EU-project:

CLOSING THE GAP – REDUCING PREMATURE MORTALITY BASELINE FOR MONITORING HEALTH EVOLUTION FOLLOWING ENLARGEMENT

Agreement number – 2003121
Acronym: HEM

INTERIM IMPLEMENTATION REPORT
Study period: 01/12/2004 – 01/12/2005
Technical report

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1. Executive summary

This document is a detailed report on one year project implementation. It contains general overview of the project aims and objectives but focuses on detailed description of applied methodology, first results of analyses and some guidelines for further work.

In the first year of the HEM project (during the period: 01/12/2004 – 01/12/2005) has realized following stages:

- The project has activated contacts in each of 8 New Member States and 2 Applicant countries and appointed Working Group and Expert Group and built up networks of collaborators at country level (See Annex 1 – Structure of the groups of collaborators)
- The project has conducted within the Expert Group many discussions on methods of analysis (See section 4 - Methodology)
- The project has conducted within the Working Group many discussions on availability of data (See section 3 – Data Sources and Annex 3 – Details on data sources, availability and ICD-codes used)
- The project has prepared joint databases of mortality and risk factors (See section 3 – Data Sources)
- The project has prepared final plan of analysis (See section 4 - Methodology)
- The project has prepared and organized I Conference on Health Transformation in Accession Countries
- The project has started analyses of the collected data
- The project has organized many meetings with the participation of Working Group members, Experts and members of Steering Committee (See Annex 2 )
- The project has prepared some reports on selected issues, some of which resulted in scientific publications in peer-reviewed journals (See section 5 – First Year Deliverables)
- The project has started working on deliverables, which resulted in given lectures and some still unpublished reports (See section 5 – First Year Deliverables)
- The project has started to prepare bibliography on risk factors influencing health in Europe.
- Organized the HEM project website (http://www.hem.waw.pl )
2. Introduction

2.1. History of the project
The project was submitted to the European Commission and has been accepted among other European Union programs in the field of public health for years 2003-2008. The grant agreement no 2003121 was signed on the 1st of December 2004, however the administrative matters allowed for using the resources only since June 2005.

2.2. People
The whole idea of the project originated from workshops and seminars, which were organized in 1990s in Cancer Epidemiology and Prevention Division, The Maria Skłodowska-Curie Memorial, Cancer Center and Institute of Oncology, Warsaw, Poland, by Professor Witold Zatoński and his co-workers.

Main analysis and scientific reports are done by the above institution’s team, with tight collaboration of such groups as Steering Committee, Working Group, Expert Group and Co-Investigators, which consist of international researchers and scientists. Witold Zatoński is the project leader and principal investigator. Marta Mańczuk is the project coordinator. This wide network of collaborators is fundamental and integral element of project’s implementation. Further information on the role and composition of these groups is given in Annex 1.

2.3. Purpose of the project
One of the most important challenges for health and economy of Central and Eastern European countries is to reduce the excess in adult premature mortality – defined for this project as death between the ages of 20 and 64. Lifestyle diseases, as cardiovascular diseases, liver cirrhosis, lung cancer, fatal injuries among young and middle-aged adults are still among the highest ever observed (e.g. in Hungary - liver cirrhosis was responsible in 1994 for around 20% of mortality in men, 20-44 years). At the same time in period of political and economic transformation (opening the market) inequalities in economic status and health increased. Additionally, accession to the EU and the change in market and regulatory institutions that it implies is a potential challenge for health if it is associated with an increase in the consumption of health damaging commodities. Trends in health losses from alcohol are of special concern in this context.
Therefore this project is aiming at analyzing the gap in adult premature mortality between the ‘EU15’ (the 15 member states as at 30/4/04) and new member states and applicant countries. Recommendations for improving the health of European Union population and for diminishing inequalities in health will be made.

The main focus will be on those risk factors for disease and injury responsible for the largest avoidable burdens of premature death. These will include tobacco, alcohol and the nutritional and physiological risk factors for vascular disease.

2.4. Why is the project mainly limited to fatal conditions?

There are 2 main reasons for this limitation:
- The limited availability and face validity of data on health levels among the living;
- The likelihood that the major causes of lost healthy time that are not also leading causes of death are not important contributors to East/West differences in overall health levels. Such conditions (as ranked by the Global Burden of Disease estimates of the WHO for Europe in 2000) include: unipolar depressive disorders, osteoarthritis, digestive diseases, adult onset hearing loss, age-related vision disorders and schizophrenia.

2.5. Objectives of the project

By realizing this project we would like to improve understanding of underlying causes of health differences between two groups of countries, one of which is EU15, which means before May 2004, and the other consists of 8 new EU member states from Central and Eastern countries and two applicant countries.

There is as well a need to identify and quantify major health determinants responsible for the gap existing in adult premature mortality between those two groups of European Union Member States.

Within this project we will try to assess the impact of enlargement process, i.e. entry of applicant countries into the single market, with special regard to alcohol; define priorities for intervention: both in general (for all accession countries) as well as specifically for each country.
The main tangible outcome of our project will be comprehensive report, called a Blueprint including major indications for public health action. The Blueprint will be presented to the European Commission and Governments of the countries of interest, in order to encourage the adoption of policies appropriate to the public health challenges faced.

Last but not least objective of this project will be to widely disseminate, in local languages, the evidence- and science-based data on health status and on the possibilities for reducing adult premature mortality, especially in 8 new EU member states from Central and Eastern countries and two applicant countries in local languages.

