Fifth meeting of the MultiCause network

Federal Institute of Drugs and Medical Devices (BfArM)

Bonn, 19&20 May, 2022

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The meeting will be held in an hybrid format.

The webex links to the meeting are:

All sessions on May 19

https://bfarm.webex.com/bfarm/onstage/g.php?MTID=ed1d47c043bbda01ac0f7c1e7a0c20b50

All sessions on May 20

https://bfarm.webex.com/bfarm/onstage/g.php?MTID=e6402f66569dfacdf489eb6a446d3b396

Registration before the meeting is needed. You can access the registration form in the window that opens when clicking on these links.

5th Meeting of the MultiCause Network

Programme

Thursday 19th May

9:00 - 9:30 Welcome

9:30 - 11:00 Session 1: Association of causes

Chair: Luisa Frova

Exploring the underlying patterns among causes of death listed in Part II of death certificates using Social Network Analysis
Mohammad Reza Baneshi, Paul McElwee, Annette Dobson
School of Public Health, University of Queensland, Australia

Analysis of the Multiple Causes of Death in Japan with Network Analysis
Futoshi Ishii 1, Reiko Hayashi 2, Emiko Shinohara 3, Motomi Beppu 2
1 Keio University, Japan
2 National Institute of Population and Social Security Research, Japan
3 University of Tokyo, Japan

Two-stage cluster analysis of multiple cause of death data to identify groups of conditions that jointly contribute to death WITHDRAWN
Karen Bishop 1, Margarita Moreno-Betancur 2 3, Chalapati Rao 1, James Eynstone-Hinkins 4, Moran L, Michelle Gourley 5, Saliu Balogun 1, Emily Banks 1 6, Grace Joshy 1
1 National Centre for Epidemiology and Population Health, Australian National University, Canberra, Australia
2 Clinical Epidemiology and Biostatistics Unit, Murdoch Children's Research Institute, Melbourne, Australia
3 Department of Paediatrics, University of Melbourne, Melbourne, Australia
4 Australian Bureau of Statistics, Canberra, Australia
5 Australian Institute of Health and Welfare, Canberra, Australia
6 The Sax Institute, Sydney, Australia.

Exploring the association between causes of death listed in Part II of death certificates by comparison of the observed and expected frequency of triads
Mohammad Reza Baneshi, Paul McElwee, Annette Dobson
School of Public Health, University of Queensland, Australia

11:00 - 11:30 Coffee break

11:30 - 13:00 **Session 2: Data quality and methods**

Chair: Sergi Trias-Llimos

Quantifying multiple causes of death: A systematic review and audit of methods and practice

Saliu Balogun 1, Karen Bishop 1, James Eynstone-Hinkins 2, Melonie Martin 1, Margarita Moreno-Betancur 3 4, Chalapati Rao 1, Grace Joshy 1
1 National Centre for Epidemiology and Population Health, Australian National University, Canberra, Australia
2 Australian Bureau of Statistics, Canberra, Australia
3 Clinical Epidemiology and Biostatistics Unit, Murdoch Children's Research Institute, Melbourne, Australia
4 Department of Paediatrics, University of Melbourne, Melbourne, Australia

A new data-driven weighting method for MCoD analysis

Paul McElwee 1, Mohammad Reza Baneshi 1, Kim-Huong Nguyen 2, Annette Dobson 1
1 School of Public Health, University of Queensland, Australia
2 Centre for Health Services Research, University of Queensland, Australia

On the comparability of international cause of death statistics: A deep artificial neural network based study

Louis Falissard 1, 2, Francesco Grippo 3, Chiara Orsi 3, Myer Glickman, Anne Campbell 4, Robert Anderson 5, Grégoire Rey 1
1 Centre for epidemiology on medical causes of death (CépiDc-Inserm), France
2 Université Paris Saclay, France
3 ISTAT, Italy
4 ONS, United Kingdom
5 NCHS, CDC, Silvers Spring, Maryland, USA

Application of Multiple Cause of Death Information to Eliminate Garbage Codes

Agnieszka Fihel 1, 2, Magdalena M. Muszyńska-Spielauer 3
1 University of Warsaw, Poland
2 Institut national d'études démographiques (INED), France
3 Wittgenstein Centre for Demography and Global Human Capital (IIASA, OeAW, University of Vienna), Vienna Institute of Demography/Austrian Academy of Sciences, Austria

13:00 – 14:00 Lunch

14:00 - 15:30 **Session 3: Miscellaneous**

Chair: Agniezska Fihiel

The concept for presentation of multi-cause data as regular statistical output

Magdaléna Baštecká,
Population Statistics Department, Czech Statistical Office

Development of multiple-cause-of-death statistics in Germany

Nela Gruba
German Federal Statistical Office (Destatis)

Multiple causes associated with COVID-19: how do demographic variables and level of education influence the association?
Simone Navarra and Silvia Simeoni*, Luisa Frova, Enrico Grande, Francesco Grippo, Stefano Marchetti, Chiara Orsi, Marilena Pappagallo.*
Division of Integrated Systems for Health, Social Assistance and Welfare, Italian National Institute of Statistics, Rome, Italy

Multiple cause of death data shows disparities in morbidity with educational status in Israel
Nehama Goldberger, Ziona Haklai
Health information division, Ministry of Health, Israel

15:30-16:00 **Coffee break**

16:00 – 17:30 **Session 4: COVID-19**

Chair: Aline Désesquelles

Analyzing complications of COVID-19 from death certificates: which ones kill most?
Chiara Orsi, Simone Navarra, Enrico Grande, Silvia Simeoni, Simona Cinque, Luisa Frova, Stefano Marchetti, Marilena Pappagallo, Francesco Grippo
Division of Integrated Systems for Health, Social Assistance and Welfare, Italian National Institute of Statistics, Rome, Italy

The impact of COVID-19-related mortality on life expectancy differences by educational level from a multiple cause-of-death approach. The case of Spain.
Jeroen Spijker, Sergi Trias-Llimós
Centre d'Estudis Demografics, Spain

COVID-19 mortality in Brazil: an analysis of multiple causes of death
Ana Maria Nogales Vasconcelos 1, 2 Lenice Istani, 3, Daisy Xavier, 3, Luana Barreto, 1, Mathews Noronha, 1, Valeria Fechine, 2, Juan Cortéz, 4, Renato Teixeira, 5, Elisabeth França, 3, 5
1 Department of Statistics, University of Brasilia, Brazil
2 Multidisciplinary Advanced Studies Center (CEAM), University of Brasilia, Brazil
3 Epidemiology and Health Assessment Research Group (GPEAS), Federal University of Minas Gerais, Belo Horizonte, Brazil
4 Pan American Health Organization (PAHO) - Brazil
5 Graduate Program in Public Health, School of Medicine, Federal University of Minas Gerais, Belo Horizonte, Brazil

