

Third International Workshop of the MultiCause Network

2-3 June 2016, University of Economics, Prague

Thursday 2nd June

9:30 - 10:00 Welcome and tour de table

10:00 - 11:00 **Session 1: Analysing differences in the number of diagnoses on death certificates**

Chair: Luisa Frova

The effect of changes in data collection system on causes of death statistics in the Czech Republic

Magdaléna Poppová and Terezie Štyglerová

Calculating standardized mortality rates for each disease by weighting multiple cause of death data

Clara Piffaretti, Margarita Moreno-Betancur, Agathe Lamarche-Vadel, Grégoire Rey

11:00 - 11:15 **Coffee break**

11:15 - 12:30 **Session 2 : Cause-specific mortality of patients: comparison with the general population**

Chair: Elena Demuru

Use of multiple causes of death to estimate the cancer-related risk of death among Italian people with AIDS

Saverio Viridone, Saverio Viridone, Antonella Zucchetto, Martina Taborelli, Enrico Grande, Laura Camoni, Marilena Pappagallo, Vincenza Regine, Francesco Grippo, Barbara Suligoj, Luisa Frova and Diego Serraino

Multiple causes of death risks and corroboration of causes amongst persons with psychiatric hospitalizations

Nehama Goldberger, Ziona Haklai and Inna Pugachova

12:30 – 14:00 **Lunch**

14:00 - 15:00 **Session 3 : Mortality differentials**

Chair: Aline Désesquelles

Using multiple causes of death to examine racial/ethnic disparities in mortality in the United States

Magali Barbieri and Irma Elo

Survival analysis with multiple causes of death: Extending the competing risks model

Margarita Moreno-Betancur, Hamza Sadaoui, Clara Piffaretti, Grégoire Rey

15:00-15:15 **Coffee break**

15:15 – 16:45 **Session 4: Data quality**

Chair: Marilena Pappagallo

Cause-of-death among the elderly in Brazil: an evaluation of data quality using multiple causes

Ana Maria Nogales Vasconcelos, Lenice Harumi Ishitani, Renato Teixeira, Daisy Abreu, Elisabeth França

The impact of coding and certification practices on recorded cerebrovascular mortality

Gleb Denissov and Luule Sakkeus

Multicausal code modifications of MUSE: Effect on German death certificates

Olaf Eckert and Torsten Schelhase (German Federal Statistical Office)

Friday 3rd June

9:30-11:00 Session 5 : Certain diseases

Chair: France Meslé

Myelodysplastic syndromes (MDS), underlying and contributing causes of death

Arnaud Bringé and Patrick Festy

Dementia in the Czech Republic: estimating prevalence from different data sources.

Marketa Pechholdova

Investigating the contribution of obesity to mortality: a multiple cause-of-death analysis comparing France, Italy and the United States of America

Magali Barbieri, Elena Demuru, Aline Désesquelles, Viviana Egidi, Luisa Frova, France Meslé, Marilena Pappagallo

11:00-12:30 **Brunch**

12:30 – 13:30 **Session 6 : Network activities**

ABSTRACTS

The effect of changes in data collection system on causes of death statistics in the Czech Republic

Poppová Magdaléna, Štyglerová Terezie (Czech Statistical Office)

Besides the implementations of ICD-10 updates, the statistics on causes of death of the Czech Republic was, relatively strongly, influenced by the implementation of automated coding (software IRIS) in 2011 and the introduction of the new death certificate along with the change in causes of death data collection system in 2013. Both changes have led in electronic processing and storing multiple-cause data since 2013. The main focus of this paper is to analyse the effect of changes in 2013. The new death certificate includes four lines in part I of the medical part of the death certificate instead of three lines. The new, two-ways, data collection system enables to process medical data directly from the death certificate instead of being rewritten in statistical report on death by Registry Offices. These changes both together increased the number of diagnoses filled in a death certificate almost by one third. From the point of view of ICD-10 chapters that influence the selection of the underlying cause of death, the most affected was a chapter IV - Endocrine, nutritional and metabolic diseases, especially diabetes mellitus. Besides diabetes mellitus, the paper analyses changes in mortality from other causes of death: vascular dementia, Alzheimer disease, hypertensive diseases, acute myocardial infarction, chronic ischaemic heart disease, heart failure, cerebrovascular diseases, atherosclerosis or pneumonia.