3. Result 1: Scope of interest

As a result of many fruitful discussions within and between the groups of collaborators (Working Group, Expert Group, Steering Committee), taking into consideration possibilities to carry out specific analyses, availability and reliability of data and thorough analysis of the project’s subject there has come to consensus in such matters as geographic scope, time scope of analyses, age groups of interest, diseases and injuries taken into consideration and considered risk factors.

3.1. Geographic Scope

The main geographic area of interest are eight new European Union member states, which joined EU in May 2004, these are Poland, Czech Republic, Slovakia, Slovenia, Hungary, Latvia, Lithuania, Estonia and two applicant countries: Romania, Bulgaria. For comparison we have been analyzing as well all EU15 countries, these are Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden and United Kingdom.

We have been analyzing data for Russia as a control country and in some particular analysis also other countries, depending on the need. For example, while analyzing alcohol burden of mortality we compared our analysis as well to some other South-Eastern European countries (for instance Moldova), where liver cirrhosis mortality is very high as in the neighbouring countries included in the project.

Depending on the analyzed condition the set of control countries might differ.

3.2. Time scope

There are three time dimensions of our analyses:
For all longitudinal epidemiological descriptive analyses, that consists mainly of
time trends we have been using data since the year 1959 (or the first year for which
mortality data are available) until the year 2002.
- For the cross sectional analyses of attributable burdens the year of reference will
be 2002 (if available), for both risk factor distributions and for mortality.
- Besides the two above approaches we would like to conduct projections for the
main causes of adult premature mortality until the year 2012. So far we have done
this for lung cancer mortality. A description of methodology can be found in
Annex 4.

3.3. Age groups of interest
The age groups were discussed at the pre application meeting in October 2003. It was decided
then that the analyses will be conducted in the ages 20-64. This period was divided into two
age ranges: premature mortality of young adults – 20-44, and premature mortality of middle-
aged adults – 45-64.
This definition of premature mortality was adopted because:
- In Eastern Europe middle age is considered to extend to 60-64 years, so it is surely
higher than World Bank definition – to 59, but definitely not to 65-69. This social
perception is concordant with a definition of (adult) deaths before 65 as
‘premature’.
- Male mortality levels for many eastern European countries are such that, half of
male deaths occur before the age of 65. This applied for example in Hungary in
2001
- 65 years is the standard retirement age. Below that age, the loss of life has a direct
effect on economic productivity in addition to its intrinsic (negative) value. Given
the increasing emphasis on the importance of health levels to economic
performance in Europe and the need for new member states to close the economic
gap with the EU15 in addition to the health gap, it makes good sense to
concentrate on the productive years.
- However as life is equally valid before and after the age of 65, we propose to
analyze as well mortality in age groups above 65 where this is likely to be
informative for the topic under consideration.
3.4. Diseases and injuries
There are four main groups of diseases that contribute in the greatest degree to the adult premature mortality in Europe. These are lung cancer (and other tobacco-related cancers), liver cirrhosis, vascular diseases and injuries. Annex 3 lists the ICD 9 and 10 codes for these groups of conditions.

3.5. Risk factors
In parallel we would like to analyze influence of such risk factors as tobacco, alcohol and selected nutritional/physiological risk factors contributing to vascular disease.

4. Result 2: Data sources
The conduct such wide-range and diversified set of analyses a comprehensive collection of reliable and valid data is important. Therefore the project team with tight collaboration of Working Group has conducted thorough search and carried discussions on availability and reliability of data, given what set of data would be really needed to carry out the project and obtain satisfactory results. These actions resulted in developing several databases. A list of needed data, and a description of data used in analyses so far can be found in Annex 3.

4.1. Mortality
As far as mortality data is concerned we have been using WHO database, where data are collated in systematic and uniform way. The calendar years for which mortality data are available for each country can be found in Annex 3.

Mortality database was first designed and then built on the ground of World Health Organization sources.

4.2. Exposure
The lifestyle risk factors exposure data are usually much more difficult to obtain although a foundation has been established by WHO’s SuRF collection and the estimates of risk factor distributions made as part of the Comparative Risk Assessment project. We have begun to extend and cross check these data by building up a network of collaborators. Usually such data come from national surveys.
There was first developed proposal and then built database of behavioural risk factors according to which data from country representatives are collected.

As far as dietary products consumption is concerned there was built user-friendly database on Food and Agriculture Organization sources.

4.3. Denominators
To ensure consistency we use population data from the same source as the mortality data – the national estimates collated in the World Health Organization database. We have cross-checked the differences between the national population estimates collated in the WHO mortality database and the UN Population Division estimates for the same countries as used for the GBD estimates in WHO. Generally the differences are small for European countries and a decision has been made to use the official national estimates collated in the WHO mortality database. These small differences in denominator estimates will create small, but generally unimportant, differences between our results and comparable statistics generated by the GBD group.

5. Result 3: Methodology
During the discussions within Expert Group and Principal Co-Investigators we have agreed that the project’s size and its multidimensional character require different analytical approaches. The particular stages of analyses have been discussed among principal co-investigators (Experts) and Steering Committee members

Final conclusions on the plan of analyses have been drawn at the annual internal meeting of collaborators (Steering Committee, Experts, Working Group) in November 2005.