COVID-19 as Cause of Death in The Netherlands: A Multiple Cause-of-Death Coding Study WITHDRAWN
P.P.M. Harteloh
Statistics Netherlands

Friday 20th May

9:00-10:30 **Session 5: Data quality and methods**

Chair: Marilena Pappagallo

Development of an Australian categorisation for MCoD analysis.
Paul McElwee, Mohammad Reza Baneshi, Annette Dobson
School of Public Health, University of Queensland, Australia

Quantification of mortality incorporating multiple causes of death: Application of different methods, including weighting strategies, to Australian data
Grace Joshy 1, Karen Bishop 1, Saliu Balogun 1, Margarita Moreno-Betancur 2 3, James Eynstone-Hinkins 4, Lauren Moran 4, Rosemary Korda 1, Chalapati Rao 1, Emily Banks 1 5
1 National Centre for Epidemiology and Population Health, Australian National University, Canberra, Australia
2 Clinical Epidemiology and Biostatistics Unit, Murdoch Children's Research Institute, Melbourne, Australia
3 Department of Paediatrics, University of Melbourne, Melbourne, Australia
4 Australian Bureau of Statistics, Canberra, Australia
5 The Sax Institute, Sydney, Australia.

Accuracy of death certification of diabetes, dementia and cancer in Australia
Zhiwei Xu, Paul McElwee, Richard Hockey, Annette Dobson
School of Public Health, University of Queensland, Australia

Studying multiple causes of death in the absence of death certificates: taking advantage of probabilistic methods to estimate causes of death (InterVA)
Ariane Sessego 1 2 3, Géraldine Duthé 1, Bruno Lankoandé 4, Dianou Kassoum 4
1 Institut national d'études démographiques (INED), France
2 École nationale supérieure (ENS) de Paris, France
3 École des hautes études en sciences sociales (EHESS), France
4 Institut supérieur des sciences de la population (ISSP), Ouagadougou, Burkina Faso

10:30 - 11:00 **Coffee break**

11:00 - 12:30 **Session 6: Specific conditions or diseases**

Chair: Markéta Majerová

The role of overweight and obesity in adverse cardiovascular disease mortality trends: an analysis of multiple cause of death data from Australia and the USA
Tim Adair 1, Alan D. Lopez 2
1 University of Melbourne, Australia
2 Institute of Health Metrics and Evaluation (IHME), University of Washington, USA

Senility Deaths in Japan
Reiko Hayashi 1, Futoshi Ishii 2, Emiko Shinohara 3, Motomi Beppu 1
1 National Institute of Population and Social Security Research, Japan
2 Keio University, Japan
3 The University of Tokyo, Japan

Different patterns of alcohol-related mortality in four European countries: preliminary results based on the Multiple-Causes-of-Death Approach
Agnieszka Fihel 1,2, Magdalena M. Muszyńska-Spielauer 3, Marketa Pechholdová 4, Sergi Trias-Llimós 5
1 University of Warsaw, Poland
2 Institut national d'études démographiques (INED), France
3 Wittgenstein Centre for Demography and Global Human Capital (IIASA, OeAW, University of Vienna), Vienna Institute of Demography/Austrian Academy of Sciences, Austria
4 Prague University of Economics and Business, Czech Republic
5 Centre d'Estudis Demogràfics, Centres de Recerca de Catalunya (CERCA), Spain

Chronic obstructive pulmonary disease-related mortality in Brazil, 2000-2019: a multiple-cause-of-death study.
Augusto Hasiak Santo 1, Frederico Leon Arrabal Fernandes 2
1 Departamento de Epidemiologia, Faculdade de Saúde Pública da Universidade de São Paulo, Brazil
2 Instituto do Coração, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, Brazil

12:30-13:30 **Lunch**

13:30 - 15:00 **Session 7: Miscellaneous**

Chair: Stefanie Weber

Multi-morbidity at death: a comparison of the patterns in four countries
Magali Barbieri 1,2, Aline Désesquelles 1, Viviana Egidi 3, Luisa Frova 4, Francesco Grippo 4, France Meslé 1, Marilena Pappagallo 4, Sergi Trias-Llimós 5
1 Institut national d'études démographiques (INED), France
2 University of Berkeley, USA
3 Sapienza University of Rome, Italy
4 ISTAT, Italy
5 Centre d'Estudis Demogràfics, Spain

Towards a practical grouping of ICD-10 blocks to facilitate analysis of associated comorbidities with the leading causes of death as recorded on death certificates
Neil Hopper, Shaun Purkiss, Ngaire Coombs and Myer Glickman
ONS, United Kingdom

Multiple causes of death and seasonality
Markéta Majerová
Prague University of Economics and Business, Czech Republic

Cause-of-death diversity from a multiple-cause perspective in the US
Sergi Trias-Llimós, Iñaki Permanyer
Centre d'Estudis Demogràfics, Centres de Recerca de Catalunya (CERCA), Spain

15:00 - 15:30 Concluding remarks

5th Meeting of the MultiCause Network

Abstracts

Session 1: Association of causes

Exploring the underlying patterns among causes of death listed in Part II of death certificates using Social Network Analysis

Mohammad Reza Baneshi, Paul McElwee, Annette Dobson
School of Public Health, University of Queensland, Australia

Aim: The set of causes listed on the death certificate describe a complex process of the simultaneous effects of several diseases. It would be of interest to explore the complex relationships that link the causes of death mentioned in Part II of the same death certificate.

Methods: Using 1.93 million records of all deaths in Australia from 2006 to 2018, we have used Social Network Analysis (SNA) to visualise the complex system of relationships linking Part II causes. We used the normalised joint frequency of causes in part II of the death certificates to describe the strength of the associations. Using various statistics of connectedness, we have explored whether conditions can be grouped into 'communities' which were highly connected to each other.

Results: As an example, for women aged over 85, the conditions were grouped together into six communities.
•Natural injuries (e.g., injury, poisoning) and external causes (including accidents, and falls);
•Several different cancers: breast, colorectal, lymph and blood, melanoma, other malignant neoplasms;
•Lung conditions: lung and tracheal cancer and chronic lower respiratory
•Several neurological conditions: dementias (including Alzheimer's disease), Parkinson's disease, cerebrovascular disease, mental and behavioural disorders, and other neurological conditions;
•A group of liver and pancreas conditions: liver disease, liver cancer, pancreatic cancer, and diabetes;
•The last group was heterogeneous.

Conclusion: SNA was able to identify complex associations between multiple conditions in Part II of the death certificate and to define meaningful communities of conditions.