Calculating standardized mortality rates for each disease by weighting multiple cause of death data

Clara Piffaretti 1,2, Margarita Moreno-Betancur 3,4,1, Agathe Lamarche-Vadel1, Grégoire Rey1

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Background

Analysis of mortality data is important to develop and evaluate health policies. In a context where deaths are often caused by more than one disease, this article presents a new method for reevaluating standardized mortality rates by disease, by considering multiple causes of death.

Methods

Using the French National cause-of-death register, we calculated age- and sex-standardized mortality rates by cause using: a) only the underlying cause of death and b) three experimental weighting multiple cause of death (WMC) methods, that assign a weight to each cause on the death certificate. While the first two WMC methods assigned non-zero weights to all causes mentioned, the third method attributed weights only to the

underlying cause and the contributive causes that were not part of the main morbid process. The sum of the weights for each death always equaled one, so that each death had an equal influence on estimates and the total number of deaths remained the same. We estimated the relative increase of the standardized mortality rates by cause with the WMC methods compared with the classic method.

Results

On average, 3.4 causes per death were listed in deaths occurring in 2010. The relative increase of standardized mortality rates obtained with the third WMC method exceeded 20% in 5 categories: Genitourinary diseases, Blood diseases, Endocrine diseases, Mental disorders and Skin diseases.

Conclusions

The WMC methods portrayed a different picture of the distribution of mortality by cause. This exploratory analysis is promising and suggests new possibilities for analyzing multiple cause of death data.

Use of multiple causes of death to estimate the cancer-related risk of death among Italian people with AIDS

Saverio Virdone¹, Antonella Zucchetto¹, Martina Taborelli¹, Enrico Grande², Laura Camoni³, Marilena Pappagallo², Vincenza Regine³, Francesco Grippo³, Barbara Suligo³, Luisa Frova² and Diego Serraino¹

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Background. Non-AIDS defining cancers (non-ADCs) have become the leading non-AIDS-related cause of death among people with HIV/AIDS. We aimed to quantify the excess risk of cancer-related deaths among Italian people with AIDS (PWA), as compared to people without AIDS (non-PWA) using a multiple causes of death (MCoD) approach.

Methods. A nationwide, population-based, retrospective cohort study was carried out among 5285 Italian PWA, aged 15-74 years, diagnosed between 2006 and 2011. Date of death and MCoD data were retrieved through a record-linkage between the National AIDS Registry and the National Register of Causes of Death. Excess mortality, as compared to non-PWA, was estimated using sex-and age-standardized mortality ratios (SMRs) and corresponding 95% confidence intervals (CIs).

Results. Among 1229 deceased PWA, 10.3% reported non-ADCs in the death certificate, including lung (3.1%) and liver cancers (1.4%). As compared to deceased non-PWA, statistically significant SMRs emerged for several non-ADC types/sites, including anus (SMR=228), Hodgkin lymphoma (SMR=122), uterus (SMR=52.5, 95% CI: 14.3-135), liver (SMR=13.2, 95% CI: 7.7-21.1), skin melanoma (SMR=10.9, 95% CI: 3.0-27.8), lung (SMR=8.0, 95% CI: 5.7-11.0), head and neck (SMR=7.8, 95% CI: 3.6-14.9), leukemia (SMR=7.6, 95% CI: 2.4-17.7), and colorectum (SMR=5.4, 95% CI: 2.6-10.0). SMRs for non-ADCs were particularly elevated for PWA infected through injecting drug use.

Conclusion. The extremely elevated risks of death for non-ADCs, confirmed by the use of MCoD, deserve anti-cancer interventions from both the preventive and clinical side to reduce the incidence and to improve the management of these cancers in PWA.

Multiple causes of death risks and corroboration of causes amongst persons with psychiatric hospitalizations

Nehama Goldberger (1), Inna Pugachova (2), Ziona Haklai (1)

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BACKGROUND: Previous studies have shown that persons affected by severe mental disorders have a significantly higher mortality risk than the general population. Will similar results be found for multiple causes of death (MCoD)?

