Original Research Article

Dementia Related Deaths: A Multiple Cause Coding Study

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ABSTRACT

Background: A multiple cause coding of death certificates is a new way of looking at mortality statistics. Death is attributed to a network of interacting pathological conditions, not just to one disease. For dementia - the leading cause of death in many countries today - this implies a revaluation on its role as cause of death.

Methods: All records mentioning dementia in the 2014-2017 Dutch cause-of-death registry were selected (n = 98 718, 18% of all records). Two internationals agreed on measures for multiple cause coding were calculated: the standardized rate of dementia begin mentioned versus dementia being underlying cause of death (SRMU) and the cause of death association index (CDAI) for relationships between dementia and other diseases or disorders mentioned on the same death certificate.

Results: Dementia was the underlying cause of death in 59% of the death certificates mentioning dementia. The SRMU was 1.68 for all forms of dementia and decreased with an increase of diagnostic specification. For men the SRMU was higher than for women. With regard to all causes being mentioned on a death certificate, several clusters causing death could be identified: 1. Dementia associated with cachexia and dehydration, 2. Dementia associated with infections (pneumonia, urinary tract), 3. Dementia associated with falls, 4. Dementia associated with cardiovascular disorders.

Conclusion: Considering a cluster of diseases as cause of death is a more meaningful way to study mortality in a 21st Century population than selecting just one underlying cause of death per deceased.

Keywords: Dementia, Cause of death, Multiple cause coding, Mortality statistics, SRMU, CDAI

INTRODUCTION
Dementia is a leading cause of death in many countries today [1-2]. This ranking is based on cause-of-death statistics showing one underlying cause of death per deceased person [3]. However, today the majority (75%) of the population in high income countries dies after the age of 70 and about 70% of the deceased have more than three diseases at the end of life [4]. It is therefore more and more difficult to select one ("the") cause of death per deceased. The reduction of the cause of death to one disease or condition masks on average two other diseases that have played a causal role in dying [4]. It also implies a selection hiding the full impact of a disease on death. In the Netherlands, dementia is mentioned as a cause of death on 17.8% of the death certificates, while the disease is selected as underlying cause of death in "just" 10.6% of the deceased. Selecting one underlying cause of death per deceased is not only hiding the full impact of a disease in dying, it is also not in accordance with contemporary views on causality. In the 20th Century, the theory of one cause-one effect has been replaced by the network idea of causality [5-7]. It is not just the smoking cigar causing a forest fire, but the (interacting) presence of oxygen, the careless smoker, the wind, the dry wood, etc. are considered causes as well. There is a network of interacting factors underlying the occurrence of an event. In line with this network idea of causality, it is a cluster of

interacting pathological conditions leading to death and not just one disease or disorder. For dementia this implies, a revaluation of its role in dying. It is not "just" the dementia - as cause-of-death statistics might suggest - , but the interaction of dementia with other pathological conditions causing death. Therefore, in this study the co-occurrence of diseases on death certificates mentioning dementia was investigated in order to better understand the causal role of dementia in dying.

MATERIALS & METHODS

This study is a secondary analysis of routinely collected cause-of-death data. Material is drawn from the 2014-2017 Dutch cause-of-death registry, containing 571 434 death certificates. These death certificates were automatically coded with Iris version 4.4.1 according to ICD-10 conventions and guidelines [8]. WHO updates for the year in question were applied [9]. The choice of these years was based on the use of the same Iris version (4.4.1) so that the results are not subjected to a change in software as might have been the case for other/later years. Iris coded about 66% of the records without human intervention and could assign an underlying cause of death in about 93% of the cases [10]. Iris enables a multiple cause coding of death certificates. All medical expressions on a death certificate are coded taking mutual relationships among codes into account.

All death certificates mentioning dementia (n= 98 718) were selected and associations with other causes of death studied by calculating a standardized Cause-of-Death Association Index (CDAI). This index represents the number of times a cause of death (c) co-occurs with an underlying cause of death (u) (numerator) by the prevalence of this cause of death (c) as such (denominator) in a standard population of deceased persons (box 1).