Analysis of the Multiple Causes of Death in Japan with Network Analysis

Futoshi Ishii 1, Reiko Hayashi 2, Emiko Shinohara 3, Motomi Beppu 2
1 Keio University, Japan
2 National Institute of Population and Social Security Research, Japan
3 University of Tokyo, Japan

As the old age mortality has been improved, main causes of deaths have shifted to chronic diseases that increased the number of people suffered from multiple diseases in Japan. It has increased the importance of the analysis of multiple causes of death.

There have been few studies that uses multiple causes of death in Japan since that kind of data has just become available in recent years. However, there is a large number of studies on the multiple causes of death in Europe and the United States. Amongst them, Egidi et al. (2018) is a seminal study that applied a network analysis to explore relationships between causes of death.

In this study, we will analyze multiple causes of death in Japan using network analysis following Egidi et al. (2018). To investigate relationship between causes of death, we will evaluate centrality measures such as degree centrality, closeness centrality and betweenness centrality. Moreover, we will apply community detection methods in network analysis for better understanding of complex relationship between causes of death, which are not examined in Egidi et al. (2018).

From the results of this study, we will show that the network analysis is effective for analyzing the relationship between the multiple causes of death for Japan.

Exploring the association between causes of death listed in Part II of death certificates by comparison of the observed and expected frequency of triads

Mohammad Reza Baneshi, Paul McElwee, Annette Dobson
School of Public Health, University of Queensland, Australia

Aim: The set of causes of death mentioned in Part II provide a valuable source of information to identify combinations of causes frequently associated with each other. Our objective is to find associated conditions among cases with the Underlying Cause of Death of Dementia (including Alzheimer's disease) (UCODD) and Ischemic Heart Disease (UCODI).

Methods: Using the Australian data from 2006 to 2018, we have used the Observed-to-Expected (O/E) ratio method to identify causes frequently associated with UCODD (N=135,475) and UCODI (N=249,077). We used causes with a minimum prevalence of 2% and extracted all triadic combinations with prevalence above 0.5%. The Expected prevalence was calculated by multiplying the prevalence in Part II of the conditions forming the triad. We assumed an O/E ratio above two indicates a strong association between the triad's conditions.

Results: Causes with the highest prevalence in both groups were hypertensive disease, diabetes, cerebrovascular disease, cardiac arrhythmia, other circulatory diseases, heart failure, and kidney disease. The prevalence of ischaemic heart disease (IHD) among UCODD and dementia among UCODI was 8.4% and 10.3%, respectively. Among UCODD, we have found 9 triads: dementia + (hypertensive disease + benign neoplasms, blood, metabolic disease), (hypertensive disease + diabetes) + (hypertensive disease + cardiac arrhythmia), (hypertensive disease + musculoskeletal disease), (IHD + cardiac arrhythmia), (IHD + heart failure), (IHD + other circulatory diseases), (IHD + kidney disease), and (cardiac arrhythmia + heart failure). Only 4 triads were found for UCODI cases: IHD + (hypertensive disease + benign neoplasms, blood, metabolic disease), (hypertensive disease + diabetes), (hypertensive disease + cardiac arrhythmia), and (cardiac arrhythmia + heart failure). Stratification by age revealed no other pattern.

Conclusion: We have found strong associations between a similar range of cardiometabolic conditions in Part II for death certificates with UCODD and UCODI.

Session 2: Data quality and methods

Quantifying multiple causes of death: A systematic review and audit of methods and practice

Saliu Balogun 1, Karen Bishop 1, James Eynstone-Hinkins 2, Melonie Martin 1, Margarita Moreno-Betancur 3 4, Chalapati Rao 1, Grace Joshy 1
1 National Centre for Epidemiology and Population Health, Australian National University, Canberra, Australia
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3 Clinical Epidemiology and Biostatistics Unit, Murdoch Children's Research Institute, Melbourne, Australia
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Background: Mortality reporting and research are typically focused on a single underlying cause of death (UCoD) selected from multiple reported causes. The need to incorporate multiple causes of death (MCoD) in mortality statistics is now recognised internationally, but there is scant methodological work to guide analytical approaches. This review aims to identify and appraise current methods and practices used to analyse MCoD data.

Methods: The Web of Science, Medline, Pubmed and Scopus (from inception to August 2020) were queried. Studies reporting MCoD alone or in comparison with single UCoD were included. The review is supplemented by qualitative interview with international experts.

Results: 4004 articles were identified; 440 full texts were included in the review. Articles can be broadly categorised by the methods used to analyse MCoD into those reporting: descriptive measures (83%, n=367), measures of pairwise associations between diseases on death certificates (53%, n=232), measures based on groups of causes (1.8%, n=8) and rates based on multiple cause weighting methods (n = 4 studies). Descriptive statistics commonly include rates based on any mention with or without comparisons to rates by underlying cause. Measures to assess pairwise disease combinations include mortality odds ratios and frequencies of associated causes. Cluster analysis methods were common among studies based on groups of causes. Weighting methods include: (i) a fixed weight to the UC of 50% with the remaining 50% equally distributed among the other causes in Part II of the death certificate; (ii) equal weighting of all causes and (iii) weighting the UC double; weights remain arbitrary in all weighting methods. Audit results will be discussed.

Conclusions: This review provides a comprehensive and updated summary of methodological approaches used to analyse MCoD data. The merit of each analytical framework is discussed.

A new data-driven weighting method for MCoD analysis

Paul McElwee 1, Mohammad Reza Baneshi 1, Kim-Huong Nguyen 2, Annette Dobson 1
1 School of Public Health, University of Queensland, Australia
2 Centre for Health Services Research, University of Queensland, Australia

Aim: To develop a data-driven method of weighting MCoD and compare the results to other methods of weighting.

Method: The multiple-cause-of-death weighting method version 3 (MCW3) of Piffaretti et al. (Bull. WHO, 2016) weights the Underlying Cause of Death (UCoD) 50% with each of the Part II (PII) causes given an equal weight so they sum to 50%.

In the new method each PII cause in a particular record has a weight given by the proportion of times that cause occurred among all records with the same UCoD divided by the number of PII causes in the particular record.

For records containing no PII causes, 100% of the cause of death was attributed to the UCoD. For records with PII causes, each cause has the weight calculated as above, and the remainder of the cause of death is allocated to the UCoD.

These two methods of MCoD weighting were applied to the death records for all people aged over 60 who died in Australia from 2006 to 2018 (1.66 million records).

Results: Compared to the Leading Causes of Death ranking based only on UCoDs, changes in ranking were greater using MCW3 compared to the new method.

Conclusion: The new method is entirely data-driven, requiring no subjective weighting between UCoD and PII causes. As expected, the rank order of causes of death is affected by how the MCoD analyses are performed, and the new method provides credible results.

