Does quality control of death certificates in hospitals have an impact on cause of death statistics?

BACKGROUND The effects of inaccurate death certificates on cause of death statistics are uncertain. Since 2008, Akershus University Hospital has systematically corrected all death certificates. The effects of these corrections on the total cause of death statistics from the hospital were studied.

MATERIAL AND METHOD ICD-10 codes for the underlying cause of death on the original and the corrected death certificates issued by Akershus University Hospital were retrieved from the Cause of Death Registry for the period 1 May 2008–31 December 2009, once the Cause of Death Registry had processed the death certificates with the aid of the computer program ACME (Automatic Classification of Medical Entities).

RESULTS Altogether 1 001 deaths were investigated (547 men and 454 women). A total of 223 death certificates were corrected. This entailed changing the underlying cause of death in 176 cases. Death certificates for women were corrected most frequently. In 121 cases, the changes entailed a change of disease chapter in ICD-10. The corrections caused a significant reduction in the number of unspecific diagnoses, such as sepsis, cardiac arrest, pneumonia with no further specification, renal failure and fractures without any specific cause. There was a significant exchange of individuals within all the large diagnostic groups, with the exception of cancer. Because of the balancing effect of exchanges within and between the disease chapters, this generated only minor effects on general statistics on causes of death.

INTERPRETATION The continuous correction of death certificates in the hospital was important for adjustments at the individual level and as a quality control of cause of death statistics, but had only minor effects on the general statistics from the hospital.

The regulations for entering information on death certificates have been determined by the World Health Organization (WHO) and are used worldwide (1). This notwithstanding, the completion of the certificates presents problems, both because doctors issue death certificates relatively rarely, and because the course of the disease is often complicated. A number of studies have shown that death certificates are often fraught with error (2-4). How these errors affect national cause of death statistics remains unclear. Studies of this issue tend to be registrybased without any control for actual case histories, they may be based on manual amendments to a small number of death certificates, or they may be retrospective with no electronically based coding (5-8).

Since 2005, the Cause of Death Registry has used the computer program Automatic Classification of Medical Entities (ACME) to identify the underlying cause of death. The computer program was developed by the US National Center for Health Statistics, and determines the underlying cause of death according to rules and guidelines established by the WHO (International Classification of Diseases, ICD), thus helping to achieve a more homogenous coding and improve international comparability (9–11).

Since 2008, Akershus University Hospital has undertaken a systematic and continuous quality control of death certificates issued after deaths occurring in the hospital (4). The reasons for the review include a desire to improve the listing of causes of death. Since May 2008, the original as well as the amended death certificates have been submitted to the Cause of Death Registry, and this provides an opportunity to study the effects of the quality control. Here we will present the effects that this continuous correction of the death certificates have produced with regard to public statistics on causes of death, after processing of the data with the aid of ACME.

Material and method

The data for the study are based on the *Doctor's declaration of death/report of death by unnatural causes* (here referred to as the death certificate) submitted to the Cause of Death Registry. A detailed review of the listing of underlying cause of death and contributing diseases as well as of the processing of death certificates by the Cause of Death Registry has previously been published in this journal (12).

In brief, the death certificate contains two fields for entering diseases. In Field I, the doctor enters the condition or disease that brought about death. The development of the course of disease can be described in steps (Ic-Ia) if this is deemed to be necessary to establish a proper understanding of the case. The various steps must be correlated in

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MAIN MESSAGE

Continuous quality assurance of death certificates in hospitals provided an important corrective at the individual level.

A considerable reduction in the number of unspecific diagnostic codes («garbage diagnoses») testified to the improved quality of the death certificates after the correction.

Because of a balanced exchange of codes between the various disease chapters, the quality assurance produced only minor consequences for the hospital's cause of death statistics as a whole.

The study permits no conclusions regarding the quality of nationwide cause of death statistics. a medically logical manner. The earliest step in the causal chain, i.e. the condition or disease that initiated the process of death, is reported as the underlying cause of death. In Field II, other serious diseases that may have had an effect on the process of death may be listed.

