CoDe

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# Pilot of the CoDe (Coding of Death) project - a standardized approach to code causes of death in HIV infected individuals

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## BACKGROUND

While absolute death rates have decreased markedly in the era of combination antiretroviral therapy, the proportion of death from non-AIDS causes has increased. However, lack of standardisation in the coding of causes of death in HIV-infected individuals has made comparisons over time and between different populations difficult.

Use of death certificates is not always a reliable source, and the ICD9/10 coding system is sometimes inadequate for the separation of AIDS- and non-AIDS related causes.

As shown (in figure 1), data from the D:A:D study published at CROI 2005 suggest that not only causes of death conventionally regarded as HIV related (i.e. death from AIDS), but also other causes of death (including death from liver failure and non-AIDS malignancies), are strongly related to CD4 count.

Hence, a panel with representation of scientific boards of several large cohort studies and ongoing randomized clinical trials developed the CoDe project throughout 2004.

The CoDe project is a standardised system for the classification and coding of death in studies of individuals with HIV-infection, based on (i) a detailed data collection of information on the causes of death and contributing factors, and (ii) a centralised coding process.

## OBJECTIVES

To describe and evaluate the pilot of CoDe using a standardised approach to classify causes of death.

## METHODS

For the pilot study of CoDe, the Coordinating Centre agreed with twelve HIV-cohorts that they would complete data on the CoDe CRF for the five most recent deaths reported by their cohort (for a total of 60 cases of death being included in the pilot). The dates of death were from February 1st 2003 until July 24th 2004. The principles for the data collection and review process in CoDe are depicted in the flow chart (in figure 2).

HIV clinicians, primarily the site-investigators, completed the CoDe pilot CRFs in order to ensure a detailed, clinical collection of causes of death and contributing factors. Data in the CRF included: demographics, HIV-markers, ART, co-morbid conditions and risk factors, a narrative detailing the sequence of events leading to death, method and certainty of diagnoses, and post-mortem reports where available.

The CoDe CRF was then sent to the Coordinating Centre where it was computerized and checked for completeness (figure 2, brown), and each case of death was finally reviewed by 2 independent HIV experts (figure 2, grey). In the pilot, six pairs of reviewers were asked to review ten cases each.
In the centralized review process, the following is achieved:

- A coding of the immediate, contributing and underlying cause(s) of death, according to the three-step classification system (as shown in figure 3 & 4).
- An assessment and coding of whether the death was related to immunodeficiency using the algorithm shown (in figure 5).

In the 1st Independent Reviewer Round, pairs of HIV experts independently review pilot CRFs by coding the diseases and conditions as immediate, contributing and underlying cause of death and classifying the immunodeficiency-relatedness of death.

Uniform guidelines are used to handle discrepancies by having a 2nd Consensus Review Round and possibly even a final 3rd Specialist Panel Round to ensure that all cases are coded and classified.

## RESULTS

All sixty CoDe pilot CRFs were received at the Coordinating Centre.

- In the 1st Independent Reviewer Round, agreement was reached on 78.5% in terms of the underlying causes of death and 78.5% in terms of immunodeficiency-relatedness. In 15% of the cases one of the reviewer had not decided, whether the case was immunodeficiency related or not.
- In the 2nd Consensus Review Round, following communication between reviewers, in situations in which they had initially disagreed, an eventual 100% agreement on the underlying cause of death and 90% on immunodeficiency relatedness was achieved. The lack of agreement for the latter 10% represented a non-response in one case and a one step discrepancy in five cases between adjacent categories, (see figure 5).

The underlying causes of death were: AIDS (40%), chronic viral hepatitis (16.5%), cardiovascular disease (10%), active substance abuse (8.5%), suicide/depression (8.5%), non-AIDS/non-hepatitis malignancy (6.5%), non-AIDS-infection (5%), accident/violent death (1.5%), and unknown causes (3.5%). The few causes with disagreement were mainly due to shift between contributing and underlying cause of death, and were easily resolved within the consensus round.