5.1. Measures of mortality
Three types of mortality measure will be employed:

- Counts (numbers of deaths)  
  These help convey absolute magnitudes.

- Rates (including age-specific and age-standardized rates) 
  These are optimal for comparing cause-specific mortality levels and trends between countries.

- Years of Life Lost (YLL) from deaths at ages 20 to 64
There are some opinions that this methodology can be useful for ranking the social importance of causes of death, however this is still not standard. The exact form of the YLL measure to be used is still under discussion. A leading candidate is the YLL component of the Disability Adjusted Life Year. This can be used with or without discounting and age-weighting.

5.2. Temporal evolution of the conditions of interest
To identify years in which trends change and to measure rates of change in the intervals between these changes in trend, the regression software Joinpoint had been used. More information on this methodology can be found in Annex 4.
Using this approach we have so far been able to analyze evolution of mortality due to lung cancer, liver cirrhosis, vascular diseases and injuries for all 25 countries of interest (check Geographic scope) according to age and sex. This has provided a useful overview of trends in conditions of interest in these countries over the past 5 decades.
Exemplary analysis on lung cancer has been presented in the paper published in British Medical Journal, in July, 2005.

5.3. Attributable mortality
For the risk factors of interest we intend to estimate the burden of attributable mortality – expressed both as counts of deaths and as YLL. For this kind of analysis, besides data on mortality we would need relative risks and estimates of the distribution of exposure levels for each risk factor of interest. Relative risks will be obtained from various meta-analyses and scientific publications. In some cases expert judgment will need to be employed, making use of relevant expertise amongst those associated with the project. Estimates of risk factor distributions have been obtained with a help of country collaborators and from the WHO SuRF database and the Comparative Risk Assessment project.

Alcohol
As of the writing of this update, we have conducted alcohol-attributable mortality analyses for Poland, Hungary, Sweden, Czech Republic, Latvia, Lithuania and France. Further information on methodology can be found in Annex 4.
This analysis together with temporal analysis of liver cirrhosis mortality, fatal injuries and oral cavity and larynx cancer mortality will provide a comprehensive account of the contribution of alcohol to adult premature mortality in Europe.
**Tobacco**

We have conducted tobacco-attributable mortality analyses using the standard methodology for Poland, Czech Republic. Further information can be found in Annex 4. We have as well adjusted the Peto Lopez method to the project needs and obtained first results for Poland. We are planning to conduct the calculations as well for all other countries of interest and compare the results to tobacco-attributable mortality analyses that were computed using Global Burden of Disease methodology. Information on the Peto Lopez method can be found in Annex 4.

This analysis together with temporal analysis of lung cancer mortality will provide a comprehensive account (useful indicators) of the contribution of tobacco to adult premature mortality in Europe.

**The nutritional/physiological risk factors contributing to vascular disease – preliminary phase: plan**

These can be divided into proximal and intermediate risk factors. Their identity and potential use in envisaged analyses are given in the table. A protocol and work plan for these analyses is yet to be agreed.

<table>
<thead>
<tr>
<th></th>
<th>Intermediate</th>
<th>Proximal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attributable</td>
<td>Tobacco, alcohol, fruit and vegetable consumption, physical inactivity</td>
<td>Usual systolic blood pressure, usual cholesterol concentration, BMI</td>
</tr>
<tr>
<td>mortality in 2002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changes over time</td>
<td>Tobacco, alcohol, index of fat type*</td>
<td></td>
</tr>
</tbody>
</table>

* From Food balance sheets and other sources

Analysis of diet has just started. We have built a functional database and filled it with data from the Food and Agricultural Organization’s Food Balance Sheets. There is a hope that these data will be useful for deriving indices of types of fat consumed. They are known not to provide valid measures of total food energy consumption. They may provide some useful indications of trends in the consumption of fresh fruits and vegetables. First descriptive analysis has already been done, details can be found in Annex 4.

We expect to be able to replicate at country level and for the year 2002, the types of attributable risk estimates for vascular disease made for the WHO sub-regions in the
Comparative Risk Assessment project. (We have already used these data in our explorations of differences between Europe A, B and C.)

5.4. Analyses of changes over time
Temporal trends in vascular mortality in this region are unlikely to be well accounted for by available data on the conventional vascular risk factors – with the partial exception of smoking. In the temporal analyses, it is planned to explore the association between the changes in fat type, resulting in part from the effects on prices of the withdrawal of large consumer subsidies for animal products, and national trends in vascular mortality. In addition we will continue to explore the implications of multi-causality for the choice of preventive strategies in populations at high absolute risk of premature death from vascular causes – already begun in our report on differences between the European sub-regions.

6. Result 4: First Year Deliverables

6.1. Scientific papers published in peer-reviewed journals
Lung cancer mortality at ages 35-54 in the European Union: ecological study of evolving tobacco epidemics.
Didkowska J, Manczuk M, McNeill A, Powles J, Zatonski W.

Changes in dietary fat and declining coronary heart disease in Poland: population based study.
Zatonski WA, Willett W.