Box 1. The cause of death association index (CDAI) [14]

$$CDAI_{u,c} = \frac{\sum_x \frac{_u d_{c,x}}{_u d_x} . \overline{d}_x}{\sum_x \frac{d_{c,x}}{d_x} . \overline{d}_x} * 100$$

In this formula:
udc, x = number of deaths at age x with the underlying cause of death u and as the leading cause of death c
udx = number of deaths at age x with the underlying cause of death u
dc, x = number of deaths at age x with the leading cause of death c (regardless of underlying cause of death)
dx = total number of deaths at age x (regardless of underlying cause of death)
dx (with dash) = standard number of deaths at age x (regardless of underlying cause of death)
The "Standardized Ratio of Multiple to Underlying Cause" (SRMU) is defined as the ratio between the number of times a cause of death is reported/mentioned on a death certificate (numerator) and the number of times it is selected as the underlying cause of death (denominator) in a standard population [11]. The SRMU represents the selection of a disease for mortality statistics. The 2013 "European Standard Population" was used as the standard [12].

RESULTS

Dementia was the underlying cause of death in 59% of the cases mentioning dementia as a cause of death. The selection rate (SRMU) of dementia decreased by an increasing number of causes on a death certificate. The SR was 100% for certificates mentioning just one cause (dementia), and 73%, 62%, 54%, 48% for certificates mentioning two, three, four and five or more causes of death, respectively. Just 4.2% of the records had dementia as the only cause of death. Most often, dementia appeared in a cluster of three (28%), four (22%), two (21%) and

five (13%) causes of death, covering 83% of all cases. In 53% of the cases mentioning dementia as a cause of death, dementia was noted on part 2 of the death certificate (the position of a contributory cause of death). The age and sex standardized rate for dementia being mentioned on a death certificate was 158 per 100 000 men and 174 per 100 000 women. The age and sex standardized rate for dementia being selected as underlying cause of death was 89 per 100 000 men and 107 per 100 000 woman (*figure 1*).

Figure 1a. Dementia as underlying cause of death (UCOD) and as cause of death being mentioned on a death certificate (Mention) for men (Dutch death registry 2014-2017)
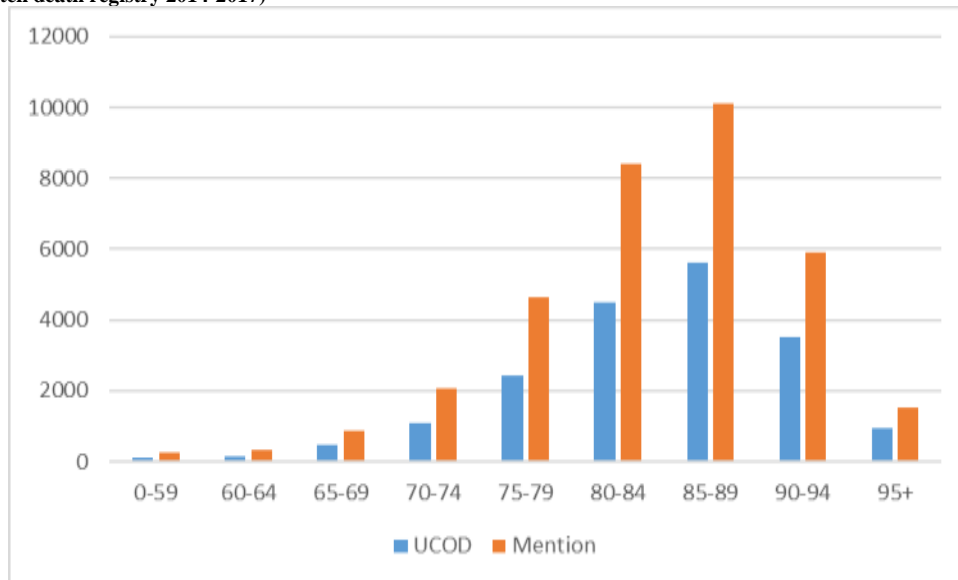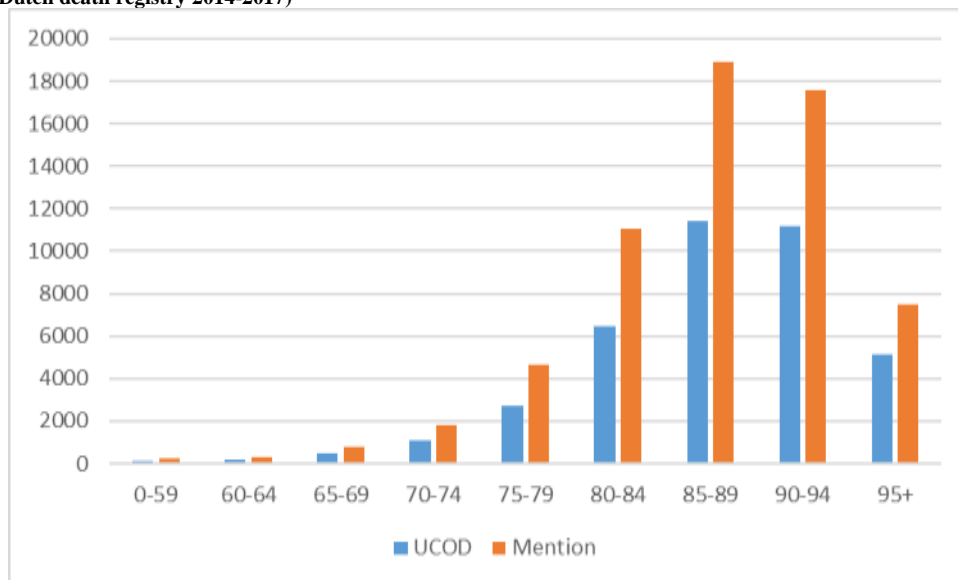