In addition, discharge data on chronic diseases in the population of persons who had a psychiatric hospitalization can be compared with MCoD data as a measure of chronic disease coverage in MCoD.

METHODS: This cohort study compared the cause specific mortality risk for underlying cause (UC) and multiple causes (MC) among persons aged 18 and over, whose psychiatric hospitalization was recorded in the National Psychiatric Case Register (NPCR) with those never hospitalized, for deaths between 2007 -2012.

The NPCR was linked to the national database on causes of death. Cause specific age adjusted rates were calculated for UC and MC for persons in the NPCR with a severe mental disease diagnosis, and those never hospitalized, and the respective rate ratios (RR), and standardized ratio of multiple to underlying rate (SRMU), for the two groups.

The prevalence of chronic diseases reported on discharge from psychiatric hospital was compared to corresponding case data in MCoD, and for those who died within a year of last discharge from psychiatric hospitalization, we checked whether the chronic diseases chosen as UC or listed amongst MC were also noted on discharge from hospital.

RESULTS: There were 12,928 deaths between 2007 -2012 of persons ever hospitalized, and 2,377 who were discharged within a year of death. The RR of ever hospitalized to non-hospitalized in MC was very similar to those for the corresponding UC, between 1.3 and 2.6 for most leading natural causes. Different RRs were found only for substance abuse, where RR was 10.0 for the UC compared to 5.3 for MC.

Leading chronic diseases reported on discharge from psychiatric hospitalization were frequently mentioned in MCoD, cancer in 61% of these cases, cardiovascular disease - 51%, diabetes or endocrinal disease - 40%, CLRD -30%, urinary tract disease - 28% and a psychiatric diagnosis in 27%.

For several leading causes mentioned in MCoD, over half were also reported in discharge data within a year of death, diabetes or endocrinal disease in 69% of cases, cardiovascular disease – 62%, CLRD - 60%, and cancer 54%.

CONCLUSIONS: The pattern of higher cause specific mortality rates found in persons after a psychiatric hospitalization compared to others were similar for UC and MC.

A relatively high correspondence was found between leading chronic diseases reported on hospital discharge, and those mentioned in MCOD, which may validate the use of MCOD diagnoses as estimators of chronic disease in the population.

Examining Differentials in Multiple Cause of Death Data by U.S. Region.

Janet Weeks (Duke University)

When examining international differences on multiple causes of death (MCOD) data, the U.S. is often characterized by high rates of diabetes and hypertension as listed multiple causes as compared to other predominately European countries such as France and Italy. Given the large landmass of the U.S., and cultural heterogeneity by region, it is possible that there is also strong regional heterogeneity in MCOD. Our focus is twofold: First, I examine whether diabetes and hypertension MCOD patterns differ by U.S. region. Second, I compare these regional rates to Italy and France. Data are taken from the public use version of the Integrated Health Interview Series for 1999-2009, linked with the National Death Index through 2010. Given that race/ethnicity, gender, and socioeconomic status (SES) are often considered fundamental causes of health differentials, I then plan to assess U.S. regional variation by race, gender, and SES.

Using multiple causes of death to examine racial/ethnic disparities in mortality in the United States

Magali Barbieri (INED/University of Berkeley), Irma Elo (University of Pennsylvania)

Our overall purpose is to investigate whether we can gain additional insights about racial/ethnic disparities in mortality in the United States when using multiple cause of death information in comparison to underlying cause of death only. To this end, we will construct cause-specific mortality rates for a shortlist of 72 categories using multiple cause-of-death information separately for non-Hispanic Whites, non-Hispanic Blacks and Hispanics. The rates will be computed by combining the race-specific life tables published by the NCHS for 2011 (or the last year available) with multiple-cause-of-death data from the Public Multiple Cause Mortality Files for the same year. We will seek to identify those cause-combinations that exhibit the largest differential between all three racial/ethnic groups and compare these differentials with those based on single (underlying) cause only. We will use two types of indicators that have been developed in the Multiple Cause of Death Project: 1) the Standardized Ratio of Multiple- to Underlying-Cause (SRMU), and 2) the Cause of Death Association Indicator (CDAI). Both types of indicators have been described in the 2010 Demographic Research article by Désesquelles et al. (2010).