In the Cause of Death Registry the diagnostic texts are translated into ICD-10 codes (International Classification of Diseases, version 10) and processed (10). The ICD-10 codes are listed in the same order as they were entered by the doctor who completed the form. The cause of death is subsequently determined automatically by the ACME computer program, which processes the data according to ICD-10 rules. Table 1 provides an example of the determination of the underlying cause of death with the application of ICD-10 rules.

Death certificates after deaths of patients at Akershus University Hospital who were aged two or older in the period 1 May 2008-31 December 2009 were compared to the patient records for an assessment of whether the underlying cause of death had been correctly reported. The same two pathologists (GCA/LGL) shared the task of undertaking the daily review. Wherever doubts regarding the correctness of the death certificate arose, the completing doctor was contacted and a new listing of causes was proposed. Amendments were proposed only for death certificates for which it was assumed that the Cause of Death Registry would record an erroneous underlying cause of death. These were primarily death certificates where the underlying cause of death was clearly wrong or omitted, or certificates where the location of the cause of death in the listing gave rise to the suspicion that the coding might end up faulty (for example identification of an underlying cause of death as a contributing disease in Field II). The death certificates were amended by the completing doctor or by a pathologist in consultation with the completing doctor and after checking the case history. The pathologists submitted the corrected death certificates after the Cause of Death Registry had completed the registration of the original submissions.

The effect of the amendments undertaken during the period 1 May 2008-31 December 2009 was investigated. For all death certificates, the originals as well as the amended versions, we were supplied with all ICD-10 codes for the underlying and the contributing causes of death («code strings»), in addition to the final ICD-10 code for the underlying cause of death after the processing of the code strings. We also received information on the gender and age of the deceased, as well as information about autopsies. Since an autopsy entails a correction of the cause of death through submission on an autopsy report, all autopsied deaths were excluded from the study.

Table 1 ACME-based determination of the underlying cause of death

a Correctly completed death certificate

Diagnoses, the death certificate	ICD-10	ACME
1a Acute myocardial infarction	121.4	Is I214 a consequence of J44.9? Yes
1b Pneumonia	J18.9	Choose as tentative underlying cause of death: J44.9
1c COPD	J44.9	Known combination?' J44.9 J18.9 J44.0 Yes Choose underlying cause of death: J44.0
II Ischaemic heart disease	125.9	

b Erroneously completed death certificate, with a logical inconsistency in the causal chain in Field I

Diagnoses, the death certificate	ICD-10	ACME
1a Acute myocardial infarction	121.4	Is I21.4 a consequence of K56.7? Yes
1b COPD	J44.9	No tentative underlying cause of death possible
1c lleus	K56.7	Is I21.4 a consequence of J44.9? Yes Is J44.9 a consequence of K56.7? No
II Chronic alcoholism	F10.2	Choose underlying cause of death: J44.9

c Erroneously completed death certificate, with the underlying cause of death listed in Field II

Diagnoses, the death certificate	ICD-10	ACME
1a Sepsis	A41.9	Is A41.9 a consequence of J18.9? Yes
1b Bronchopneumonia	J18.9	Further direct sequences? ²
II Renal cancer, chronic respiratory failure	C64, J44.9	Is J18.9 a consequence of C64? Yes Choose underlying cause of death: C64

¹ ICD has separate code numbers for several known combinations. The combination of pneumonia and COPD has the code J44.0, which is used for the underlying cause of death instead of J.44.9.

² ACME always tests the tentative underlying cause of death in Field I against further sequences in Field II, but this does not appear on the analytic printout if the underlying cause of death is determined by sequences in Field I.

All statistical analyses were undertaken with the aid of PASW Statistics 18. The chisquare test was used for statistical testing. P-values < 0.05 were regarded as statistically significant.

All data from the Cause of Death Registry had been anonymised.

Results

Over the period 1 May 2008–31 December 2009, a total of 1 230 deaths were recorded. For 229 of these an autopsy was performed. The remaining 1 001 deaths comprised 547 men and 454 women. The median age at death was 77 years for men and 80 years for women. There were no significant differences between the age and gender distributions for 2008 and 2009.