The contribution of leading diseases and risk factors to excess losses of healthy life in eastern Europe: burden of disease study
Powles J, Zatonski W, Vander Hoorn S, Ezzati M
BMC Public Health 2005, 5:116

Infant mortality in Central Europe: effects of transition.
Zatoński WA, Mikucka M, LaVecchia C, Boyle P
Under revision – Gaceta Sanitaria
6.2. Other project publications
On the basis of the materials- prepared by our team, there were pieces of text published in WHO book: Preventing Chronic Diseases a vital investment.
World Health Organization 2005

6.3. Lectures
Lectures on adult premature mortality, cardiovascular diseases, and other non-communicable diseases in Eastern Europe:

The health implications of an expanded EU: threats or opportunities for the UK and Europe?, Royal College of Physicians, London, 10 March, 2005

6th International Conference of Preventive Cardiology”, Iguassu , 21-25 May, 2005

Population Health Research Institute, McMaster University and Hamilton Health Sciences, Hamilton, 28 July, 2005

UK Presidency of EU: Tackling Health Inequalities Summit”, London, 17-18 October, 2005

7. Expected results of the project
The main long-term aim of the Project is to help speed up the decline of premature mortality from preventable causes, improving the health of European Union population in addition to securing the intrinsic benefits of better health

It is expected that main determinant factors of present health situation, especially of premature mortality will be identified. The impact on mortality of each factor, including alcohol, tobacco and selected nutritional factors will be quantified as well. The analysis will be included in the Blueprint.

Recommendations for public health intervention aimed at improving health status in the applicant countries as a region, as well as for each country separately will be produced. The recommendations will be included in the Blueprint.
The results will be disseminated (in English and in local languages) among policy makers, politicians, scientific community, and public opinion. The channels of dissemination will include: scientific and political conferences (the conferences will be accompanied by press conferences and media releases), publications in peer-reviewed journals, production as well as publication of a Blueprint, containing recommendations for health politics, project website in English and local languages.

8. Forthcoming activities in the second year of project implementation
(period from 01/12/2005 – 01/12/2006)

In the second year of the HEM project (during the period: 01/12/2005 – 01/12/2006) has planned to realize following stages:

Collaboration with Working Group:
- Deadline for submitting data (end of January 2006),
- Registering collected data into projected databases,
- Discussions on comparability of collected data
- Meeting with Working Group Member – Slovenia (26-27 January 2006)
- Meeting with Working Group Member – Bulgaria (24 February 2006)
- Meeting with Working Group Member – Hungary (3-4 April 2006)

Analysis of collected data:
- Workshop on projections (December 2005);
- Finalizing analysis of alcohol-attributable mortality in particular countries and preparing comparative analysis
- Finalizing analysis of tobacco-attributable mortality in particular countries and preparing comparative analysis)

Expert group discussions on methods and results of analysis:
- Meeting of Principal Co-Investigators (30-31 January 2006)
- Further meetings and teleconferences aiming at discussing implementation of the project
- Meeting of Principal Co-Investigators (19-20 June 2006)

Preparing reports on selected issues (YLL and life expectancy, premature mortality, lung cancer, liver cirrhosis, vascular diseases, injuries, smoking, alcohol drinking, obesity)

Preparation of the Country reports
- Writing and editing exemplary country report for Poland
- Setting out tasks for country representatives and guidelines for country reports
- Writing country reports
- Edition and preparation for publishing
II Working Meeting On Adult Premature Mortality in European Union – Internal conference:

- October 16-17, 2006
- Presenting methodology of analyses (alcohol-attributable fraction, tobacco-attributable fraction)
- Presenting final results of analyses
- Discussing details of publishing and disseminating the Blueprint

Preparation preliminary version of the Blueprint and recommendations:

- Publication of the Blueprint:
- Discussion on the recommendation within co-principal investigators, Expert group and Steering Committee
- Preparing conclusions for the final publication

List of the Annexes

Annex 1 – Structure of the groups of collaborators
Annex 2 – Schedule of the meetings carried out during the first year of the project
Annex 3 – Details on data sources, availability and ICD-codes used
Annex 4 – Details on methodology
Annex 1 – Structure of the groups of collaborators

**Steering Committee**

1. Terms of reference
Preparing merits of the project and plan of analysis, contributing to analyzing the data, preparing individual reports and the Blueprint.

2. Membership
Leif Aaro,
Research Center for Health Promotion, Norway
Peter Boyle,
International Agency for Research on Cancer, France
Anna Gilmore,
European Centre on Health of Societies in Transition London School of Hygiene and Tropical Medicine, United Kingdom
Eric Jougla,
Centre d’Epidemiologie sur les Causes Medicales de Deces, France
Jose Martin – Moreno,
Catedratico de Medicina Preventiva y Salud Publica Universitat de Valencia, Spain
Eva Negri,
Department of Epidemiology Instituto di Reserche Farmacologiche "Mario Negri", Italy – CHAIR
Fred Paccaud,
Institute for Social and Preventive Medicine, Faculty of Biology and Medicine of Lausanne, Switzerland
Richard Peto,
Clinical Trial Service Unit, United Kingdom
Vesna-Kerstin Petric,
Sector for Health Promotion and Healthy Life Styles Ministry of Health, Ljubljana, Slovenia
Pekka Puska,
National Public Health Institute, Finland
Mike Quinn,
National Cancer Intelligence Centre, United Kingdom

**Principal Co-investigators**

Paolo Boffetta
Genetics and Epidemiology Cluster, IARC, France
John Powles
Department of Public Health and Primary Care; Institute of Public Health, Cambridge, UK
Jurgen Rehm
Addiction Policy, Public Health Sciences, Faculty of Medicine, University of Toronto, Canada
Carlo LaVecchia
Laboratory of Epidemiology, Instituto di Reserche Farmacologiche "Mario Negri", Italy
Walter Willet
Department of Nutrition, Harvard School of Public Health, USA

**Working Group / Expert Group (will be extended)**
Terms of reference
Creating joint database, co-interpreting data, participation in preparing reports on selected issues, contributing to preparing the Blueprint.