Figure 1b. Dementia as underlying cause of death (UCOD) and as cause of death being mentioned on a death certificate (Mention) for women (Dutch death registry 2014-2017)

For all forms of dementia there was a substantial selection with regard to its occurrence in cause-of-death statistics. They were 1.68 times more cases of dementia mentioned on a death certificate than selected as underlying cause of death. SRMU's were varying from 2.1 for vascular dementia to 1.5 for Lewy-body dementia. In general, the SRMU decreased with an increased specification of the diagnosis. For women the SRMU was lower than for men (*table 1*).

Table 1. The SRMU for different forms of dementia (Source: Dutch death registry 2014-2017)

SRMU	Women	Men	Total	Rate per 100 000 EPS*
Vascular dementia (ICD-10: F01)	2.21	2.04	2.11	8.3
Dementia not otherwise specified (ICD-10: F03)	1.69	1.84	1.76	61.8
Dementia Alzheimer Type (ICD-10: G30)	1.58	1.71	1.63	24.0
Pick's disease (ICD-10: G31.0)	1.45	1.64	1.55	0.8
LewyBody disease (ICD-10: G31.8)	1.43	1.55	1.51	2.2
All forms	1.62	1.77	1.68	98.0

*European Standard Population [12]

With regard to causal sequences mentioned on a death certificate six meaningful clusters of causes explained almost 90% of the cases (table 2).

Table 2. Frequency of causal sequences when dying from dementia (n = 98 718)

Death Certificate [3]					
Part	1a (Direct CoD: disease or condition leading directly to death)	1b (Intermediate CoD: disease or condition, if any, leading to 1a)	1c (Underlying CoD: the *start* of the causal sequence leading to death, i.e. to 1b, if any, or to 1a) **	2 (Contributory CoD: disease or condition without which the patient would not have died, not being part of the causal chain 1a-1c.)	
Causal sequence (in order of importance/frequency of occurrence)					Causal mechanism
1 (47%)	Dehydration/cachexia	Stop eating/drinking	Dementia		Neurodegeneration (ND)
2 (22%)	Pneumonia/lower resp. tract infection		Dementia		Irregular/shallow breathing due to neurodegeneration
	Respiratory failure	Pneumonia/lower resp. tract infection		Dementia	Low resistance
3 (7%)	Urinary tract infection/sepsis		Dementia		Incontinence/retention
	Sepsis	Urinary tract infection		Dementia	Low resistance
4 (5%) *	Complications of (femur) fracture/fall		Dementia		Instability gait/posture due to ND
5 (4%)	Complications of cerebrovascular accident			Dementia	Atherosclerose
6 (4%)	Congestive heart failure		Dementia		Immobility/cachexia due to ND
7 (3%)	Aspiration (pneumonia)		Dementia		Difficulties swallowing due to ND
8	Others (less than 1%)				

