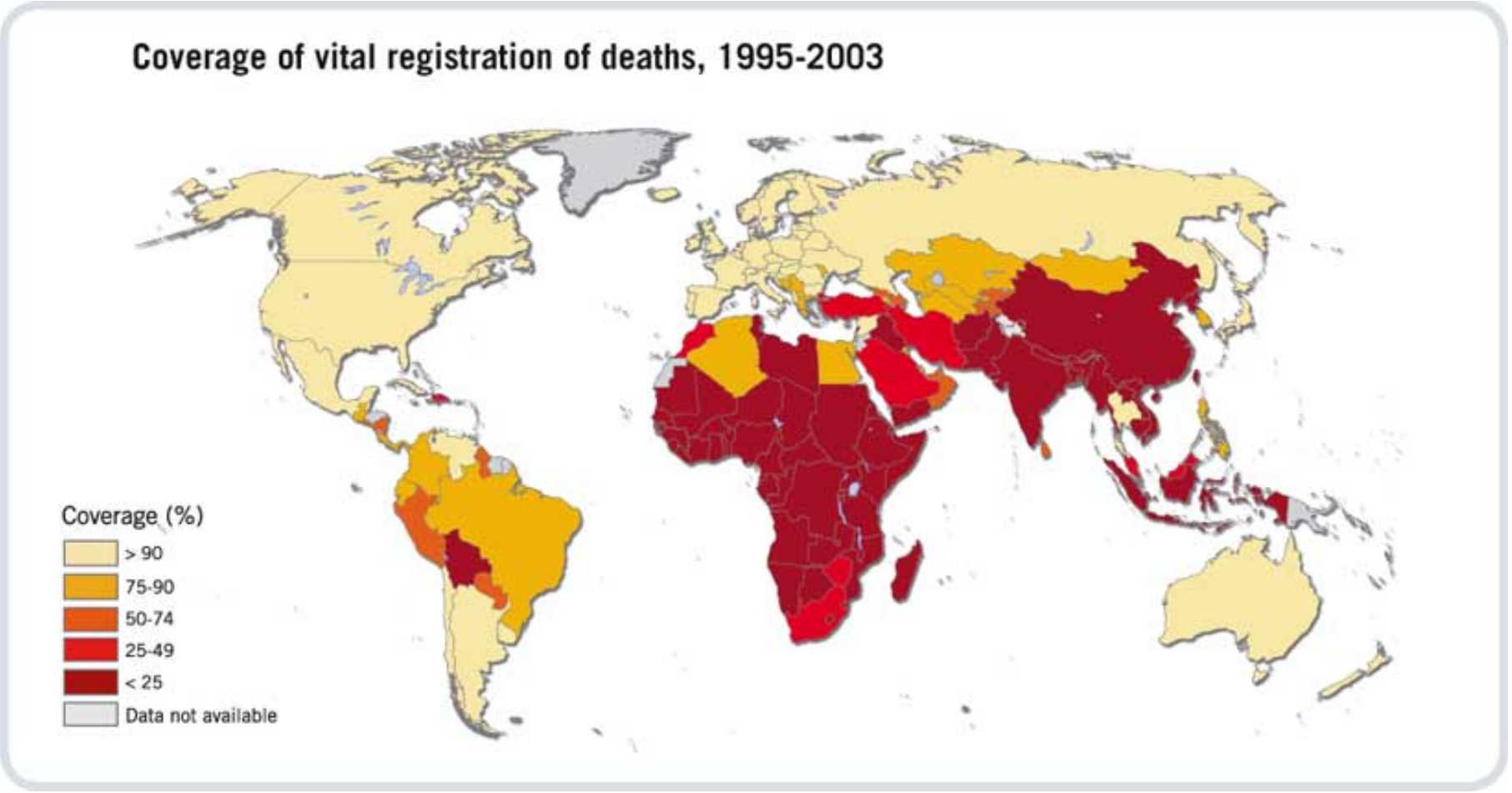
cism
centro de
investigação
em saúde de
manhiça

An introduction to Cause of death ascertainment

In developing countries, what is the best way to estimate the cause of death?