## CONCLUSION

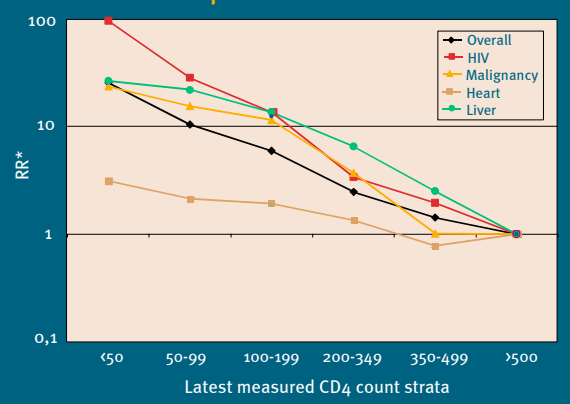
Uniform data collection forms were successfully utilized to obtain detailed information on the deaths from the site clinicians.

Providing specific guidelines enabled expert reviewers to arrive at consensus regarding underlying cause of death and whether it was related to immunosuppression.

Following the experience and evaluation of the CoDe pilot, this method has been implemented widely in HIV cohorts, and will be subject to continuous evaluation.

Figure 1

### Death Rate Ratios (RRs) according to immunofunction and specific causes of death




* Adjusted for HIV RNA, age, race, cohort and smoking status

R. Weber, CROI 2005

Figure 2

### Process Flow Chart (Generic)

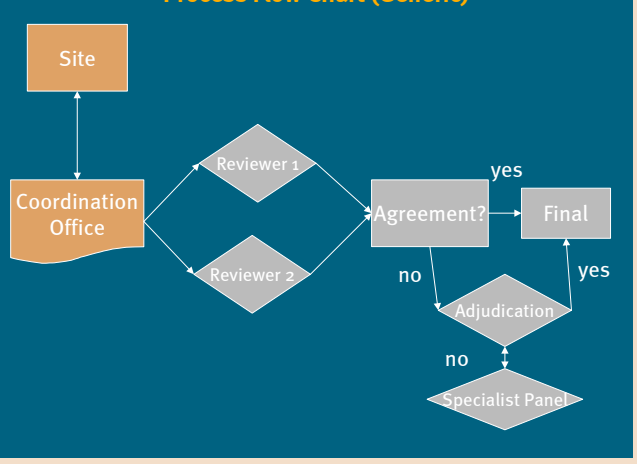
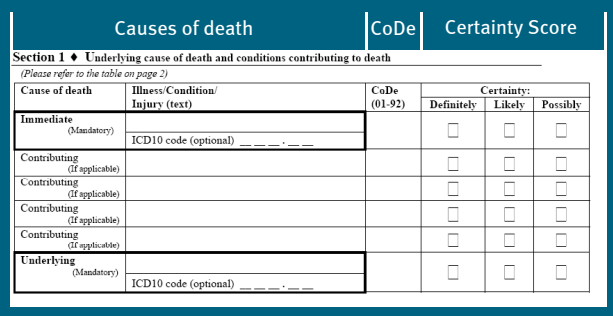



Figure 3

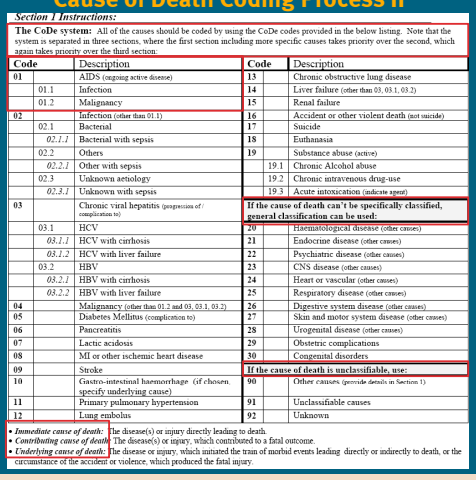
### Cause of Death Coding Process I




ICD10 lookup tool: http://www3.who.int/icd/vol1htm2003/fr-icd.htm

Figure 4

### Cause of Death Coding Process II



*Section 1 Instructions:*

**The CoDe system:** All of the causes should be coded by using the CoDe codes provided in the below listing. Note that the system is separated in three sections, where the first section including more specific causes takes priority over the second, which again takes priority over the third section.