CoD = cause of death; *According to ICD-10 conventions an external cause of death; ** the disease or condition thought to be the underlying cause of death should appear in the lowest completed line of part I [3]

Underlying death, there was a cluster of: 1. Dementia associated with cachexia and dehydration (47%), 2. Dementia associated with pneumonia, lower respiratory tract infections, respiratory failure or sepsis (22%), 3. Dementia associated with urinary tract infections or sepsis (7%), 4. Dementia associated with complications of trauma (5%), 5. Dementia associated with congestive heart failure (4%), and 6. dementia associated with complications of a cerebrovascular accident (CVA) (4%). These clusters of causes could be attributed to neurodegeneration with its loss of voluntary reflexes (breathing, swallowing, posture, gait) or executive functions (drinking, eating), a reduced immunological resistance and atherosclerosis as underlying pathological processes (*table 2*).

The CDAI showed statistically significant associations for dementia and cachexia/dehydration, dementia and urinary tract infections and for dementia and pneumonia. Reported sequences of dementia followed by sepsis, lower respiratory tract infections, stroke (cerebrovascular accident, cva), congestive heart failure and accidental fall could not be validated by a statistically significant CDAI (*table 3*).

Table 3. CDAI for dementia and some other causes of death

	CDAI	95%-CI	
		lower limit	upper limit
cachexia/dehydration	333	205	541
urinary tract infection	203	106	390
pneumonia	146	125	172
sepsis	112	79	158
lower respiratory tract infection	60	47	79
stroke (CVA)	56	44	71
heart failure	36	28	45
cardiovascular disease	14	13	15
fall	11	9	15
cancer	8	6	10

DISCUSSION

The role of dementia as cause of death was studied by a multiple cause coding of death certificates. Dementia was identified as part of several pathological clusters leading to death. Attributing the cause of death to a cluster of diseases is in accordance with contemporary views on causality in which the co-occurrence of determinants (a set of necessary and sufficient factors) forming a network in time-space may constitute an event, instead of a sequence of consecutive events in time [5-7]. For dementia, three pathological clusters could be distinguished as cause of death: 1. Dementia with cachexia and or dehydration, 2. Dementia with pneumonia, and 3. Dementia with urinary tract infections. The first cluster can be explained by a progress of the neuro-degeneration underlying dementia [13-15]. The second and third clusters show the diminished resistance towards infectious diseases accompanying the neurodegenerative process [16] [17]. The clusters reflect the findings at autopsy [18]. The reported causal sequences of dementia with falls, cerebrovascular accidents or congestive heart failure could not be validated by a CDAI. Reporting a fall as external cause of death probably hinders the study of a causal connection with dementia. WHO should reconsider its instructions with regard to this as in aging populations external causes are more and more in line with underlying diseases. The co-occurrence of dementia and congestive heart failure is probably a spurious correlation based on the widespread occurrence of heart failure as direct cause of death at the end of life. The co-occurrence of dementia and a cerebrovascular accident can be explained by an atherosclerotic process underlying both pathological conditions, i.e. the vascular aspect of dementia.

On both epidemiological and philosophical grounds, "the underlying cause of death" is an outdated concept raising problems when studying mortality in an aging population. It requires selection of *one, i.e. the* cause of death [19], not justifying the increasing occurrence of multi-morbidity at the end of life on the one hand and the clinical reality of certifiers confronted with a network of causal conditions on the other [20]. Multiple cause coding of death certificates is an alternative [21]. It requires no selection rules, just the coding of all causes mentioned on a death certificate. Its limitation is a well filled in death certificate which is not always the case [22]. Over all, multiple cause coding shows the role of a disease in dying by meaningful clusters, serving etiological insights of clinicians and epidemiological information for research or health care policy.

CONCLUSION

The attribution of death to a cluster of diseases or disorders is a meaningful way to study mortality in a 21st Century population. It provides a more valid picture of mortality than the traditional selection of one underlying cause of death. It enables to differentiate between spurious and true causal connections as the case of dementia shows. Not dementia as such is a cause of death, but the co-occurrence of dementia with cachexia/dehydration, pneumonia or urinary tract infections are leading to death. The pathological relationships between

dementia and cerebrovascular accident or congestive heart failure could not be validated and need further investigation.