1. **Death certificates**
2. **Clinical records**
3. **Post mortem examinations**
4. **Verbal autopsy**
5. **None of the above?**

Death certificates– Vital registration



Mathers et al. *Counting the dead and what they died from: an assessment of the global status of cause of death data*. WHO Bulletin 83, 2005, 171-177.

"… in Africa and Asia most people are born and die without leaving a trace in any legal record or official statistic."

"the scandal of invisibility"

"In Africa and Asia most people die at home"

Setel PW et al. A scandal of invisibility: Making everyone count by counting everyone. Lancet 2007; 370: 1569-77

Clinical records

OPEN ACCESS Freely available online

PLoS MEDICINE

Clinico-Pathological Discrepancies in the Diagnosis of Causes of Maternal Death in Sub-Saharan Africa: Retrospective Analysis

Jaume Ordi[1,2*], Mamudo R. Ismail[3], Carla Carrilho[3], Cleofé Romagosa[1,4], Nafissa Osman[5], Fernanda Machungo[5], Josep A. Bombi[1], Juan Balasch[6], Pedro L. Alonso[2,4], Clara Menéndez[2,4]

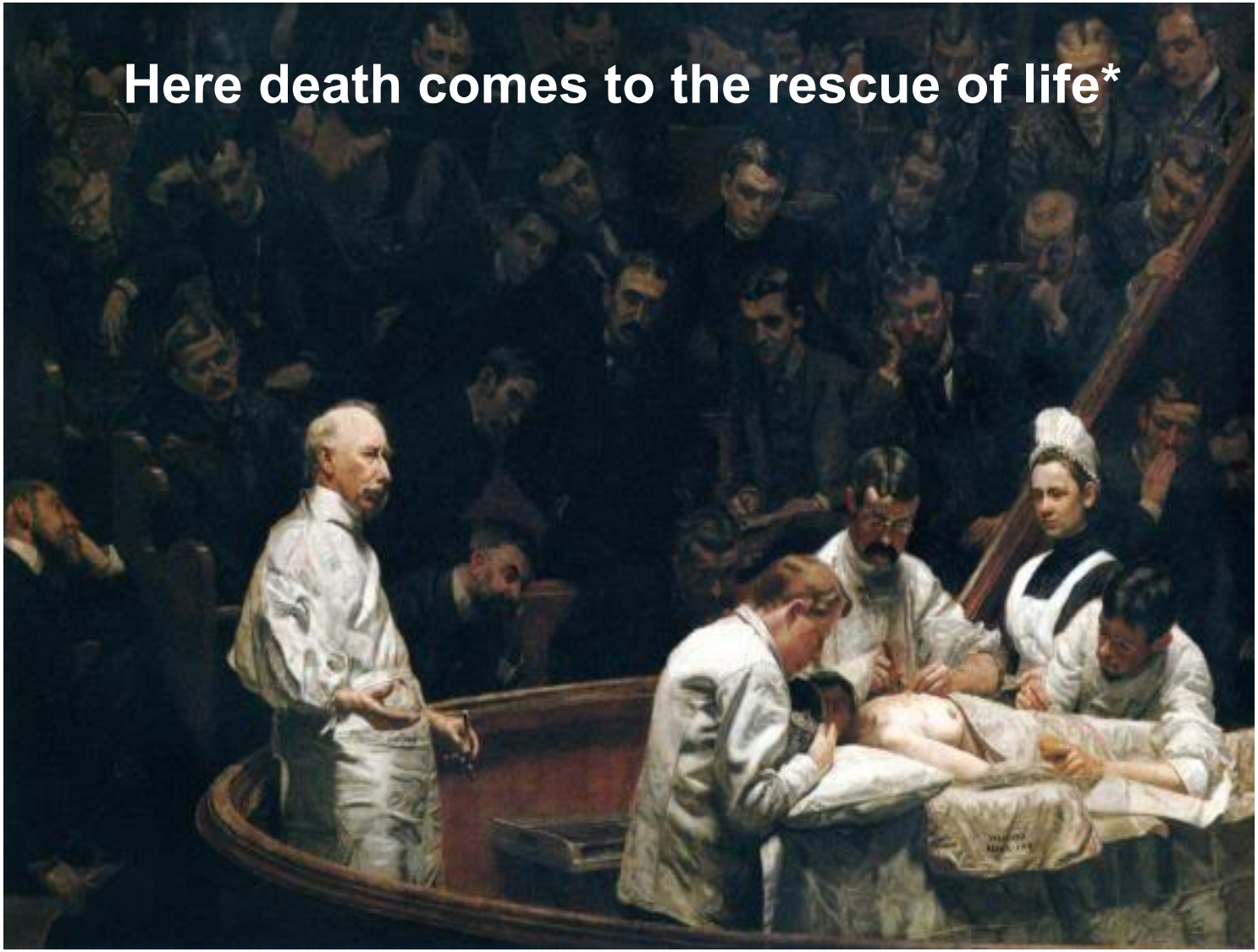
1 Department of Pathology Hospital Clinic, Universitat de Barcelona, Institut d'Investigacions biomèdiques August Pi I Sunyer (IDIBAPS), Barcelona, Spain, 2 Barcelona Centre for International Health Research (CRESIB), Hospital Clinic/Universitat de Barcelona, IDIBAPS, Barcelona, Spain, 3 Department of Pathology, Maputo Central Hospital Universidad Eduardo Mondlane, Maputo, Mozambique, 4 Manhiça Health Research Center (CISM), Manhiça, Mozambique, 5 Department of Obstetrics and Gynecology Hospital Central de Maputo, Universidad Eduardo Mondlane, Maputo, Mozambique, 6 Department of Obstetrics and Gynecology, Hospital Clinic, University of Barcelona Barcelona, Spain