References

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Survival analysis with multiple causes of death: Extending the competing risks model

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Statistics on mortality related to each disease are usually based on the so-called 'underlying cause of death', which is selected from the diseases declared on the standardized death certificate using international rules. However, the assumption that each death is caused by exactly one disease is debatable, particularly with an aging population in an era where infectious diseases are replaced by chronic and degenerative diseases. The need to consider multiple causes of death has been acknowledged in epidemiological research, with a growing body of literature producing statistics based on any mention of a disease on the death certificate. Yet, there has not been a formal framework proposed for the statistical modeling of death arising from multiple causes. We propose a model for multiple cause of death data grounded on an empirical approach that assigns weights to each cause on the death certificate. We describe how this model for multiple-cause mortality, which extends the usual competing risks model used to conceptualize single-cause mortality, can serve to study the burden and etiology of mortality related to each disease, particularly using Cox regression methodology. We discuss how the multiple-cause, single-cause and 'any-mention' approaches compare in this regard. A simulation study and an application to a study of socioeconomic inequalities in mortality show the value of the proposed methods for exploiting this precious source of data to gain new insights, especially for certain diseases.

Cause-of-death among the elderly in Brazil: an evaluation of data quality using multiple causes.

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Background: Analysis of the quality of cause-of-death data represents an important matter in Brazil due to the incompleteness of mortality statistics and errors in reporting cause-of-death. In Brazil, the Ministry of Health (MoH) has been responsible for the nationwide collection and regular publication of data on mortality. In 1976 the Brazilian Mortality Information System (MIS) was created by MoH and since that this system has improved on

mortality data quality toward several initiatives. The MIS have used a standard medical certificate throughout the country and cause-of-death statistics collected systematically and coded using the International Classification of Diseases (ICD). Despite these efforts, this issue have been considered as a challenge, and evaluations of quality of cause-of-death statistics should be done systematically.

This situation is even more important for the elderly population due to the high proportion of deaths from ill-defined causes because the morbid profile is more difficult to identify, just like the lack of medical care and the high proportion of home deaths.

Furthermore, among older adults, several potentially fatal disease processes may be present or there may be a set of conditions that jointly contribute to death. The application of multiple cause-of-death can be used to better determine the impact of some diseases that can, in combination with others, accelerate fatal processes. Some of these events are not often identified as the underlying cause-of-death. Multiple cause-of-death analyses can rank a cause based on its prevalence as the underlying cause or as one of the reported or multiple causes of death.

The objective of this study is to assess the quality of statistics of cause-of death among the elderly in Brazil and regions in 2013 through the analysis of multiple causes.

Methods: Data on deaths among the elderly (≥ 60) occurred in 2013 and recorded in the Brazilian MIS (available on www.datasus.gov.br) are analyzed. Underlying cause of death and all diagnoses mentioned in the certificate for each death recorded in MIS, including immediate causes and other associated causes listed in lines a, b, c and d of the death certificate – Part 1, as well, significant conditions contributing to the death listed in Part 2, were considered in analysis. The number of causes reported in the certificate and how they were reported (if in Part 1, the specific line, or in Part 2) were investigated. The causes of death are coded according to the 10th Revision of International Classification of Diseases (ICD-10).