A new version of the death certificate was submitted to the Cause of Death Registry for 223 deaths (22%). Women were overrepresented, accounting for 52% of the group of corrected death certificates, against 43% of the non-corrected group. The age distribution in the corrected group was not different from the non-corrected (the median age of corrected and non-corrected women was 79 and 80 years respectively). The correction of the death certificates led to a new ICD-10 code for the underlying cause of death in 176 cases (Table 2). In 121 of these cases (12.1% of the total), the change of ICD-10 code entailed a relocation to another disease chapter.

Table 2 The significance of quality assuranceof death certificates for ICD-10 codes of theunderlying cause of death. Non-autopsieddeaths at Akershus University Hospital inthe period 1 May 2008–31 December 2009.(N = 1 001)

	Number (%)
No change proposed	778 (77.7)
The proposed change had no effect on coding	47 (4.7)
Change resulted in a new code, but within the same chapter	55 (5.5)
Change entailed relocation to another chapter	121 (12.1)
Total	1 001 (100)

Table 3 ICD-10 coding of the underlying cause of death before and after correction of 223 death certificates issued at Akershus University Hospital during the period 1 May 2008–31 December 2009. For each chapter, the table shows the number of codes before the changes (i.e. based on the original death certificates) and the result after the changes had been made. The number of cases that were relocated to another code chapter as a result of the correction is also stated.

ICD-10		Underlying cause of death				
Chapter, codes	Disease group	Before change	After change	Relocated to another chapter	Relocated from another chapter	
I: A 00- B99	Infections	22	6	19	3	
II: C00-C9	Malignant neoplasms	27	44	2	19	
III: D50-D89	Diseases of the blood and the immune system	4	2	3	1	
IV: E00-E90	Endocrine, nutritional and metabolic diseases	5	8	4	7	
V: F00-F99	Mental disorders	4	9	2	7	
VI: G00-G99	Diseases of the nervous system	1	9	0	8	
IX: 100-199	Diseases of the circulatory system	74	60	36	22	
X: J00-J99	Diseases of the respiratory system	34	17	23	6	
XI: K00-K93	Diseases of the digestive system	23	28	7	12	
XII: L00-L99	Diseases of the skin	0	0	0	0	
XIII: M00-M99	Diseases of the musculoskeletal system	1	2	1	2	
XIV: N00-N99	Diseases of the genitourinary system	12	2	11	1	
XVII: Q00-Q99	Congenital malformations	1	1	1	1	
XVIII: R00-R99	Unspecified, symptoms	0	1	0	1	
XIX: V01-Y89	Injuries	15	34	12	31	
Sum		223	223	121	121	

Table 4 Cardiovascular diseases as underlying cause of death in death certificates that were corrected (n = 223) at Akershus University Hospital in the period 1 May 2008–31 December 2009. The number of codes in the various disease groups in ICD-10 chapter IX based on the original death certificates and number after correction are shown. For the corrected death certificates, the table shows the number of codes that remained unchanged, that were changed within the same chapter or retrieved from another chapter. The number of cases of cardiovascular disease in the entire material (N = 1 1001) after the inclusion of corrected certificates is shown in the right-hand column.

	Underlying cause of death, certificates that were corrected					
Disease (ICD-10 codes)	Before change	After change	No change	Relocated within chapter IX	Retrieved from another chapter	Underlying cause of death, all certificates
Hypertension (I10–15)	1	6	0	3	3	9
Ischaemic heart disease (I20–25)	23	20	5	5	10	131
Pulmonary heart disease/ circulatory (I26–28)	1	2	0	1	1	7
Other heart disease (105, 130–52)	25	15	4	5	6	59
Whereof cardiac arrest (146)	3	0	0	0	0	2
Intracerebral haemorrhage (161–62, 169.1)	10	1	1	0	0	11
Cerebral infarction, «stroke» [163–64, 169.4]	12	12	8	3	1	33
Other vascular disease I67, I70–74, I81	2	4	2	1	1	31
Sum	74	60	20	18	22	281

Table 5ICD-10 codes for the underlying cause of death for 1 001 deaths at Akershus University Hospital in the period 1 May 2008–31 December2009, based on original death certificates without any corrections and after quality assurance, involving correction of 223 death certificates.The proportion of codes is listed as a percentage of all deaths.