- **Clinico-pathological discrepancies were frequent**
  - ◇ Clinical errors present in 62% of maternal deaths
  - ◇ A major clinical error detected in 40.3% maternal deaths

- **High rate of false negative diagnosis for infectious diseases**

◇ Underestimation of prevalence

Postmortem examination – The full autopsy



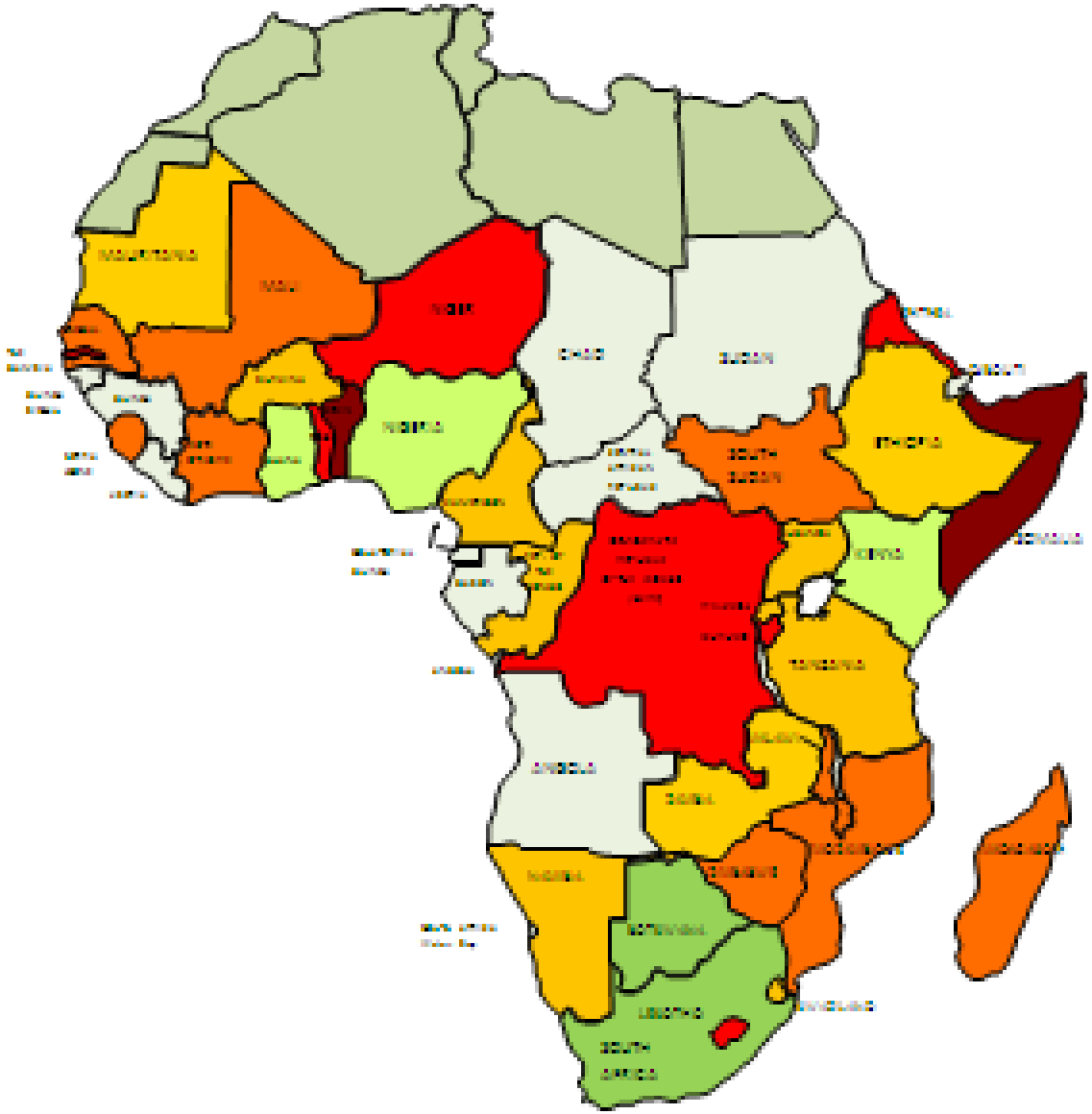
Thomas Eakins, The Clinic of Dr. *Agnew*, 1889

Postmortem examination – The full autopsy

Indisputably the gold standard for CoD ascertainment, but…

- Few pathologists available
- Little acceptability & feasibility
- A procedure seldom performed outside reference hospitals and for legal reasons

Number of People Served By Each Pathologist in Sub-Saharan Africa



- No Active Pathologist
- >5.0 million
- 2.5-5.0 million