Declarations by the author

Ethical Approval: According to Dutch Civil Law (Article 7: 458) no ethical approval is required for a secondary analysis on anonymized data of deceased persons.

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Conflict of Interest: The author declares no conflict of interest.

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REFERENCES

1. Eurostat, causes of death - deaths by country of residence and occurrence [cited 28 May 2018]. Available from: http://appsso.eurostat.ec.europa.eu/nui/submitViewTableAction.do (dementia).
2. Prince M, Wimo A, Guerchet M, Ali GC, Wu YT, Prina M. World Alzheimer Report 2015: The Global Impact of Dementia. An analysis of prevalence, incidence, cost and trends. London: Alzheimer's Disease International; 2015.
3. World Health Organisation (WHO) International Statistical Classification of Diseases and Related Health Problems, 10th Revision. Volume 2 (Instruction manual). Geneva: WHO; 1993.
4. Désesquelles A, Gamboni A, Demuru E and the MultiCause network. We only die once… but from how many causes? Population and Societies 2016 (Number 543): 1-4.
5. Schaffer J. The Metaphysics of Causation. In: Zalta EN (ed.). The Stanford Encyclopedia of Philosophy (Fall 2016 Edition): https://plato.stanford.edu/archives/fall2016/entries/causation-metaphysics.
6. Vineis P. Causality in epidemiology. Sozial- und Präventivmedizin 2003*;* 48:80-87.
7. Araújo de LFS, Dalgalarrondo P, Banzato CE. On the notion of causality in medicine: addressing Austin Bradford Hill and John L. Mackie. Archives of Clinical Psychiatry 2014*;* 41:56-61.
8. IRIS Institute. IRIS User Reference Manual V4.4.1. Cologne: IRIS Institute; 2014. Available from; www.iris-institute.org.
9. World Health Organization (WHO). List of Official ICD-10 Updates. https://www.who.int/classifications/icd/icd10updates/en/, accessed 8-1-2020.
10. Harteloh PPM. The implementation of an automated coding system for cause-of-death statistics. Informatics for Health and Social Care. Doi: 10.1080/17538157.2018.1496092.
11. INED. Institut National d'études Démographiques. Guidelines for the computation of the standard MCOD indicators. Paris: INED, 2009.
12. Eurostat. Revision of the European Standard Population: Report of Eurostat's task force. Luxembourg: Publications Office of the European Union, 2013
13. Brunnström HR, Englund EM. Cause of death in patients with dementia disorders. Eur J Neurol 2009;16;488-492. doi: 10.1111/j.1468-1331.2008.02503. x.
14. Foley NC, Affoo RH, Martin RE. A systematic review and meta-analysis examining pneumonia-associated mortality in dementia. Dement Geriatr Cogn Disord 2015; 39:52-67. doi: 10.1159/000367783.
15. WHO. World health Organization. Dementia. Available from: http://www.who.int/mediacentre/factsheets/fs362/en/.
16. Burns A, Lliffe S. Dementia. BMJ 2009*;*338:b75.
17. Guhne U, Matschinger H, Angermeyer MC, Riedel-Heller SG. Incident dementia cases and mortality. Results of the leipzig Longitudinal Study of the Aged (LEILA75+). Dement Geriatr Cogn Disord 2006; 22:185-93. doi: 10.1159/000094786.
18. Degerskär ANW, Englund EM. Cause of death in autopsy-confirmed dementia disorders. Eur J Neurol. 2020; 27:2415-2421. doi: 10.1111/ene.14450.
19. World Health Organization (WHO). International Statistical Classification of Diseases and Related Health Problems, 10th Revision. Volume 2 (Instruction manual). Geneva: WHO, 2016.
20. Grippo F, Désesquelles A, Pappagallo M, Frova L, Egidi V, Meslé F. Multi-morbidity and frailty at death: A new classification of death records for an ageing world.

Population Studies 2020; 74: 437-449. DOI: 10.1080/00324728.2020.1820558

21. Israel RA, Rosenberg HM, Curtis LR. Analytical potential for multiple cause-of-death data. Journal of Epidemiology 1986; 124: 161-179.

22. Kotabagi RB, Chaturvedi R, Banerjee A. Medical Certification of Cause of Death. *Med J Armed Forces India* 2004; 60: 261-

72. https://doi.org/10.1016/S0377-1237(04)80060-1

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