Membership

CZECH REPUBLIC
Jana Brozova
Institute of Health Information and Statistics
Zdenek Kucera
Health and health policy, Institute of health policy and economics
Alexandra Pilipcincova
Institute of Clinical and Experimental Medicine
Rudolf Poledne
Institute of Clinical and Experimental Medicine

SLOVAKIA
Hana Vrbanova
Department of Health Promotion and Health Education, Regional Institute of Public Health
Tibor Baska
Department of Epidemiology, Institute of Public Health, Jessenius Faculty of Medicine, Comenius University (JFM CU)

SLOVENIA
Tit Albreht
Institute of Public Health

HUNGARY
Monika Bene
Hungarian Central Statistical Office, Budapest
Csilla Kaposvari
Head of Department of Health Monitoring and Epidemiology of NCDs, National Center for Epidemiology

LATVIA
Iveta Pudule
Strategy Development Department Health Promotion State Agency

LITHUANIA
Jurate Klumbiene
Preventive Medicine Department, Institute of Biomedical Research, Kaunas University of Medicine

ESTONIA
Raul Kiivet
Head of the Department of Public Health, University of Tartu

BULGARIA
Lyubomir Ivanov
Plamen Dimitrov
National Center of Public Health Protection, Sofia

ROMANIA
Vladimir Bacarea
University of Medicine and Pharmacy, Targu Mures
Annex 2 – Schedule of the project’s meetings

Meetings already held

<table>
<thead>
<tr>
<th>DATE</th>
<th>NAME OF THE MEETING – AIM</th>
</tr>
</thead>
<tbody>
<tr>
<td>14-16 December 2005</td>
<td>Meeting of Experts on future project plan</td>
</tr>
<tr>
<td>2-3 March 2005</td>
<td>Meeting of Experts on Alcohol-attributable Mortality analysis</td>
</tr>
<tr>
<td>13 June 2005</td>
<td>Meeting of Experts on alcohol and tobacco burdens – preparation for workshop in July</td>
</tr>
<tr>
<td>20 October 2005</td>
<td>Meeting of Working Group members – details of collaboration</td>
</tr>
<tr>
<td>21-23 November 2005</td>
<td>I Working Meeting On Adult Premature Mortality In European Union – Internal conference</td>
</tr>
</tbody>
</table>

Meetings to be held

<table>
<thead>
<tr>
<th>DATE</th>
<th>NAME OF THE MEETING – AIM</th>
</tr>
</thead>
<tbody>
<tr>
<td>19-23 December 2005</td>
<td>Workshop on projections</td>
</tr>
<tr>
<td>26-27 January 2006</td>
<td>Meeting with Working Group Member – Slovenia</td>
</tr>
<tr>
<td>30-31 January 2006</td>
<td>Meeting of Principal Co-Investigators</td>
</tr>
<tr>
<td>24 February 2006</td>
<td>Meeting with Working Group Member – Bulgaria</td>
</tr>
<tr>
<td>3-4 April 2006</td>
<td>Meeting with Working Group Member – Hungary</td>
</tr>
<tr>
<td>19-20 June 2006</td>
<td>Meeting of Principal Co-Investigators</td>
</tr>
<tr>
<td>October 16-17, 2006</td>
<td>II Working Meeting On Adult Premature Mortality In European Union – Internal conference</td>
</tr>
</tbody>
</table>
Annex 3 – Details on data sources, availability and ICD-codes used

Detailed list of needed data

**Mortality data**
Critical review of WHO mortality database
Overall mortality and population according to education
Eventually chosen conditions according to education

**Incidence data**
HIV/AIDS
Hepatitis (B, C),

**Risk factors data**
tobacco (long term data)
alcohol (long term data)
diet (long term data)

Detailed description of the data on deaths and rates used in our analyses

**Data on deaths:**
In all analyses of mortality we use WHO database, which is available at WHO website. The details are described at 325 pages of WHO Mortality Data base documentation, which is as well available at WHO website (http://www3.who.int/whosis/mort/text/download.cfm?path=whosis,inds,mort,mort_download&language=english).

Deaths on specific causes according to ICD codes as well as population are derived from above source in 5 years age groups, according to sex. The last age group is 85+.

**Rates per 100 000 population:**
Age-specific rates are computed in 5 years age groups dividing number of deaths by population per 100 000.

To standardize rates we use direct method and world population weights. A standardized rate in given age range is nothing more than the weighted average of age-specific rates, weighted with world population weights in given 5 years age groups.

**Years of life lost:**
Given the established international currency of Burden of Diseases methodology and the YLL methodology within it, a decision has been taken to use this particular procedure. Such a choice implies the selection of the same reference life table against which years of life lost are calculated. The issue then remains whether or not to use time discounting and age weights in procedures as employed in GBD methodology.

One provisional solution to this is to calculate YLL using both methods: with 3% discounting and age weights and with nor discounting neither age weighting.

To calculate YLL we used table of life expectancies at the average ages of death derived from WHO website and age-specific rates of mortality. Time lost due to premature mortality (20-64) was discounted using 3% discount rate. The picture below shows number of years of life lost among males and females and time lost due to premature mortality.