Results: In 2013, approximately 770,000 deaths of 60 and over were reported to the MIS (25% of 60-69, 32% of 70-79 and 43% of 80+). The top four groups of underlying cause of death were: diseases of the circulatory system (34.7%), neoplasms (17.2%), diseases of the respiratory system (14.5%) and endocrine, nutritional and metabolic diseases (7.7%). The importance of neoplasm as underlying cause of death decrease with the age (24% in 60-69 to 11.6% in 80+) and respiratory diseases increase (9,9% in 60-69 to 18% in 80+). Deaths with ill-defined causes were 6.2%, increasing to 7.5% for the age group 80+. The average number of diagnosis listed in death certificate among elderly was 3.1 for the whole country, varying from approximately 3.0 in North, Northeast and South regions to 3.5 in the Center-West. Differences ($p < 0,01$) were also observed among groups of underlying causes: endocrine and metabolic diseases (3.70), digestive diseases (3.55), circulatory and respiratory diseases (3.20), neoplasms (2.97) and ill-defined causes (1.20). The average number of diagnosis varied by color of the skin and level of education of deceased (3.16 among white vs 3.01 among non-white; 3.33 for high level of education vs 3.07 for low level). Considering only the natural causes (excluding ill-defined), the average number of diagnosis was significant higher for deaths with medical assistance (3.34 vs 3.06) or for certificates of death signed by the physician who attend the deceased (3.31 vs 3.11).

Concerning on how the causes are originally reported in death certificate, 96.5% of all certificates presented at least one diagnosis in line a, 78.7% in line b, 51.0% in line c, 22.2%

in line d and 37.5% in Part 2. In 7.8% of certificates, there was more than one diagnosis reported in the same line of Part 1 of the certificate, and in 16.8% in the same line of Part 2. Abbreviations of causes and more than one cause informed in the same line may cause difficulties in the collect of data.

Regarding to the diagnosis reported and their contribution to understand the process resulting in death, 34% of all certificates, excluding those with ill-defined as underlying cause, presented at least one diagnosis coded in the Chapter XVIII of ICD10 (Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified). This proportion increased to 43% in Center-West region and among age 80+ (36.4%). In 50.3% of these certificates, there were at least one diagnosis classified as garbage code (expanded list WHO-2013), including cardiac arrest (I46), heart failure (I50) and respiratory failure (J96). Considering all diagnoses reported, 13,5% was coded as ill-defined (codes R), 33,6% as garbage code (unspecific codes) and 52,9% as specific causes.

CONCLUSIONS: The findings indicate how the multiple causes' analysis could be helpful in mortality studies for specific population as elderly. This approach could be also an useful method for clarify issues to improve the quality of statistics of cause-of death in Brazil.

The impact of coding and certification practices on recorded cerebrovascular mortality

Gleb Denissov (Head of Estonian Causes of Death Registry), Luule Sakkeus

Cerebrovascular diseases (I60-I69) is a frequent cause of death recorded by official statistics. Due to new treatment methods it is on decline. However, this indicator is dependent on certification and coding practices and therefore should not be used without a quality assessment. Our study demonstrates the impact of certification and coding on recorded cerebrovascular mortality in Estonia. A half of the decrease in cerebrovascular mortality in 2004-2013 was due to increased selection of hypertensive diseases (I10-I15) the underlying cause of death in cases where both conditions were reported on medical death certificate. More detailed certificates were more affected: in cases where a cerebrovascular disease was mentioned and selected the underlying cause of death, the mean number of diagnoses per record was 2.45, in cases where a cerebrovascular disease was mentioned, but hypertension selected the underlying cause of death, the mean number of diagnoses was 3.15.

Multicausal code modifications of MUSE: Effect on German death certificates*Gleb Olaf Eckert and Torsten Schelhase (German Federal Statistical Office)*

"Multicausal and Unicausal Selection Engine" (MUSE) is a software that has been developed by the German Federal Statistical Office. It is used by statistical offices of the federal states since 2012 for standardised electronic processing of causes of death certificates. MUSE will be the coding kernel of the upcoming international Iris versions after 2016. Its decision logics can be modified simply by changing a configuration file. This file contains unicausal and multicausal instructions executed by the coding kernel. The unicausal part covers decision tables provided by Iris Core Group/Iris Institute. Additionally

multicausal coding instructions were prepared in collaboration with the German Institute for Medical Documentation and Information (DIMDI) and Iris Core Group. Now about 10.000 multicausal instructions are implemented. 69.000 German certificates have been processed by MUSE two times. In the first run multicausal processing is enabled, in the second run it is disabled. In this manner the influence of MUSE on multicausal coding and the selection of underlying causes can be shown. More than 10% of certificates are changed by code modifications. Many details (e.g. frequency of recodings, recoding of cancer certificates) and typical examples will be presented. A systematical testing of code modifications is required because systematical errors and an information loss by recoding should be avoided.