On the comparability of international cause of death statistics: A deep artificial neural network based study

Louis Falissard 1, 2, Francesco Grippo 3, Chiara Orsi 3, Myer Glickman, Anne Campbell 4, Robert Anderson 5, Grégoire Rey 1
1 Centre for epidemiology on medical causes of death (CépiDc-Inserm), France
2 Université Paris Saclay, France
3 ISTAT, Italy
4 ONS, United Kingdom
5 NCHS, CDC, Silvers Spring, Maryland, USA

Background: The availability of up-to-date, reliable data on causes of death is a matter of significant importance in public health monitoring. However, the coding of underlying causes of death from death certificates is a process that is nowadays undertaken by humans with assistance from expert systems, such as the Iris software. It is, consequently, an expensive process, that can suffer from geospatial discrepancies, thus potentially severely impairing the comparability of death statistics at the international level.

Objective: This study assesses potential discrepancies in international cause of death statistics using an artificial neural network based model

Methods: The investigated dataset was based on data contained from French, Italian, American and British and Welsh death certificate from several time periods ranging from 2000 to 2018, containing the chain of events leading to his or her death, for a total of around 70 million observations. A deep neural network-based model was then designed and fit to the dataset in order to predict the underlying cause of death from this information. Error rates were then assessed on the test set while having the country of origin vary, in order to assess whether the model's learnt decision process depends on this predictive variable.

Results: The portability of the deep learning algorithm to the international scale was validated, with performance results even better than previously reported for some countries. The

experiment shows that overall, mortality statistics (at least for the included countries) are fairly comparable, although some cases requiring further investigations were identified.

Conclusions: This study shows that the performances of the deep learning model are very similar on various countries, and that the causes of death statistics are globally fairly comparable, although some cases of potential differences between international coding processes were identified.

Application of Multiple Cause of Death Information to Eliminate Garbage Codes

Agnieszka Fihel 1, 2, Magdalena M. Muszyńska-Spielauer 3
1 University of Warsaw, Poland
2 Institut national d'études démographiques, France
3 Wittgenstein Centre for Demography and Global Human Capital (IIASA, OeAW, University of Vienna), Vienna Institute of Demography/Austrian Academy of Sciences, Austria

With more than 20% of deaths annually assigned to ill-defined cardiovascular conditions, the mortality level due to well-defined causes of death is under-registered in Poland. As the reliability of mortality analyses depends on the quality of data, WHO excludes Poland from international comparisons. In this study, we aim to use the multiple causes of death (MCoD) data in order to reclassify the underlying causes of death from cardiovascular garbage codes (GCs) into well-defined causes. Based on these results, we seek to approximate mortality levels due to well-defined (underlying) causes of death in Poland. We aim also to examine the usefulness of the MCoD approach for correcting low-quality data on the underlying causes of death.

Based on the unique MCoD dataset for Poland, death counts due to cardiovascular GCs were reassigned to well-defined underlying causes in two steps: (1) manually for death records that included MCoD information constituting a logical chain of conditions leading to death and (2) with coarsened exact matching for the remaining death records. Age-specific and age-standardised death rates for large groups of causes were calculated before and after redistribution and compared to those of other Eastern European countries with relatively good data quality. Of deaths originally assigned to cardiovascular GCs, 86,856 were reclassified, mostly to well-defined cardiovascular diseases, cancers, endocrine, nutritional and metabolic diseases, and respiratory diseases. The age-standardised death rate due to well-defined ischaemic heart diseases increased by 43%, and the rate due to cerebrovascular diseases by 22%. Cardiovascular mortality structure by large groups of causes became similar to the structure registered in other Eastern European countries characterised by a low prevalence of GCs.

Our study shows that coarsened exact matching performs relatively well when abundant MCoD information is available and enhances the comparability of cause-of-death data between countries.

Session 3: Miscellaneous

The concept for presentation of multi-cause data as regular statistical output

Magdaléna Baštecká,
Population Statistics Department, Czech Statistical Office

The underlying cause statistic ceases to be sufficient for the explanation of mortality patterns in regard to the growth of chronic diseases or covid-19 pandemic existence. Multi-cause statistics will be necessary as a regularly published output of the Czech Statistical Office. This

study presents efforts to create a multi-cause shortlist corresponding to national purposes. The study tries to find out how to define contributing causes of death and as well to create a shortlist for contributing causes of deaths and to incorporate it in the multi-cause shortlist. Finally, the list is checked if will be convertible into the ICD-11, which is coming into force.

Development of multiple-cause-of-death statistics in Germany

Nela Gruba
German Federal Statistical Office (Destatis)

In times of increasing life expectancy and consequently an increasing proportion of multimorbidity, the current unicausal cause of death statistics is no longer a sufficiently suitable measure for assessing the health status of the population. At least since the Sars-Cov-2 pandemic, there has been a great need for more up-to-date and well-founded information on causes of death than the annual unicausal statistics can currently provide.

To serve this public interest, the Federal Statistical Office started publishing provisional results on causes of death on a monthly basis since July 2021. With regard to these data and in particular because of the COVID-19 deaths, not only underlying causes of death are presented.

For the first time, this analysis also includes multicausal data of COVID-19 deaths (died with COVID-19). In the future, these monthly statistics of provisional causes of death will also include a multiple-cause-of-death analysis. One focus is to identify the most common comorbidities and multiple combinations of comorbidities in those who have died of/with COVID-19 in order to be able to make statements about which people have an increased risk of dying of/with Sars-CoV-2.

Additionally, the pilot project of a nationwide electronic death certificate is also comprehensively evaluating the causes of death in a multicausal manner. One focus of this project will be to analyse the data quality of multicausal causes of death. However, first calculations are showing the advantages and disadvantages of multiple-cause-of-death German data. On the one hand, a multicausal evaluation promises an enormous gain in knowledge regarding the true extent of multimorbidity in aging societies. On the other hand, the analysis all causes of death also reveals the problems of doctors in determining the existing diseases and causes of death of deceased people solely on basis of first external examinations.

Multiple causes associated with COVID-19: how do demographic variables and level of education influence the association?

Simone Navarra and Silvia Simeoni*, Luisa Frova, Enrico Grande, Francesco Grippo, Stefano Marchetti, Chiara Orsi, Marilena Pappagallo.*
**equal contributions*
Division of Integrated Systems for Health, Social Assistance and Welfare, Italian National Institute of Statistics, Rome, Italy

People with comorbidities show an increased vulnerability to developing of severe forms of COVID-19. There are also important differences among age groups and gender in conditions associated with COVID-19, as well as in complications.