**References:**
Standard life tables. Available on the worldwide web at www.who.int/entity/healthinfo/bodreferencestandardlifetable.xls

Detailed data range for each country

Mortality data:
European Union until May 2004
Austria, 1959-2002
Belgium, 1959-1997
Denmark, 1959-2000
Finland, 1959-2002
France, 1959-2000
Germany, 1990-2001
Greece, 1961-2001
Ireland, 1959-2001
Italy, 1959-2001
Luxembourg, 1967-2002
Netherlands, 1959-2000
Portugal, 1959-2002
Spain, 1959-2001
Sweden, 1959-2001
UK, 1959-2002

New European Union Member States since May 2004
Czech Republic, 1970-2002
Estonia, 1981-2002
Hungary, 1959-2002
Latvia, 1980-2002
Lithuania, 1981-2002
Poland, 1963-2002
Slovakia, 1971-2002
Slovenia, 1985-2002
Malta, 1965-2002
Cyprus – no data

Applicant countries
Bulgaria, 1964-2002
Romania, 1969-2002

Control countries
Russia, 1980-2002

Exposure data (collected so far):
European Union until May 2004
France, alcohol 2002
Italy - tobacco: 2005
Sweden, alcohol 2002
New European Union Member States since May 2004
Hungary, alcohol 2002
Latvia, alcohol 1999
Lithuania - alcohol 2002, tobacco: 2004
Slovakia – tobacco: 2003,

Detailed ICD codes for the conditions of interest

Temporal evolution of mortality analyses:

<table>
<thead>
<tr>
<th>Condition</th>
<th>ICD-9</th>
<th>ICD-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant neoplasm</td>
<td>B08-B14</td>
<td>C00-C97</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>B101</td>
<td>C33-C34</td>
</tr>
<tr>
<td>Oral cavity and pharynx, Larynx</td>
<td>B08, B100</td>
<td>C00-C06, C09, C10, C12-C14, C32</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>B347</td>
<td>K70, K74</td>
</tr>
<tr>
<td>CVD</td>
<td>B25-B30</td>
<td>I00-I99</td>
</tr>
<tr>
<td>Injuries</td>
<td>B47-B56</td>
<td>V01-Y98</td>
</tr>
</tbody>
</table>

Outstanding issues:
Consistent aggregations of causes of death for use to cross different goals and components of the project.
The question of adjustment of the raw mortality data to allow for between countries variation in the use of ill defined codes. This issue still requires resolution.
Annex 4 – Details on methodology applied

Working paper on Joinpoint regression program

This software calculates the simple regression with 0 up to 3 breakpoints so there are 4 models:
JP0 – no breakpoints,
JP1 - 1 breakpoint,
JP2 - 2 breakpoints,
JP3 - 3 breakpoints.

Then the models are tested by conducting various statistical tests and best fit is being chosen. The software estimates as well annual percentage change between the breakpoints.
Joinpoint is statistical software for the analysis of trends using joinpoint models. The software takes trend data (e.g. cancer rates) and fits the simplest joinpoint model that the data allow. The user supplies the minimum and maximum number of joinpoints. The program starts with the minimum number of joinpoint (e.g. 0 joinpoints, which is a straight line) and tests whether more joinpoints are statistically significant and must be added to the model (up to that maximum number). This enables the user to test that an apparent change in trend is statistically significant. The tests of significance use a Monte Carlo Permutation method. The models may incorporate estimated variation for each point (e.g. when the responses are age adjusted rates) or use a Poisson model of variation. In addition, the models may also be linear on the log of the response (e.g. for calculating annual percentage rate change). The software also allows viewing one graph for each joinpoint model, from the model with the minimum number of joinpoints to the model with maximum number of joinpoints.

Estimated Annual Percent Change
In the joinpoint analysis, the best fitting points (the “joinpoints”) are chosen where the rate changes significantly. The analysis starts with the minimum number of joinpoints (e.g. zero joinpoints, which is a straight line), and tests whether one or more joinpoints (up to three) are significant and must be added to the model. In the final model, each joinpoint (if any) indicates a significant change in the slope. The estimated annual percent change (EAPC) is then computed for each of those trends by fitting a regression line to the natural logarithm of the rates using calendar year as a regressor variable [i.e. given \( y = ax + b \), where \( y = \ln(rate) \) and \( x = calendar\ year \), the EAPC is estimated as: \( 100 \cdot (e^b - 1) \)].

REFERENCES:
http://srab.cancer.gov/joinpoint/

Methodology of alcohol-attributable mortality analysis

OBJECTIVE: To estimate the number of deaths and the years of life lost attributable to alcohol in 2002.
METHOD: Distribution of exposure should be taken from national survey, and adjusted for real per capita consumption (moonshine included).
The prevalence data of different levels of current alcohol consumption should be collected in four drinking categories.

For chronic disease, risk relations were taken from the published literature and combined with exposure to calculate age- and sex-specific alcohol-attributable fractions (AAFs).

Information on mortality, with cause of death coded according to the International Classification of Diseases version 10 (ICD-10) was obtained from WHO database. The relative risk for each condition was combined with different levels of alcohol consumption for each sex and age group and an attributable fraction was obtained using the following formula:

$$ AAF = \frac{\sum_{i=1}^{k} P_i(RR_i - 1)}{\sum_{i=0}^{k} P_i(RR_i - 1) + 1} $$

i: exposure category with baseline exposure or no alcohol i=0.
RR(i): relative risk at exposure level i compared to no consumption
P(i): prevalence of the i-th category of exposure.