Myelodysplastic syndromes (MDS), underlying and contributing causes of death

Arnaud Bringé and Patrick Festy (INED, France)

As most deaths are concentrating at older ages, where individuals suffer from complex groups of pathologies, it becomes increasingly relevant to refer to multiple causes of death that include not only underlying but also contributing causes. Such an analysis is generally performed for frequent pathologies, which result in numerous deaths. We deal here with a specific and rare cause, myelodysplastic syndromes (code D46 in the 10th revision of the International Classification of Diseases), because it is characterized by a heavy concentration of deaths at older ages (beyond 70). D46 is in an intermediate position between chapter II in ICD10 (Neoplasms) and chapter III (Diseases of the blood), where diseases are characterized respectively by low proportions of contributing causes and very high proportions.

From annual records of deaths for France, we measure the frequency of D46 and the distributions of associations with other causes whether MDS are underlying or contributing causes. The analysis includes sex and age. After identifying the most frequent associations, we try to visualize their mutual relationships through network analysis to reveal complementarities between myelodysplastic syndromes and groups of associated causes. We compare these groupings with medical state-of-the-art on death of patients suffering from MDS. We conclude by questions on validity of cause of death statistics concerning a rare disease recently introduced in WHO classification.

Dementia in the Czech Republic: estimating prevalence from different data sources

Markéta Pechholdová (University of Economics, Prague)

Background: The issue of dementia in Central and Eastern Europe (CEE) is largely uncovered by research. In fact, the only estimates of dementia prevalence for the Czech Republic are derived from foreign studies such as EuroDEM or EuroCoDe. According to epidemiological studies, main cause of dementia is Alzheimer disease, a condition primarily affecting the brain tissue. However, countries of the CEE have experienced a long-term crisis of cardiovascular mortality, which may put them in an increased risk of dementia related to cerebrovascular conditions (mainly the vascular dementia).

Methods: Based on the multiple cause-of death data for the Czech Republic, we explore the prevalence of different types of dementia divided into Alzheimer and other types. At first,

we look at total mentions of dementia and their changes since 1998. At second, we explore and compare the comorbidity of the two types of dementia using the CDAI indicator.

Results: Non-Alzheimer type of dementia in the Czech Republic is much higher than expected from epidemiological studies: for one case of Alzheimer, there are almost five cases of “other” dementia. Analysis of comorbidity shows that while both Alzheimer and non-Alzheimer dementia share very similar comorbidity patterns, the link with cerebrovascular disease was observed only for the highly prevalent non-Alzheimer dementia.

Conclusion: The real burden of dementia in the countries of Central and Eastern Europe (CEE) remains unknown: dementia mortality is underestimated in the underlying cause-of-death statistics and information from health surveys is lacking. Multiple causes of death provide a better estimate and reveal that CEE countries are more at risk for dementia due to cerebrovascular disease while less at risk for ageing-related organic dementia (Alzheimer), compared to Western countries. Further research including more detailed international comparison and more data sources is still needed.

Investigating the contribution of obesity to mortality: a multiple cause-of-death analysis comparing France, Italy and the United States of America

M.Barbieri (INED/University of Berkeley), E. Demuru (Sapienza University of Rome), A.Désesquelles (INED), V.Egidi (Sapienza University of Rome), L.Frova (ISTAT), F. Meslé (INED), M.Pappagallo (ISTAT)

For many years now the prevalence of obesity has been on a strong upward slope in many countries. France, Italy and the United States, the three countries considered in our research, are no exception to this trend. According to the most recent surveys, the prevalence of self-reported obesity in the adult population was 35% in the US while it was only 15% in France and 11% in Italy. As the literature provides support for a positive link between obesity and mortality, we expect that these differences are reflected in the obesity-related mortality levels of the three countries. We first compare the underlying- and multiple-cause obesity death rates of France, Italy and the USA at ages 50-89. Then we use a multiple correspondence analysis and a cluster analysis to describe and compare the different cause-of-death patterns involving obesity.