ICD-10		Underlying causes of death, proportion in per cent		
Chapter, codes	Disease group	Original death certificates	Death certificates after quality assurance	
I: A 00- B99	Infections	4.2	2.6	
II: C00-C9	Malignant neoplasms	36.4	38.1	
III: D50-D89	Diseases of the blood and the immune system	1.7	1.5	
IV: E00-E90	Endocrine, nutritional and metabolic diseases	1.5	1.8	
V: F00-F99	Mental disorders	0.7	1.2	
VI: G00-G99	Diseases of the nervous system	1.5	2.3	
IX: 100-199	Diseases of the circulatory system	29.5	28.1	
X: J00-J99	Diseases of the respiratory system	11.7	10	
XI: K00-K93	Diseases of the digestive system	5.5	6	
XII: L00-L99	Diseases of the skin	0.1	0.1	
XIII: M00-M99	Diseases of the musculoskeletal system	0.8	0.9	
XIV: N00-N99	Diseases of the genitourinary system	1.5	0.5	
XVII: Q00-Q99	Congenital malformations	0.1	0.1	
XVIII: R00-R99	Unspecified, symptoms	0.1	0.2	
XIX: V01- Y89	Injuries	4.7	6.5	
Sum		100	100	

The differences in the ICD-10 codes for the underlying cause of death before and after the correction of the death certificates are shown in Table 3. A major proportion of the changes after correction resulted from replacement of unspecified diagnostic codes with more specific diagnoses. The number of diagnoses of sepsis in Chapter 1 was reduced from 17 to one, the number of cardiac arrest diagnoses in Chapter IX from three to zero, the number of unspecified pneumonias in Chapter X from ten to three, the number of renal failure diagnoses in Chapter XIV from nine to one, and the number of unspecified fractures in Chapter XIX from 12 to three. Codes for hypertension or atherosclerosis with no specified cause, respiratory failure, and cancer without any reported location were also considered as unspecified. The proportion of unspecified diagnoses in the corrected death certificates was reduced by 79%, from 57 before the correction to 12 afterwards. The disease chapters cancer and injuries increased noticeably after the corrections. As shown in Table 3, there was a comprehensive exchange of individuals between all the different chapters.

Nearly half of all cases that originally were coded as deaths from diseases of the circulatory system were replaced as a result of the corrections (36 of 74) (Table 3). The changes in this largest chapter are specified in Table 4. After the corrections there was total agreement on the diagnosis of ischaemic heart failure in only five of 20 cases, and half of the changes were relocated from other chapters. Approximately one tenth of all diagnoses of ischaemic heart disease thus resulted from corrections to death certificates (15 of 131). The largest changes involved ten deaths which originally had been coded as intracerebral haemorrhage. With one exception, all these were relocated to disease groups where anticoagulants or thrombolytic treatment had been administered.

In 47 of 223 death certificates (21%) the corrections did not entail a change to the underlying cause of death. The main reason for this absence of change after correction was the WHO rule that permits drawing on information from Part II if Part I has been completed incorrectly (Table 1c). These cases were thus corrected identically by the manual procedure and by ACME. The most frequent occurrences applied to cases of cancer (nine certificates), chronic obstructive pulmonary disorder (six certificates), stroke (four certificates) and ischaemic heart disease (three certificates). Some cases of absent corrections were due to the fact that not all medical correlations are approved by the ICD-10 regulations.

The effects of the changes to underlying

causes of death on the death certificates for the total number of non-autopsied deaths at Akershus University Hospital for the study period are shown in Table 5. On the whole, the corrections had only minor effects for cause of death statistics. The proportion coded as malignant neoplasms (Chapter II) or injuries (Chapter XIX) had an absolute increase of 1.7% and 1.8% respectively, while diseases of the circulatory system (Chapter IX) and the respiratory system (Chapter X) were correspondingly reduced. The increase of 17 new death certificates where the cause was reported as a malignant neoplasm was only in four cases due to malignancy being discovered during the review of the case history, without having been referred to in the original death certificate.

The number of deaths from external causes increased mainly at the expense of deaths caused by diseases of the circulatory system and unspecified infections. No disease groups stood out in terms of the cause of relocations within or between the other chapters.