- 1.0-2.5 million
- 500,000-1 million
- 200,000-500,000
- Data Not Available

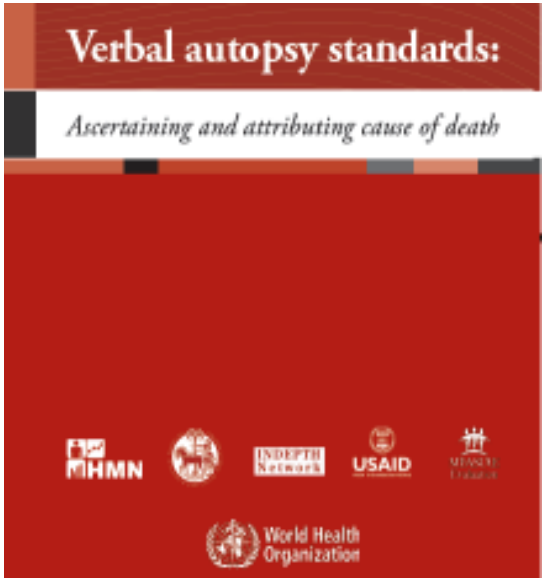
Number of People Per Pathologist:
UK*: 15,108
US**: 19,232

*Royal College of Pathologists, 2012,
**Anatomic and Clinical Pathologists, AAMC, 2007

Slide courtesy of Drucilla Roberts

Verbal autopsies

- An indirect and protocolized approach for establishing CoD by interviewing relatives or witnesses of the death
- Generally performed >1 month after the death occurs, to respect the families' mourning period
- Can be performed by an adequately trained field worker
- Follows a standardized questionnaire
- Requires about 45-60 minutes of interview
- Contains “open narrative” but also “closed questions”
- Is divided into two parts:
    - 1) Data collection 2) Data interpretation