The aim of the study is to identify the most frequent causes of death associated with COVID-19 by age and gender, but also to evaluate the impact of socioeconomic conditions (SEC) on the comorbidity associated with Covid-19. In this study, we use the educational level, information available for each death, as a proxy of the SEC. The role of the educational level is poorly explored and represents a novelty in the study of the association among COVID-19 and other conditions.

We analyzed all causes of death reported on the death certificates, grouping them according to a detailed list. We compared deaths occurred in Italy in March-April 2020 mentioning COVID-19 anywhere on the death certificate (cases) with non-COVID-19 deaths (controls). As the control group, we used deaths occurred in 2018 (March-April) in order to avoid the confounding effect of underreporting of COVID-19 in non-COVID-19 deaths during the early pandemic phase in 2020. For each cause of death, we used logistic regression models to calculate the odds ratio of having mentioned the specific cause in COVID-19 compared to non- COVID-19 deaths using age, sex, region of residence and month of death as control variables. Successively, in order to identify the differences in the association in a specific subgroup of decedents, we performed analyses stratified by sex, age group and educational level.

Multiple cause of death data shows disparities in morbidity with educational status in Israel

Nehama Goldberger, Ziona Haklai
Health information division, Ministry of Health, Israel

Background: This study investigated morbidity as reflected in multiple cause of death data in Israel, by educational and ethnic status.

Method: A mortality follow-up of multiple causes of death, 2007- 2017, for a cohort of Israeli residents aged 25-69 in 2007. Educational status was grouped into under 8/missing, 9-11, 12, 13-15 and 16+ years of education. Direct age adjustment was used to calculate the SRMU ratio and indirect adjustment to calculate SMRs by sex and educational group for lower educational groups compared to 16 and above, for mention of multiple causes. A Cox regression model was used to assess the relative risk of different natural multiple causes controlling for age and ethnic group (Jews and Others/ Arabs).

Results: 2.7 million persons were included of whom 137 thousand (5.1%) died. A clear educational gradient in mention of all multiple causes was found, with the exception of suicide, and cancer in females. The highest SMR for multiple natural causes was found for diabetes, 4.15 (95% CI 4.06 - 4.23) for males and 4.58 (95% CI 4.49 -4.67) for females for the lowest educational group compared to the highest. The SRMU's increased and the percentage of deaths with multiple cause mention decreased by educational group for most natural causes, with the exception of cancer.

Hazard ratios from Cox regression showed a similar educational gradient, and were highest for males for multiple mention of dementia, respiratory diseases and diabetes 4.12 (95% CI 3.44 - 4.93), 3.62 (95% CI 3.43 – 3.82) and 3.43 (95% CI 3.19 – 3.68), respectively, for lowest v highest educational group and for diabetes, respiratory and infectious diseases in females, 3.70 (95% CI 3.34 - 4.09), 3.23 (95% CI 3.00 – 3.47) and 3.14 (95% CI 2.92 – 3.37), respectively.

Conclusion: Multiple cause of death disease mention shows educational and ethnic differences in morbidity.

Session 4: COVID-19

Analyzing complications of COVID-19 from death certificates: which ones kill most?

Chiara Orsi, Simone Navarra, Enrico Grande, Silvia Simeoni, Simona Cinque, Luisa Frova, Stefano Marchetti, Marilena Pappagallo, Francesco Grippo
Division of Integrated Systems for Health, Social Assistance and Welfare, Italian National Institute of Statistics, Rome, Italy

Death certificates are the basis for cause-of-death statistics and contain the whole sequence of diseases leading to death. This information is useful for understanding pathways from disease to death. Several complications are associated with COVID-19, nevertheless limited data are still available on complications and comorbidities reported on death certificates of patients with COVID-19.

We identified a method to individuate causal relations among conditions reported on the death certificates. It allows identifying, for a given condition, which are the complications, the precipitating conditions or the antecedent conditions or causes. We analyzed Italian data (March-April 2020) to identify the most relevant complications and precipitating conditions of COVID-19. To show its general applicability, we applied the method to the data for the year 2018 evaluating causal relations of pneumonia and diabetes with other diseases.

Respiratory conditions, such as pneumonia, respiratory failure, respiratory symptoms, adult respiratory distress syndrome, systemic inflammatory response syndrome, are complications of COVID-19. Pneumonia is the most frequent one. Other conditions, mainly non-respiratory, are precipitating conditions, meaning that the causal relation might be not direct, but mediated by other conditions associated to COVID-19. The most frequent are heart failure, sepsis, shock, renal failure. Neoplasms, chronic lower respiratory diseases, cerebrovascular accidents, hypertensive heart diseases, and dementia resulted to be antecedent conditions, meaning that they are not direct causes of COVID-19 but they are pre-existing diseases that increased the risk of dying.

Complications of pneumonia are very similar to those of COVID-19; however, pneumonia is also a complication of chronic lower respiratory diseases, extrapyramidal and movement disorders, some disorders of the immune mechanism. Diabetes is not a complication of any disease. It has only one group of antecedent conditions: congenital malformations and chromosomal anomalies. Several conditions, especially cardiovascular ones, are complications of diabetes.

The method succeeds in highlighting patterns among conditions on death certificates.

The impact of COVID-19-related mortality on life expectancy differences by educational level from a multiple cause-of-death approach. The case of Spain.

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While research on the impact of COVID-19 on life expectancy in Spain is already well-covered, little is yet known on its impact on causes of death, especially from a multiple cause-of-death (MCOD) perspective. Likewise, the study of educational differences in life expectancy has also attracted attention over the last decade, but its role in COVID-19 related mortality has not yet been investigated. We, therefore, propose to analyse the impact of COVID-19-related mortality in Spain on life expectancy differences by educational level from a MCOD approach.

We will use multiple cause-of-death (MCOD) mortality data and population data for Spain (2018–2020; and 2021 if it becomes available before the workshop) by age, sex, and educational attainment from the Spanish National Statistics Institute.

We will first compare, also by educational attainment, the distribution of the main causes of death in 2020 with the previous two years by selecting COVID-19 (ICD10 U07.1, U07.2) as both the underlying cause of death (UCOD) and MCOD. To this end, we will also analyse COVID-19 deaths together with conditions frequently reported in patients with undiagnosed

infection (flu, pneumonia (J09-J18) and selected respiratory diseases (J80, J84.9, J96), especially during the initial stages of the pandemic.

This is followed by an estimate of the educational inequalities in COVID-19-related mortality using the absolute and relative inequality measures RII and SII.

Lastly, we aim to estimate the role of COVID-19 in educational inequalities in both all-cause mortality (life expectancy) and lifespan variation in Spain. We will do this by comparing the corresponding values for the whole population and excluding COVID-19-related deaths.