Discussion

Information on causes of death is crucial to monitor the patterns of illness in the population, and provides the foundation for planning and implementation of health-related programmes (13). Quality control of the data that go into these statistics is therefore essential. Our review of data from nonautopsied hospital deaths showed that there was a considerable reallocation of individual cases. A change of ICD-10 code occurred in 17.6% of the death certificates – to another disease chapter for 12.1% of the certificates and to another disease code within the same chapter for 5.5%. The effects of these changes on cause of death statistics from the hospital were less significant, and did not exceed 2% for any of the large disease chapters.

We have no knowledge of similar investigations of the effect of continuous quality control of death certificates in a hospital material, including the use of ACME. A retrospective, manual study of 4 644 deaths in hospitals in Thailand documented large differences between the hospitals and changes in 6-48% of the death certificates after they had been reviewed by a coding team (8). A Swedish registry-based study did not check the case histories, but correlated the ICD-10 codes in 69 818 death certificates with the discharge codes from the last hospitalisation. This changed the underlying cause of death in 11% of the cases (5). The results from these studies are not directly comparable to ours, but illustrate the large variation in the quality of the death certificates and the methodological problems involved in quality control of them.

In our material, the death certificates were corrected more frequently in cases where the deceased was a female. The reasons for this are uncertain, especially since the age difference between the genders was no more than three years of median age, and no age differences were detected in the corrected group when compared to the non-corrected. Explanations of the fact that the quality of death certificates fails to improve despite medical progress include multi-morbidity and complex disease conditions resulting from increasing life expectancies (14). However, the age difference between the genders in our material is unlikely to be sufficiently large to explain the difference in gender representation. We have no information on whether the disease pattern of the women in general was more complex than that of the men.

The use of «garbage diagnoses» is a known problem in cause of death statistics, and has been described in detail by Naghavi and collaborators (15). Sepsis, pneumonia, renal failure and fractures without specification of cause were among the most common unspecified diagnoses in our material. On the whole, this group of «garbage diagnoses» was reduced by 79% as a result of the review. Codes from ICD-10 Chapter XVIII (symptoms, signs and similar), on the other hand, figured only rarely as original diagnoses. The observation that these symptom codes were used only in exceptional cases may be related to the fact that our

study did not include autopsies, in which such codes are used more frequently (12). Nationwide, the proportion of symptom codes in the death certificates accounts for 3-4% (12).

The proportion of corrected death certificates in our material is a minimum figure. Because the proposals for amendments were discussed with the completing doctor, we cannot exclude the possibility that some of the death certificates were corrected manually by the clinician after the discussion and before submission. The fact that 47 of the corrections made by the pathologists did not include a change to the underlying cause of death may be partly due to such double corrections. If the pathologists had been better trained in the use of the ICD-10 coding system, many of the corrections that were caused by «backtracking» of the underlying cause of death from Field II in the death certificates could probably have been avoided as well.

The submission of death certificates to the Cause of Death Registry normally goes via a public medical officer, who checks their completion. However, the scope of the changes that occur as a result of the check made by the public medical officer is not recorded by the registry. We have thus no information as to whether any of the original death certificates in our study have been amended by a public medical officer.

Continuous quality control, such as that undertaken by us at Akershus University Hospital, has several obvious advantages: The deaths have occurred only recently, and the case history can easily be recapitulated. In addition, the completing doctor and others who were familiar with the patient are immediately available for consultation. We have also on a previous occasion documented how continuous feedback on the completion of death certificates has an effect on their quality (4). The learning effect may thus be assumed to have contributed to a smaller proportion of changes in our material when compared to what could be expected in other hospitals of the same size. The fact that in our hospital, the death certificates are normally completed by the youngest doctors and that a large number of doctors participate in this, means that each individual doctor has little practice in it. Consistent continuous follow-up will therefore be required to maintain the quality of the death certificates.

Continuous quality control of the death certificates produced only small percentage changes among the ICD-10 disease chapters in the statistics from our hospital. The quality of the total cause of death statistics for non-autopsied deaths occurring in the hospital may thus be denoted as acceptable, also without the corrections. However, the small effects on the statistics were not caused by a small number of changes, but by a relatively even distribution of reallocations within and between the various disease chapters.

