

Online Data Supplement

Ascertainment of Cause-Specific Mortality in COPD -- Operations of the TORCH Clinical Endpoint Committee

Lorcan P. McGarvey, Matthias John, Julie A. Anderson, Michael Zvarich, Robert A. Wise

APPENDIX A

Clinical Endpoint Committee – Principles of Operation

Assignment of Cause of Death

The Clinical Endpoint Committee will designate cause of death by probable cause. Causes of death will be grouped by general categories, e.g. Respiratory, Cardiovascular, Cancer, or Other. If a cause of death cannot be ascertained, the cause of death will be classified as Unknown. The general principles and methods used in this classification are listed:

1. All diagnoses of cancer should be corroborated by the primary medical record. This should include imaging studies, histologic diagnoses, operative or procedure notes, and records of treatment. If the primary medical record cannot be obtained to confirm the diagnosis, this should be affirmatively stated in the documentation, and the committee will determine a diagnosis based on their best judgment.

Patients who die with an uncured cancer will be designated as dying from the cancer. For example, a patient with documented gastric cancer who dies of gastrointestinal hemorrhage will be classified to have died from gastric cancer. A patient who dies from neutropenic sepsis while undergoing chemotherapy for lymphoma will be classified as dying from lymphoma.

2. Death certificates should be sought in all cases. If they cannot be obtained, it should be affirmatively stated in the documentation.

3. If medical records are inadequate and cannot be obtained as affirmatively stated in the documentation, a cause of death will be adjudicated based on the best available evidence of record. If a probable cause of death cannot be adjudicated, it will be classified as unknown.

4. The primary cause of death should be attributed to the disorder that causes the patient to present for medical treatment. This should be distinguished from terminal events that are the immediate cause of death.

- For example, if a patient is admitted to the hospital with a COPD exacerbation, from which they do not fully recover, and the patient subsequently develops complications such as pneumonia, respiratory failure, renal failure, sepsis, or myocardial infarction, the primary cause of death will be attributed to COPD.
- For example, if a patient undergoes surgery for cancer and dies from complications of the surgery or during the immediate post operative period, the primary cause of death will be attributed to cancer, even if the cancer was potentially curable by the surgery.
- For example, if a patient is admitted to the hospital with pneumonia and develops complications such as respiratory failure, gastrointestinal bleeding, etc. the cause of death will be attributed to pneumonia. If it is unclear if a patient is admitted with a COPD exacerbation or pneumonia, the cause of death will be based on the hospital admission chest radiograph. If pneumonia is present on the admitting chest radiograph, the cause of death will be designated pneumonia. If pneumonia is

present only on subsequent chest radiographs, the cause of death will be designated as COPD.

5. Sudden death is defined as death that occurs within 24 hours of being observed alive and without evidence of a deteriorating medical condition. If the interval between death and last being observed alive is greater than 24 hours, and there is no other known cause of death, the cause of death will be classified as unknown.

The diagnosis of myocardial infarction will require pathologic evidence, or evidence of medical record including electrocardiographic tracings, blood enzyme measurements, and compatible clinical findings.

6. In cases of out of hospital death, the site coordinator or site physician should interview family or witnesses to ascertain the following information:

- When was the person last known to be alive?
- When was the person found to be deceased?
- What were the events surrounding the death?
- Did the decedent have any symptoms or change in health status that preceded the death? Special reference should be made to dyspnea, febrile illnesses, chest pain, abdominal pain, syncope, seizures, paralysis and change in mental status.
- Were there recent medical visits or recent changes in medication?
- Was an autopsy performed?
- Permission to obtain medical records should be requested from next-of-kin.

Determination of COPD relatedness.

All cases will have a secondary classification to determine whether the death is related to COPD. The possible choices are YES, NO, UNKNOWN, POSSIBLE, PROBABLE.

1. All cases where primary cause of death is COPD will be classified as YES
2. In cases where primary cause of death is NOT COPD the classification of COPD relatedness will be based on the sequence of terminal events:
 - If the terminal event is documented to be hypercapnic respiratory failure or failure to wean from a ventilator the case will be classified YES
 - For example, patient dies in hospital on ventilator but succumbs to fatal pneumonia, arrhythmia, or care is withdrawn.
 - If the patient would have been judged to have survived the terminal illness had COPD not been present, the case will be classified YES
 - For example, patient dies from Stage I lung cancer because they have insufficient lung function to undergo surgery.
 - For example, patient has pneumonia or influenza that is fatal.
 - If the death occurs at home, where the patient is receiving palliative care for advanced COPD, the case will be classified YES
 - For example, a patient receiving continuous oxygen, confined to bed and chair, with cor pulmonale, or with advanced malnutrition.