COVID-19 mortality in Brazil: an analysis of multiple causes of death

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Since the beginning of the pandemic, in March 2020, there have been more than 600,000 deaths by COVID-19 in Brazil. Knowing and describing the morbid process and the contributing causes are the objectives of the present communication. We used the Ministry of Health's mortality information system (SIM) microdata and a multiple-cause-of-death approach, including all conditions, diseases, and injuries mentioned on the death certificate. For 2021, the data are still preliminary. All data are available on the Ministry of Health Department of Informatics (Datasus) website - www.datasus.gov.br. We considered causes that appeared in "Part I" of the death certificate and indicated complications of COVID-19 as a chain-of-event of COVID-19 mortality. Conditions associated with severe COVID-19, which mainly appeared in "Part II," were considered a contributing condition. The analysis includes the region of residence (North, Northeast, Southeast, South, and Center-West), gender, age (< 5; 5-29; 30-60; 70+), race/skin color (black/non-black), local of occurrence of death (inside hospital/ outside hospital) and investigation of the cause of death (yes/no). In 2020, 1,531,524 deaths were reported in SIM, of which 206,646 (14%) were due to COVID. The most frequent chain-of-event causes on the death certificate were lower respiratory infections, mostly pneumonia (46.5%), followed by acute respiratory failure (35.1%) and sepsis (25.2%). Contributing causes were hypertension (30.3%) and diabetes mellitus (25.2%). We observed variations by characteristics of the deceased and circumstances of the death. With the contribution of the multiple-cause-of-death approach, we can better comprehend the morbid process of COVID-19 mortality. But it is essential that certifier physicians report correct and ultimately all causes that led to death.

COVID-19 as Cause of Death in The Netherlands: A Multiple Cause-of-Death Coding Study

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On 27th February 2020, the first patient with COVID-19, the illness caused by SARS-CoV-2 was reported in the Netherlands. It was the start of an epidemic that continues to this day counting more 2 million (reported) cases of COVID-19. Not everyone who is infected with SARS-CoV-2 will succumb to it. Death is due to an interaction between the virus, the host and

the environment. The question addressed in this study is therefore why people with COVID-19 actually die? For answering this question, the relationship between COVID-19 and other causes of death reported by attending physicians on death certificates is studied using the multiple cause-of-death coding method. In the Netherlands from March 2020 to June 2021, 33 008 (12,9 percent) death certificates mentioned COVID-19 as cause of death. In almost 24 percent of these cases, COVID-19 is the only cause of death mentioned on the death certificate. This percentage is also observed in other countries and seems to be an indication of the virulence of the SARS-CoV-2 virus. In 64 percent of cases, 1-3 other diseases played a role as cause of death (co-mortality). When other diseases are also reported as cause of death, there appears to be a statistically significant association (CDAI) between COVID-19 and dementia, Parkinson's disease, COPD, asthma, diabetes mellitus and obesity. These diseases are associated with a reduced resistance (immunological defense) or promote an infection (cytokine storm or increased number of ACE2 receptors). Three patterns of dying emerge: COVID-19 in conjunction with 1. neurodegenerative disorders, 2. chronic respiratory disorders, or 3. metabolic syndrome. The associations found in this study are in agreement with research in other countries. The association between death from COVID-19 and cardiovascular diseases or cancer reported in other studies could not be confirmed.

Session 5: Data quality and methods

Development of an Australian categorisation for MCoD analysis

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Aim: To propose an Australian specific categorization of causes of death for MCoD analysis of multi-morbidity among older people.

Method: Beginning with the “Leading causes of death, Australia” from the Australian Bureau of Statistics, a frequency table of underlying causes of death was produced for the 1.93 million records of all deaths in Australia from 2006 to 2018. This produced groups of varying sizes and obscured details relevant for deaths among older people with multi-morbidity.

This initial grouping was refined using the “Australian Burden of Disease Study” from the Australian Institute of Health and Welfare which grouped injuries into natural (e.g., injury, poisoning) and external causes (including accidents).

Additionally, cause of death groups particularly relevant for the older people were created (e.g., a group comprising dementia and Alzheimer’s disease).

Finally, ICD chapters were used to group the remaining causes of death.

Results: This categorization resulted in 41 groups.

Conclusion: The Australian specific categorization proposed is a hybrid grouping of causes of death reflecting the needs for MCoD analysis for older age groups.

Quantification of mortality incorporating multiple causes of death: Application of different methods, including weighting strategies, to Australian data

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Background: Mortality statistics are typically based on a single underlying cause of death (UC). Although UC provides a useful construct, the relevance of assuming that a single disease caused the death is diminishing, especially with increased life expectancy and high proportions of deaths in older ages from chronic/degenerative diseases. We quantified mortality incorporating multiple causes (MC) of death in Australia.

Methods: All deaths registered in Australia from 2015-2017 (478,454 deaths) and coded using International Classification of Diseases Version 10 were classified using an extended cause list (n=136 causes) based existing causes of death categories. Age-standardised rates were estimated using: (1) UC alone (ASRUC); (2) 'any-mention' (ASRAM) (3) and a weighting method (ASRW) - UC weighted 0.5, remaining 0.5 apportioned to the contributing causes in Part II of the death certificate. Causes were ranked according to magnitude of ASRUC, ASRAM and ASRW, and leading causes compared.

Results: Deaths involved on average 3.4 causes; 18% of deaths involved a single cause, 21% had 2 causes and 61% involved ≥3 causes. Ischaemic heart disease (ASRUC=73.3, ASRAM=135.8, ASRW=63.5), dementia (ASRUC=51.1, ASRAM=98.1, ASRW=52.1) and cerebrovascular diseases (ASRUC=39.9, ASRAM=76.7, ASRW=33.5) ranked as leading causes by all methods. Causes with high RR (ASRAM/ASRUC) included hypertension (ASRUC=2.2, RR=35.5), atrial fibrillation (ASRUC=8.0, RR=6.5) and diabetes (ASRUC=18.5, RR=3.5); the corresponding ASRW were 12.5, 12.6 and 24.0 respectively. Renal failure, atrial fibrillation and hypertension ranked among the ten leading causes by ASRW but not by ASRUC. Rates based on alternative MC weighting methods were similar. Practical considerations in working with MC data are discussed.

Conclusions: Despite similarities in leading causes under the three methods, several preventable diseases emerged as leading causes with integration of MC. Mortality indicators incorporating MC enhance traditional measures of mortality and offer a richer additional perspective for population health monitoring and policy development.

Accuracy of death certification of diabetes, dementia and cancer in Australia

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Aim: To assess how well the chronic conditions a person is known to have in their lifetime are reflected on their death certificate.