The cause of death is used as an end point in most epidemiological and clinical studies, and erroneous classification at the individual level will weaken the reliability of such studies. This is especially crucial, since quality control of public statistics on causes of death in the form of autopsies is decreasing in importance (12). The results do not permit any conclusions as regards nationwide statistics on causes of death, since hospital deaths currently account for only 35 % of the total (16). There is no reason to assume that the completion of death certificates in hospitals is more difficult than in nursing and health institutions, where the majority of the population currently dies. A systematic study of deaths outside hospitals, especially deaths occurring in nursing and health institutions, is therefore required to draw any conclusions regarding the quality of Norwegian statistics on causes of death in general.

Conclusion

Continuous correction of death certificates is a useful method for adjustments at the individual level and important as quality assurance of public statistics on causes of death.

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References

- Certification WHO. ICD-10. http://apps.who.int/ classifications/apps/icd/icd10training/ ICD-10%20Death%20Certificate/html/index.html (17.5.2012).
- Maudsley G, Williams EM. «Inaccuracy» in death certification – where are we now? J Public Health Med 1996: 18: 59–66.
- Johansson LA, Westerling R. Comparing hospital discharge records with death certificates: can the differences be explained? J Epidemiol Community Health 2002; 56: 301–8.
- Alfsen GC, Lyckander LG, Lindboe AW et al. Kvalitetssikring ved dødsfall i sykehus. Tidsskr Nor Legeforen 2010; 130: 476-9.
- Johansson LA, Westerling R. Comparing Swedish hospital discharge records with death certificates: implications for mortality statistics. Int J Epidemiol 2000; 29: 495–502.
- Santo AH, Pinheiro CE, Rodrigues EM. Comparative evaluation of underlying causes of death processed by the Automatied Classification of Medical Entities and the Underlying Cause of Death Selection Systems. Rev Saude Publica 1998; 32: 1–6.

- Pritt BS, Hardin NJ, Richmond JA et al. Death certification errors at an academic institution. Arch Pathol Lab Med 2005; 129: 1476–9.
 Pattaraarchachai J, Rao C, Polprasert W et al.
- Pattaraarchachai J, Rao C, Polprasert W et al. Cause-specific mortality patterns among hospital deaths in Thailand: validating routine death certification. Population Health Metrics 2010; 8: 12. www.pophealthmetrics.com/content/8/1/12 (17.5.2012).
- Om statistikken. Oslo: Statistisk sentralbyrå, 2010. www.ssb.no/vis/emner/03/01/10/dodsarsak/ om.html (20.12.2010).
- International statistical classification of diseases and health related problems ICD. 10th revision, version for 2007. Genève: World Health Organization, 2007. www.who.int/classifications/icd/ icdonlineversions/en/ (18.6.2012).
- Lu TH. Using ACME (Automatic Classification of Medical Entry) software to monitor and improve the quality of cause of death statistics. J Epidemiol Community Health 2003; 57: 470–1.
 Alfsen GC, Mæhlen J. Obduksjonens betydning for
- Alfsen GC, Mæhlen J. Obduksjonens betydning for registrering av dødsårsak. Tidsskr Nor Legeforen 2012; 132: 147–51.
- Hill K. Making deaths count. Bull World Health Organ 2006; 84: 162.
 Lu TH, Anderson RN, Kawachi I. Trends in fre-
- Lu TH, Anderson RN, Kawachi I. Trends in frequency of reporting improper diabetes-related cause-of-death statements on death certificates, 1985–2005: an algorithm to identify incorrect causal sequences. Am J Epidemiol 2010; 171: 1069–78.
- 1069-78.
 15. Naghavi M, Makela S, Foreman K et al. Algorithms for enhancing public health utility of national causes-of-death data. Population Health Metrics 2010; 8: 9. www.pophealthmetrics.com/content/8/ 1/9 (25.6.2012).
- Dødsfall, etter dødssted. 2010. Oslo: Statistisk sentralbyrå, 2010. http://statbank.ssb.no/ statistikkbanken/Default_FR.asp?Productid=03.01 &PXSid=0&nvl=true&PLanguage=0&tilside= selecttable/MenuSelP.asp&SubjectCode=03 (26.6.2012).

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