REFERENCES:

Methodology of tobacco-attributable mortality analysis

OBJECTIVE: To estimate the number of deaths attributable to tobacco.
METHOD: Distribution of exposure should be taken from aggregated data from national surveys.

Risks relations were taken from the published literature and combined with exposure to calculate age- and sex-specific tobacco-attributable fractions (TAFs).

Information on mortality, with cause of death coded according to the International Classification of Diseases version 10 (ICD-10) was obtained from WHO database. The relative risk for each condition was combined with different levels of tobacco smoking for each sex and age group and an attributable fraction was obtained using the following formula:

$$ TAF = \frac{\sum_{i=1}^{k} P_i(RR_i - 1)}{\sum_{i=0}^{k} P_i(RR_i - 1) + 1} $$

i: exposure category with baseline exposure or no smoking i=0.
RR(i): relative risk at exposure level i compared to no smoking
P(i): prevalence of the i-th category of exposure.
Potential Years of Life Lost (PYLL) (due to alcohol and tobacco):

Potential Years of Life Lost (PYLL) is an indicator of premature mortality. Persons dying due to alcohol (tobacco) consumption would have lived longer if they had not drunk alcohol (smoke). The average extra time such individuals would have lived is known as the residual life expectancy.

The sum of these extra times for all people dying from alcohol consumption is known as PYLL due to alcohol (tobacco).

PYLL for each sex-age group category can be estimated from the observed mean age at death in the age interval and the standard life expectancies tables at the exact ages defining the age interval through interpolation.

In calculating the mean ages within the intervals, the rules specified by the Global Burden of Diseases (GBD) study should be followed (Mathers et al., 2001).

PYLL due to death in Poland will be calculated for each age group (20-44, 45-64, 65+) by multiplying the number of deaths by the interpolated life expectancy for the observed mean age at death in the interval.

Peto method description


Description:

This method is based on the following assumption: current lung cancer mortality provides a better measure of the exposure of interest – lifetime tobacco smoking – than does current smoking prevalence. Moreover comparable data on smoking prevalence are usually not that easily available as lung cancer mortality data.

By comparing population lung cancer mortality with that expected in a (reference) population of non-smokers one can derive a ‘Smoking Impact Ratio’ (SIR).

Properties of SIR:

SIR=1 is equivalent to a population comprised entirely of lifetime smokers (in the reference population).

SIR=0 is equivalent to a population comprised entirely of never smokers. (The reference population used is the American Cancer Society second cohort study (CPS II) from the 1980s.).

Note: where indoor air pollution from coal fires is a significant cause of lung cancer in never smokers – most notably in China – the non-smoker lung cancer rates must be estimated separately.

4. The SIR (which only requires lung cancer mortality data (by sex and age) can be used to summarize the ‘maturity’ of the smoking epidemic in a given population:

When the epidemic is in its early phases, the SIR is high in the younger age groups and low in the older

When the epidemic is ‘mature’ the elevated SIR extend across the age-range

When the epidemic is declining the SIR in the younger age groups declines.

The SIR can also be used to estimate the total mortality attributable to smoking:

First the value of SIR is taken to be equivalent to a proportion of lifetime smokers in a hypothetical mixture of (reference population) smokers and never smokers.

Then the excess mortality attributable to smoking in such a mixture is estimated

For lung cancer, the attributable mortality is the absolute excess over the reference rate for non-smokers (CPS II)

For causes other than lung cancer, the excess relative risk in the reference population is reduced by 30%.
For "other medical causes the excess relative risk is reduced by 50%.
Note: until 1992 for all causes the excess relative risk was reduced by 50%.

The Smoking Impact Ratio

\[ SIR = \frac{C_k - N_k}{S_k - N_k^*} \]

Where the terms refer to age-sex-specific values as follows:
- \( C_k \) observed lung cancer mortality in the population of interest
- \( N_k \) assumed lung cancer mortality in never-smokers in the population of interest (taken as equal to \( N_k^* \) (below) in populations without significant indoor air pollution).
- \( S_k^* \) lung cancer mortality for smokers in the reference population (CPS II).
- \( N_k^* \) lung cancer mortality for never-smokers in the reference population (CPS II)

SIR is a measure that ranges: \((0;1]\):
Recommended practice appears to vary according to whether it is the SIR that will be used alone to describe the cumulated hazard of smoking – in which case it is recommended to make all calculated SIR that exceed 1.0 to be equal to 1.0
Practice when SIR < 0 (it might happen in the youngest age groups) is not determined, but it would be symmetrically if we rounded them up to 0. (This issue should be consulted with M. Ezzati).

Using the SIR to estimate smoking attributable mortality (SAM)

Lung cancer:

\[ SAM = \frac{C_k - N_k}{C_k} D \]

Where \( D \) is number of lung cancer deaths in the population of interest

Other neoplasms, respiratory diseases, cardiovascular diseases, liver cirrhosis:

\[ SAM = \frac{((RR \times SIR + 1 \times (1 - SIR)) - 1) \times 0,7}{(((RR \times SIR + 1 \times (1 - SIR)) - 1) \times 0,7) + 1} D \]

where
- \( RR \) – risk for current smokers – look table 1.