Methods: The subjects were the nationally representative random sample of 9056 women born in 1921-26 who participated in the Australian Longitudinal Study on Women's Health. We used record linkage from multiple sources (including regular surveys since 1996, hospital admissions, doctor visits, prescribed medications, cancer registrations and aged care assessments) to identify women with selected chronic conditions. These conditions were: diabetes (chosen because it can be diagnosed from any age and leads to multimorbidity), dementia (almost exclusively in old age) and cancer (well documented in cancer registries). The accuracy of recording these conditions on the death certificate, as the underlying cause of death

(UCOD) or among the multiple causes of death (MCOD) in Part II, was assessed using sensitivity, specificity and positive and negative predicted values.

Results: Sensitivities for UCOD were: diabetes, 12.3% (95% confidence interval (CI) 11.0%, 13.7%), dementia 25.2% (23.7%, 26.7%) and cancer 57.7% (55.9%, 59.5%). The corresponding sensitivities for the conditions mentioned as the UCOD or MCOD were: diabetes, 40.9% (38.8%, 42.9%), dementia 52.3% (50.6%, 54.0%) and cancer 67.1% (65.4%, 68.7%). In contrast the specificity values exceeded 97% indicating that if the condition was mentioned on the death certificate it was very likely the woman had a record of it during her lifetime.

Conclusion: These findings show that mortality statistics, even if based on UCOD and Part II, substantially underestimate the contributions of these conditions to burden of disease.

Studying multiple causes of death in the absence of death certificates: taking advantage of probabilistic methods to estimate causes of death (InterVA)

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In low- and middle- income countries (LMICs), the burden of non-communicable diseases is increasing due to the combination of aging and lifestyle changes. While interest in multimorbidity has been rising to study more precisely the complex morbid processes that adults experience, health data in LMICs are scarce and rarely allow such investigations. Focusing on multimorbidity leading to death, we aim to develop an approach to estimate multiple causes of death using available data. In settings where certification of death by physicians is not available, verbal autopsies (VAs) have been developed to diagnose likely causes of death from information collected via a structured interview with final caregivers about the signs and symptoms leading to death. With an increasing use of probabilistic models to interpret VAs, we investigate their potential for identifying multiple causes using a database of 72,330 adult deaths (15 and older) from 22 Health and Demographic Surveillance System (HDSS) sites located in Asia and Africa, and detailed VA data from the Ouagadougou HDSS in Burkina Faso (1,700 deaths). The Bayesian model InterVA-4 attributes multiple likely causes to 11% of deaths. However, some combinations result more from uncertain diagnosis than multimorbidity. Elaborating an index of similarity between causes based on the InterVA's probability matrix, we aim to differentiate competing causes (uncertainty) from co-occurring causes (multimorbidity). Selecting the most dissimilar associations of causes, we highlight the importance of associations between infectious and non-communicable diseases, as well as the burden of diabetes and cardiovascular diseases among the multimorbidity identified.

Session 6: Specific conditions or diseases

The role of overweight and obesity in adverse cardiovascular disease mortality trends: an analysis of multiple cause of death data from Australia and the USA

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Background: In recent years, there have been adverse trends in premature cardiovascular disease (CVD) mortality rates (35–74 years) in the USA and Australia, which have the highest

adult obesity prevalence of high-income countries. This study investigates the role of overweight and obesity in their recent CVD mortality trends by using multiple cause of death (MCOD) data.

Methods: We identified overweight- and obesity-related mortality as any CVD reported on the death certificate (CVD MCOD) with one or more of diabetes, chronic kidney disease, obesity, lipidemias or hypertensive heart disease (DKOLH-CVD), causes strongly associated with overweight and obesity. DKOLH-CVD comprises 50% of US and 40% of Australian CVD MCOD mortality. Trends in premature age-standardized death rates were compared between DKOLH-CVD and other CVD MCOD deaths (non-DKOLH-CVD). Deaths from 2000-2017 in the USA and 2006–2016 in Australia were analyzed. Trends in in age-specific DKOLH-CVD death rates were related to cohort relative lifetime obesity prevalence.

Results: Each country's DKOLH-CVD mortality rate rose by 3% per annum in the most recent year, but previous declines had reversed more rapidly in Australia. Non-DKOLH-CVD mortality in the USA increased in 2017 after declining strongly in the early 2000s, but in Australia it has continued declining in stark contrast to DKOLH-CVD. There were larger increases in DKOLH-CVD mortality rates at successively younger ages, strongly related with higher relative lifetime obesity prevalence in younger cohorts.

Conclusions: The increase in DKOLH-CVD mortality in each country suggests that overweight and obesity has likely been a key driver of the recent slowdown or reversal of CVD mortality decline in both countries. The larger recent increases in DKOLH-CVD mortality and higher lifetime obesity prevalence in younger age groups are very concerning and are likely to adversely impact CVD mortality trends and hence life expectancy in future.

Senility Deaths in Japan

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Senility deaths (R54) are increasing, counting 132,440, 9.6% of total death in 2020 and it is the third-largest cause of death in Japan. Although they decreased after the application of ICD-6 in 1950, in which senility was assigned to the ill-defined cause, they are increasing again in recent years. The age-specific senility death rate is increasing as well, so the increase is not caused by the increase of deaths of very old persons.

By the examination of death registration information, it was found that 95.1% of senility deaths had only one meaningful description out of eight fields of death certificate form (cause I-a,b,c,d, II, dissection, additional notes, remarks). However, there was a certain number of cases that the deaths were attributed to nothing else than senility, without any other underlying cause. While easy usage of senility should be avoided in writing the death certificate, senility could be re-considered as a well-defined cause of death.

Different patterns of alcohol-related mortality in four European countries: preliminary results based on the Multiple-Causes-of-Death Approach

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In this study, we aim to investigate the pattern of alcohol-related mortality in selected European countries using the Multiple Causes of Death (MCoD) approach. The analysis is performed for Austria (2019–2020), the Czech Republic (2013–2019), Poland (2013) and Spain (2016–2019). For diseases and external causes of death that can be attributed to the abuse of alcohol, we estimate age- and sex-specific death rates and calculate the age-standardised ratios of multiple to underlying causes (SRMUs).

The analysis reveals important differences between the countries under study. First, in Austria, the Czech Republic and Poland mortality is higher and concerns younger persons than in Spain, both in terms of the underlying and multiple causes. Second, the most important underlying cause is alcoholic liver disease in Austria, the Czech Republic and Poland, whereas in Spain it is chronic liver disease. In all countries under study, MCoD ata highlights the importance of chronic conditions as contributing causes of death: 1) chronic liver disease for men in Austria and Poland and for women in four countries, and 2) alcoholic psychosis and chronic alcohol abuse for both sexes in Austria, the Czech Republic and Poland. The SRMUs evidence the following conditions that are the most undervalued in the standard approach based only on the underlying causes of death:alcoholic psychosis, chronic alcohol abuse and alcohol disorders of nervous system.