Verbal autopsy standards:
Ascertaining and attributing cause of death
HMN
USAID
World Health Organization

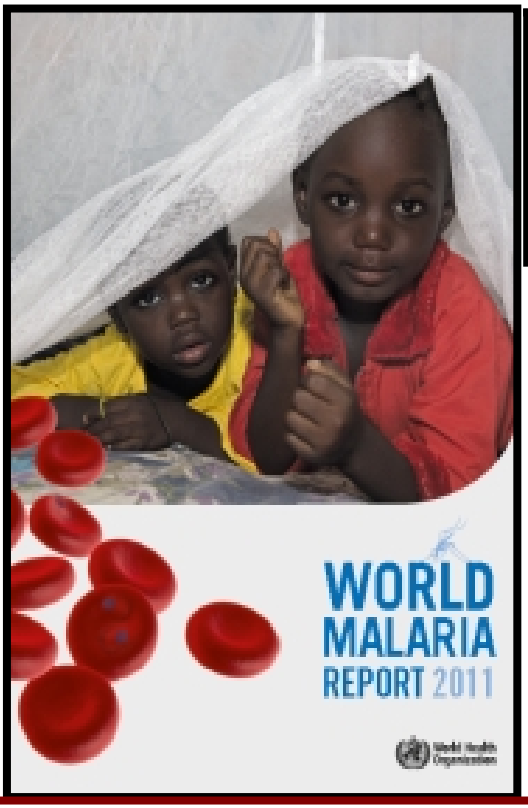
Verbal autopsies: Advantages

- Can target any death, also those occurring at home
- Data collection is simple, and can be performed by an adequately trained field worker
- Timing is not an issue. Does not require contact with the deceased
- Is non-invasive, and generally well accepted
- Interpretation of data can be done by physicians or by computer algorithms
- A good method for obtaining a reasonable estimate of the cause structure of mortality at a community/population level (rather than at the individual level)

Verbal autopsies: Drawbacks

- Not performed widely within countries, generally restricted to sites with HDSS or research
- Recall issues when done a few months after the death
- **High degree of misclassification errors**
- Deaths associated with non-specific signs/symptoms (i.e “fever”, “Vomiting”) or in specific age groups (perinatal) particularly problematic
- Never been validated in deaths studied with pathological autopsy used to determine CoD
- Requires a clinician (or a computer algorithm in place) for final review and diagnosis

An example of the difficulties regarding estimations of CoD: The case of Malaria



WHO World malaria report (2011):
- 655,000 deaths
- 91% in Africa
- Globally 86% children<5 years of age

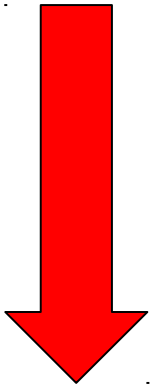
Murray (2010):
- 1,238,000 deaths
- 91% in Africa
- Globally Only 57.7% children<5 years of age
- In Africa: <5 only 61.7%
- Outside Africa: <5 only 14.5%

Lancet 2012; 379: 413–31

Global malaria mortality between 1980 and 2010: a systematic analysis

Christopher J L Murray, Lisa C Rosenfeld, Stephen S Lim, Kathryn G Andrews, Kyle J Foreman, Diana Haring, Nancy Fullman, Mohsen Naghavi, Rafael Lozano, Alan D Lopez

Verbal autopsies



- **A "better than nothing" method but with clear limitations**
- **Often the only thing we have!!! (so we need to use it wisely, without forgetting its (many) limitations**

VA -Methodology

Data collection & processing

- Information of death come from DSS/study reports
- FW after 3 months visit the family – Interview
- Is study-specific death, the sooner the better
- Questionnaires need to be in local language and locally-adapted
- VA interviews by physicians (MD), medical students, supervisor and field workers - previous written informed consent
- The person interviewed needs to feel comfortable and not pressed
- Photo aids can be utilized to illustrate non-straightforward terminology ("jaundice", "rash"…)
- Information from health card (if available) should also collected
- For "closed questions":
  - Codes 1=Yes; 2=No; 888=N/A; 999=Can't remember/doesn't know