Note:
- \((RR \times SIR + 1 \times (1 - SIR)) - 1\) – risk for population mixture (weighted average of risk for non-smokers – 1 and for smokers – RR; diminished by risk for non-smokers -1.)

"other medical causes"

\[ SAM = \frac{((RR \times SIR + 1 \times (1 - SIR)) - 1) \times 0,5}{(((RR \times SIR + 1 \times (1 - SIR)) - 1) \times 0,5) + 1} D \]

Outstanding issues:
Which set of relative risks should be used for this analysis?
How should be the relative risk from the group 35-59 redistributed among the inclusive 5-years age groups (aren’t there any methodological contraindications to use this method for any age group)? This is needed to conduct the analysis in our age ranges of interest.
Would it be possible to apply this method to calculate tobacco-attributable deaths in disease categories the same as used in TAF calculation (see Annex 4) to compare the results?
References:

Projections
Example – lung cancer

The basis for the projections:
The data on lung cancer deaths in central European countries in the period 1959-2002. Population data for the same time period. Forecast of the size and the age structure of the populations in the future. Predicted populations:
New cancer cases were grouped into 13 five-year age groups,
Age groups 0-4 ... 25-29 were aggregated into one age category (0-29 years of age) due to small number of lung cancer deaths in these groups
To evaluate changes in mortality over time in males and females, age-standardized rates were calculated for all ages combined using the weights of the World Standard Population. The joinpoint regression was applied to estimate annual percentage changes (EAPCs), corresponding 95% confidence intervals (95%CI) were calculated for each EAPC. The most recent periods of unchanged EAPCs, indicated by joinpoint analysis, were used as bases for the predictions.

The predicted numbers of lung cancer deaths in 2012 were estimated by:
(1) predicting the incidence rates on the basis of observed rates for period , according to the methods described by Dyba and Hakulinen*
(2) Multiplying these rates by the population forecast for 2015, derived from sources described above.

Four models of mortality rates as a function of population and time were made; the model fit statistics were compared and the best-fit models were chosen.
The analyzed models were:

\[
\text{case}(i,t) = \text{pop}(i,t) \cdot (\alpha(i) + \beta(i) \cdot t)
\]
\[
\text{case}(i,t) = \text{pop}(i,t) \cdot \exp(\alpha(i) + \beta(i) \cdot t)
\]
\[
\text{case}(i,t) = \text{pop}(i,t) \cdot \exp(\alpha(i) + \beta \cdot t)
\]
\[
\text{case}(i,t) = \text{pop}(i,t) \cdot (\alpha(i) \cdot (1 + \beta t))
\]

where \(\text{case}(i,t)\) is the expected number of the deaths in age group \(i\) and period \(t\). \(\alpha\) and \(\beta\) are unknown parameters.

The period \(t\) can be regarded as a surrogate variable for the changes in the collective impact of various carcinogens to which a population was exposed at a particular point in time.

All models are adjusted for possible over-dispersion and prediction intervals were calculated. Prediction intervals consist of the confidence interval for the expected value of the observation itself, which depends on the fit of the model plus the variance of the expected deaths given by the parameter values and the year of prediction.

References:
* Dyba T., Hakulinen T. Comparison of different approaches to incidence prediction based on simple interpolation techniques. Statistics in Medicine, vol. 19, 1-12, 2000
* Hakulinen T., Dyba T. Precision of incidence predictions based on Poisson distributed observations. Statistics in Medicine, vol. 13, 1513-1523, 1994
  

Diet

Following the introduction of market economy and dynamic growth of foreign trade in many European countries in the 1990s significant changes in food consumption patterns took place.

In order to identify the relationships between diet changes and mortality indicators a model (staple) for the food availability data in selected 25 countries (current EU members, excl. Malta and Cyprus, plus Bulgaria and Romania) was created. The dietary data was collected from FAO Food Balance Sheets database (www.fao.org) and included variables on:

- Annual per capita food availability of main foodstuffs (incl. main vegetal and animal products, fats and oils, fruits and vegetables);
- Daily total food energy availability and food energy availability from fats and oils (kcal/capita/day)
- Daily dietary fat and protein availability (g/capita/day).

On the basis of FAO data the share (%) of fat, proteins and carbohydrates as sources of energy as well as intake of visible and invisible fats in estimated national food supplies was calculated. The data are presented in the form of tables and figures showing trends in estimated food availability in years 1961-2002 in each country. Although these data are known not to provide valid estimates of absolute intakes, they may provide useful guides to changes in the relative proportions of different food types in national food supplies. Also if biases within national reporting systems are assumed to remain constant they may provide useful indications of temporal changes within countries.

Data on sodium consumption is desirable, especially in populations with high stroke mortality. This is not generally available from routine sources and specific information sources will need to be sought within each country.

Data on food availability at household level has been collated from national household budget surveys in 14 EU countries (including Hungary) in the DAPHNE data bank. Data of this kind is known to be available for other countries of interest – including Bulgaria.
The next steps of the research are:
Identification of the specific changes in the last 15-20 years (depending on which year major economical reforms occurred and mortality indicators changed) in each country (EU-8, Bulgaria and Romania).
The collection of secondary data from national household budget surveys and market research results (based on questionnaires) in specific age groups
Merging the dietary database with existing data on premature mortality in the studied countries.
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