| Code | | Description | Code | | Description |
|---|---|---|---|---|---|
| 01 | | AIDS (ongoing active disease) | 13 | | Chronic obstructive lung disease |
| | 01.1 | Infection | 14 | | Liver failure (other than 03, 03.1, 03.2) |
| | 01.2 | Malignancy | 15 | | Renal failure |
| 02 | | Infection (other than 01.1) | 16 | | Accident or other violent death (not suicide) |
| | 02.1 | Bacterial | 17 | | Suicide |
| | *02.1.1* | Bacterial with sepsis | 18 | | Euthanasia |
| | 02.2 | Others | 19 | | Substance abuse (active) |
| | *02.2.1* | Other with sepsis | | 19.1 | Chronic Alcohol abuse |
| | 02.3 | Unknown aetiology | | 19.2 | Chronic intravenous drug-use |
| | *02.3.1* | Unknown with sepsis | | 19.3 | Acute intoxication (indicate agent) |
| 03 | | Chronic viral hepatitis (progression of / complication to) | **If the cause of death can't be specifically classified, general classification can be used:** | | |
| | 03.1 | HCV | 20 | | Haematological disease (other causes) |
| | *03.1.1* | HCV with cirrhosis | 21 | | Endocrine disease (other causes) |
| | *03.1.2* | HCV with liver failure | 22 | | Psychiatric disease (other causes) |
| | 03.2 | HBV | 23 | | CNS disease (other causes) |
| | *03.2.1* | HBV with cirrhosis | 24 | | Heart or vascular (other causes) |
| | *03.2.2* | HBV with liver failure | 25 | | Respiratory disease (other causes) |
| 04 | | Malignancy (other than 01.2 and 03, 03.1, 03.2) | 26 | | Digestive system disease (other causes) |
| 05 | | Diabetes Mellitus (complication to) | 27 | | Skin and motor system disease (other causes) |
| 06 | | Pancreatitis | 28 | | Urogenital disease (other causes) |
| 07 | | Lactic acidosis | 29 | | Obstetric complications |
| 08 | | MI or other ischemic heart disease | 30 | | Congenital disorders |
| 09 | | Stroke | **If the cause of death is unclassifiable, use:** | | |
| 10 | | Gastro-intestinal haemorrhage (if chosen, specify underlying cause) | 90 | | Other causes (provide details in Section 1) |
| 11 | | Primary pulmonary hypertension | 91 | | Unclassifiable causes |
| 12 | | Lung embolus | 92 | | Unknown |

- *Immediate cause of death:* The disease(s) or injury directly leading to death.
- *Contributing cause of death:* The disease(s) or injury, which contributed to a fatal outcome.
- *Underlying cause of death:* The disease or injury, which initiated the train of morbid events leading directly or indirectly to death, or the circumstance of the accident or violence, which produced the fatal injury.

Figure 5

### Review and Consensus Coding Process

Cause of death immunodeficiency related or not?

*Section 2 Instructions:*

*Please evaluate the relatedness of the death with immunodeficiency by using the below algorithm. The CD4 counts that should be taken into consideration are the CD4 count prior to last stopping ART, and the most recent prior to death. The former (CD4 count at last stopping ART) should be weighed the highest.

| *CD4 counts prior to death* | *CD4 < 50 cells/µL* | *CD4 50-199 cells/µL* | *CD4 ≥ 200 cells/µL* |
|---|---|---|---|
| *Sudden* | **Possibly** immunodeficiency-related | **Assumed not** immunodeficiency-related | **Assumed not** immunodeficiency-related |
| *Not sudden* | **Likely** immunodeficiency-related | **Possibly** immunodeficiency-related | **Assumed not** immunodeficiency-related |

***'Yes, definitely'***: underlying or contributing cause of death a CDC C disease or Hodgkin's lymphoma
***'Yes, likely', 'Yes, possibly' or 'Assumed not'*** : see table above
***'No, definitely not'***: the underlying, contributing and immediate causes of death is of such a nature that it is inconceivable that the person died of causes related to immunodeficiency.

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