z-score standardize mortality.



Map 1: EuroMOMO partner countries having sent data for week 2010-47 and their mortality level expressed in standard deviation (Z-score) for the same week.

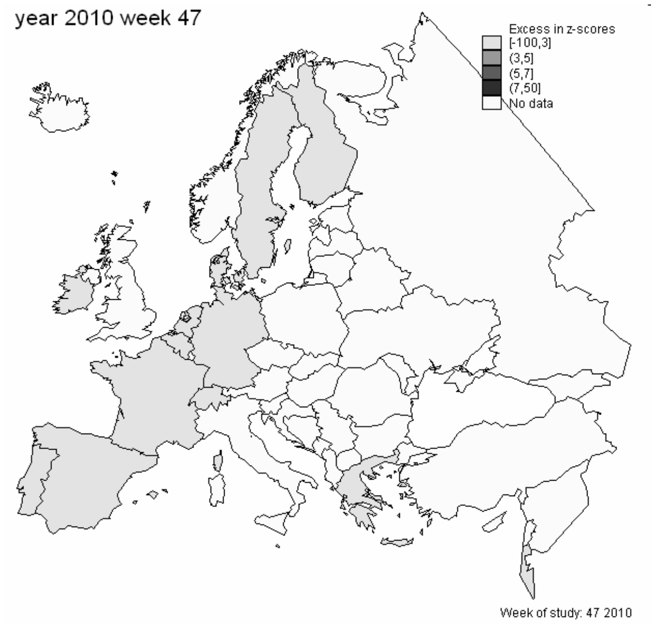
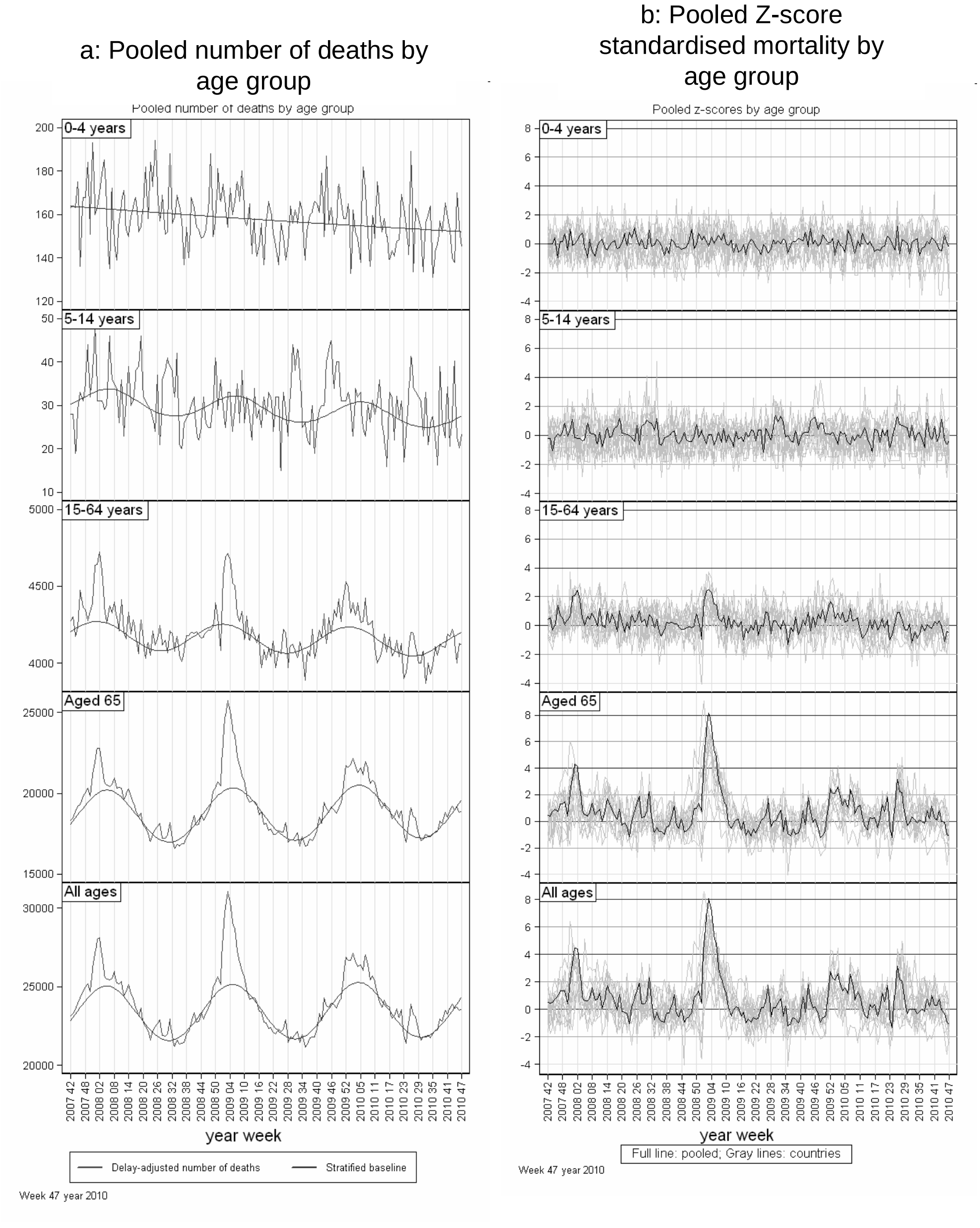


Figure 7: Pooled weekly mortality indicators in the 12 out of 13 countries that reported data to the EuroMOMO Hub week 2010-47.



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