- If the terminal event is NOT respiratory, and would be likely fatal for patients without COPD, the case will be classified NO.
 - For example, death from metastatic cancer, cerebral hemorrhage, severe cardiomyopathy, or cardiogenic shock.

- If there is another clear explanation for terminal respiratory failure that would likely have occurred in patients without COPD, then the case will be classified NO
 - For example respiratory failure secondary to CVA, drug overdose, or asphyxia.

3. If the data are inadequate to make a clear YES or NO classification, it will be designated as UNKNOWN, POSSIBLE, or PROBABLE based on the best evidence available.

Appendix B. Discrepancies in CEC adjudications with respect to specific cause of death

Case Number	Pathophysiologic Classification, First adjudication	Specific cause of death, First adjudication	Pathophysiologic Classification, Second adjudication	Specific cause of death, Second adjudication	Relationship to COPD, First Adjudication	Relationship to COPD, Second Adjudication
1	Cancer	Other Adenocarcinoma, unknown primary	Cancer	Lung	No	No
2	Pulmonary	COPD	Pulmonary	Pneumonia	Yes	Yes
3	Unknown	Unknown – Possible Sudden death	Cardiovascular	Sudden Death	Unknown	No
4	Unknown	Unknown – Possible Sudden death	Cardiovascular	Sudden Death	Unknown	No
5	Pulmonary	Pneumonia	Other	Staph Sepsis	Yes	Yes
6	Cancer	Other – Myelodysplasia	Cancer	Lung	No	No
7	Cardiovascular	Sudden Death	Pulmonary	COPD	Unknown	Yes
8	Unknown	Unknown – Possible Sudden Death	Cardiovascular	Sudden Death	Unknown	No
9	Pulmonary	COPD	Cardiovascular	Myocardial Infarction	Yes	Yes
10	Pulmonary	COPD	Cardiovascular	Sudden Death	Yes	Possibly
11	Unknown	Unknown – Likely COPD exacerbation	Cancer	Lung	Possibly	No
12	Pulmonary	Other – Asphyxia from upper airway obstruction	Other	Other – Aspiration of food bolus	No	No
13	Cardiovascular	Myocardial Infarction	Cardiovascular	Other – Cardiogenic Shock	No	No
14	Pulmonary	COPD	Pulmonary	Pneumonia	Yes	Yes
15	Unknown	Unknown– Possible acute GI hemorrhage	Other	GI Hemorrhage	Unknown	Unknown

16	Pulmonary	COPD	Cardiovascular	CHF	Yes	Yes
17	Unknown	Unknown	Cardiovascular	Sudden Death	Unknown	No

Appendix C. Discrepancies in CEC adjudications with respect to COPD causality

Case Number	Pathophysiologic Classification, First adjudication	Specific cause of death, First adjudication	Pathophysiologic Classification, Second adjudication	Specific cause of death, Second adjudication	Relationship to COPD, First Adjudication	Relationship to COPD, Second Adjudication
1	Unknown	Unknown	Cardiovascular	Sudden Death	Unknown	No
2	Unknown	Unknown	Cardiovascular	Sudden Death	Unknown	No
3	Cancer	Other Melanoma	Cancer	Other Melanoma*	Unknown	No
4	Cardiovascular	Sudden Death	Cardiovascular	Sudden Death*	No	Unknown
5	Cardiovascular	Sudden Death	Pulmonary	COPD	Unknown	Yes
6	Pulmonary	Pneumonia	Pulmonary	Pneumonia*	Probably	Yes
7	Unknown	Unknown– Possible Sudden death	Cardiovascular	Sudden Death	Unknown	No
8	Cardiovascular	Sudden Death	Cardiovascular	Sudden Death*	Unknown	No
9	Pulmonary	COPD	Cardiovascular	Sudden Death	Yes	Possibly
10	Cardiovascular	Congestive Heart Failure	Cardiovascular	Congestive Heart Failure	No	Possibly
11	Other	Other – Drug Overdose	Other	Other – Drug Overdose*	No	Probably
12	Other	Other –Post Op Thoraco-Abdominal Aneurysm	Other	Other – Surgery for Thoracic Aneurysm*	Probably	No

13	Unknown	Unknown – Likely COPD exacerbation	Cancer	Lung	Possibly	No
14	Cancer	Lung	Cancer	Lung*	No	Yes
15	Cardiovascular	CVA	Cardiovascular	CVA*	Yes	No
16	Unknown	Unknown	Cardiovascular	Sudden Death	Unknown	No