In the conclusions we discuss the methodological problems and limitations of the study resulting, in the first place, from national differences in MCoD data quality and certification practices.

Chronic obstructive pulmonary disease-related mortality in Brazil, 2000–2019: A multiple-cause-of-death study

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Chronic obstructive pulmonary disease (COPD) remains a compelling cause of morbidity and mortality; however, it is underestimated and undertreated in Brazil. Using multiple causes of death data from the Information System on Mortality, we evaluated, from 2000 to 2019, national proportional mortality; trends in mortality rates stratified by age, sex, and macro-region; and causes of death and seasonal variation, considering COPD as an underlying and associated cause of death. COPD occurred in 1,132,968 deaths, corresponding to a proportional mortality of 5.0% (5.2% and 4.7% among men and women), 67.6% as the underlying, and 32.4% as an associated cause of death. The standardized mortality rate decreased by 25.8% from 2000 to 2019, and the underlying, associated, male and female, Southeast, South, and Center-West region deaths revealed decreasing standardized mortality trends. The mean age at death increased from 73.2 (±12.5) to 76.0 (±12.0) years of age. Respiratory diseases were the leading underlying causes, totaling 69.8%, with COPD itself reported for 67.6% of deaths, followed by circulatory diseases (15.8%) and neoplasms (6.24%). Respiratory failure, pneumonia, septicemia, and hypertensive diseases were the major associated causes of death. Significant seasonal variations, with the highest proportional COPD mortality during winter, occurred in the southeast, south, and center-west regions. This study discloses the need and

value to accurately document epidemiologic trends related to COPD in Brazil, provided its burden on mortality in older age as a significant cause of death, aiming at effective planning of mortality prevention and control.

Session 7: Miscellaneous

Multi-morbidity at death: a comparison of the patterns in four countries

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With increased life expectancy, an ever-growing population is living with several diseases. Multi-morbid patients are at higher risks of dying. Additionally, they represent a major challenge for health systems and caregivers. The Covid pandemic highlights the need to monitor the contribution of multi-morbidity to death processes.

At the 4th meeting of the MultiCause network, we presented a method to classify cause-of-death records according to the presence/absence of multi-morbidity. We implemented this algorithm for all deaths at age 50 and over that occurred in Italy in 2014. Since then, we have improved our classification computer script in various ways, and we have run it on the data for three additional countries: France, Spain, and the United States. We will present the results of this new analysis and compare the patterns of "multi-morbidity at death" in the four countries.

Towards a practical grouping of ICD-10 blocks to facilitate analysis of associated comorbidities with the leading causes of death as recorded on death certificates

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Introduction: The illnesses that are thought to contribute to a death but deemed unrelated to those within the causal sequence of conditions leading to that death are recorded in Part 2 of the medical certificate of cause of death (MCCD). These conditions are in general important comorbidities, often chronic, noted within the background of a person's health profile with likely significant effects on their wellbeing and the utilisation of health resources prior to death. The information contained within Part 2 could therefore be used as a resource to further understand the burden of ill health on individuals and society.

Method: We classified entries in Part 2 of the MCCD into categories built from ICD-10 Blocks. Using these categories, we examined the conditions reported in Part 2 of the MCCD in deaths registered in England and Wales in 2018-19 and the patterns of multimorbidity based on frequency of individual conditions and the specific combinations of comorbidities recorded and associated with death, as well as their relationships with the causal sequence of events leading to death.

Results: Our study demonstrated frequent patterns of conditions associated with mortality that can be quantified and visualized for analysis. Circulatory problems featured in over 80% of

death certificates assessed. Respiratory and endocrine conditions are also common and feature with high recorded prevalence in over 40% of death certificates. The main patterns of comorbidities recorded as contributing to death also had these three conditions in various combinations.

Conclusion: Part 2 of the MCCD provides a valuable resource on societal wellbeing and healthcare needs. It potentially provides information that can further improve our understanding of the major contributors to deaths in England and Wales. Progress on our co-morbidity grouping methodology and analysis will be presented.

Multiple causes of death and seasonality

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The seasonal mortality fluctuations stem from both the cold spells and the heat waves as well as from epidemics. Humans thrive the best at temperatures between 18 and 20 degrees. Deviations from this optimum result in increasing of mortality at a measurable slope, typically with a J-, U- or V-shape, depending on the context and the measurement. Quite well described are the effects of cold, associated with winter season. Summer mortality peaks were quite frequent until the late 19th century, and were historically related to higher exposure to infections due to poor hygiene and contamination of food. Recently, climate change has led to more frequent, intense and longer-lasting heat waves with potentially severe health outcomes.

As seasonal deaths are typically acute (e.g. in heat waves they occur few days after the temperature passes a risk threshold), we focus our attention at immediate causes of death (the most acute cause reported on death certificate, such as dehydration or organ failure). The aim of the study is thus to explore the seasonality with regard to immediate causes of death. Individual data of deaths by cause will be used covering Czechia over the period 1998-2020. Seasonality indices will be computed and analysed. Furthermore, immediate causes seasonality patterns will be assessed using time series and machine learning methods.

Cause-of-death diversity from a multiple-cause perspective in the US*

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Patterns in causes-of-death are known to be key indicators of population well-being. While much is known about leading causes of death and how they have shifted over time, much less is known about the diversity of causes from which individuals die at a given point in time and how it has evolved over time. The diversity in causes of death is unarguably an important marker of health heterogeneity, with higher values suggesting more difficulties both in diagnosis/treatment (i.e., micro-level effects) and health planning (i.e., macro-level effects). The study of cause-of-death diversity has received very little attention despite its important practical implications – especially in the swift ageing process that is sweeping the world. In this paper, we propose a new approach to measure cause-of-death diversity that has been adapted to the specificities prevailing in lowmortality settings, and therefore that is able to account for multiple causes of death (MCOD). We do so by proposing and measuring it in the more general 'Multiple Causes of Death' (MCOD) settings in 2003-18. Our approach is an adaptation of popular approaches commonly applied to assess heterogeneity in human societies or animal ecosystems. Cause-of-death diversity increased in the studied period, and specially up to 2012. These trends were driven by increases in ages 65 and over. The inclusion of MCOD resulted in higher increases in cause-of-death diversity over time compared to merely using underlying causes of death, except for older men where no differences were observed. The observed

increases in cause-of-death diversity should be monitored to better understand mortality dynamics in ageing populations. Our new MCOD diversity measures suggest that traditional approaches relying on single causes

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