VA –Assigning the cause of death

The "specialists consensus method"

- Each physician (2 or 3), based on the questionnaire, should give the specific etiological cause
- Avoid unspecific general diagnosis such as "cardio-respiratory failure"
- Each physician can give up to 2 causes of death, to avoid bias introduced by physician's preferred option
- If 2 causes are given, they have to be **different and NOT related**, so for instance the physician should choose between asthma and pneumonia, but not write both
- **Diagnoses are additive, not alternative**
- If related, they have to constitute 2 well differentiated clinical entities (i.e malaria and anemia)
- Diagnoses are picked from a "VA-simplified" ICD-10 classification of diseases
- The order in which the two diagnoses are written down is not important, although it may seem logical that the major cause of death is written as Diagnosis 1

VA –Assigning the cause of death

The independent final review

- An independent MD reviews the questionnaire and the previous diagnoses given by the 3 physicians, contrasting them
- The reviewer will choose a final diagnosis, based on the agreement of at least two of the three physicians' diagnoses
  - If 2 physicians have given 2 diagnoses each, and there is agreement in 2, then those will be the 2 diagnoses
  - If there is only agreement in one, then only one diagnosis will be given
  - If 2 diagnoses are chosen, NONE will be prioritized, they will be both given as primary diagnoses
  - If there is NO agreement at all between any of the 3 physicians' diagnoses, the cause will be assigned as "UNKNOWN CAUSE"
- **The independent reviewer has access to the questionnaire, but has no right to give a fourth diagnosis. When choosing the final diagnosis, the algorithm needs to be applied strictly, and there is no right to override it!**

VA -Questionnaires

- **0-28 days**
- **29 days-12 years**
- **>12 years-Adults (includes pregnancy and perinatal deaths)**

- 192 cause of death related indicators
- Subdivided into 4 (+/-1) sections and 118 subgroups
  1. Personal information
  2. Information on the respondant
  3. Cause of death
  4. Background and context
  5. Recommended optional open narrative text field

Cause of death questions

a. Medical history
b. General signs and symptoms
c. Signs and symptoms associated with pregnancy
d. Neonatal and child history, signs and symptoms
e. History of injuries and accidents
f. Risk factors
g. Health service utilization

1A110	Was the deceased female or male?	FEMALE MALE
1A200	Is date of birth known?	YES NO
1A210	+ When was the deceased born?	DAY MONTH YEAR
1A220	Is date of death known?	YES NO
1A230	+ When did s/he die?	DAY MONTH YEAR
1A240 1A250	How old was the deceased when s/he died? IF AGE IS LESS THAN 1 YEAR RECORD IN MONTHS	AGE IN YEARS AGE IN MONTHS

NO.	QUESTIONS AND FILTERS	CODING CATEGORIES
	SECTION 4. RESPONDENT'S ACCOUNT OF ILLNESS/EVENTS LEADING TO DEATH	
	Could you tell me about the illness/events that led to her his/death?	
	CAUSE OF DEATH 1 ACCORDING TO RESPONDENT	
	CAUSE OF DEATH 2 ACCORDING TO RESPONDENT	
	SECTION 5. CONTEXT AND HISTORY OF PREVIOUSLY KNOWN MEDICAL CONDITIONS	
	I would like to ask you some questions concerning the contexts and previously known medical conditions the deceased had; injuries and accidents that the deceased suffered; and signs and symptoms that the deceased had/showed when s/he was ill. Some of these questions may not appear to be directly related to his/her death. Please bear with me and answer all the questions. They will help us to get a clear picture of all possible symptoms that the deceased had.	
3A100	Was there any diagnosis of Tuberculosis?	YES ☐ NO ☐ DON'T KNOW ☐
3A110	Was there any diagnosis of HIV/AIDS?	YES ☐ NO ☐ DON'T KNOW ☐
3A120	Did s/he have a recent positive test for Malaria?	YES ☐ NO ☐ DON'T KNOW ☐
3A130	Did s/he have a recent negative test for Malaria?	YES ☐ NO ☐ DON'T KNOW ☐
3A140	Was there any diagnosis of Measles?	YES ☐ NO ☐ DON'T KNOW ☐

3B100	Did s/he have a fever?	YES NO DON'T KNOW	☐ ☐ ☐
3B110	+ For how long did s/he have a fever?	NUMBER OF DAYS NUMBER OF WEEKS DON'T KNOW	☐☐ ☐☐ ☐
3B120	+ Did s/he have night sweats?	YES NO DON'T KNOW	☐ ☐ ☐
3B130	Did s/he have a cough?	YES NO DON'T KNOW	☐ ☐ ☐
3B140	+ For how long did s/he have a cough?	NUMBER OF DAYS NUMBER OF WEEKS DON'T KNOW	☐☐ ☐☐ ☐
3B170	+ Did s/he make a whooping sound when coughing?	YES NO DON'T KNOW	☐ ☐ ☐
3B150	+ Was the cough productive with sputum?	YES NO DON'T KNOW	☐ ☐ ☐
3B160	+ Did s/he cough out blood?	YES NO DON'T KNOW	☐ ☐ ☐
3B180	Did s/he have any breathing problem?	YES NO DON'T KNOW	☐ ☐ ☐
3B190	+ Did s/he have fast breathing?	YES NO DON'T KNOW	☐ ☐ ☐

Physician coded vs. Automated methods

- Automated should remove the variability inherent with physician coding of VA
- Fully standardised and increasingly better algorithms
- Does not require physicians (very time consuming)
- Various methods, only Inter-VA4 currently recommended by WHO
- Highly competitive area!!!

International classification of diseases 1993 (ICD-10) based diagnoses

- Full code list available at:
  - http://apps.who.int/classifications/icd10/browse/2010/en
- 22 chapters organised by disease, disorder or event
- 3 chapters which do not apply to CoD
- In case you cannot reach a diagnosis use R99 (Adults or children) or P96 (neonates)

A00-B99	Certain infectious and parasitic diseases	Chapter I
C00-D48	Neoplasm	Chapter II
D50-D89	Diseases of the blood and blood forming organs	Chapter III
E00-E90	Endocrine, nutritional, and metabolic diseases	Chapter IV
F00-F99	Mental and behavioural disorders	Chapter V
G00-G99	Diseases of the nervous system	Chapter VI
H00-H59	Diseases of the eye and adnexa	Chapter VII
H60-H95	Diseases of the ear and mastoid process	Chapter VIII
I00-I99	Diseases of the circulatory system	Chapter IX
J00-J99	Diseases of the respiratory system	Chapter X
K00-K93	Diseases of the digestive system	Chapter XI
L00-L99	Diseases of the skin, and subcutaneous tissue	Chapter XII
M00-M99	Diseases of the musculoskeletal system	Chapter XIII
N00-N99	Diseases of the genito urinary system	Chapter XIV
O00-O99	Pregnancy, childbirth, and the puerperium	Chapter XV
P00-P96	Certain conditions originating in the perinatal period	Chapter XVI
Q00-Q99	Congenital malformations and chromosomal abnormalities	Chapter XVII
R00-R99	Symptoms, signs, and abnormalities not elsewhere classified	Chapter XVIII
V01-Y98	External causes of morbidity and mortality	Chapter XX

Note: As mentioned above, we do not use codes S00-T98 (injury, poisoning), Z00-Z99 (factors influencing health status or contact with health service), or U00-U99 (special purposes).

The underlying COD is defined as:

The disease which initiated the train of morbid events leading directly to death

OR

The circumstances of the accident or violence which produced the fatal injury

The terminal event that occurred just before the death is called mode of death (e.g. aspiration pneumonia, cerebral oedema, shock). While constructing the chain of events, **it is essential to note that modes of death such as respiratory failure, cardio-respiratory arrest, brain death, etc., should NOT be considered as the underlying causes of death.**

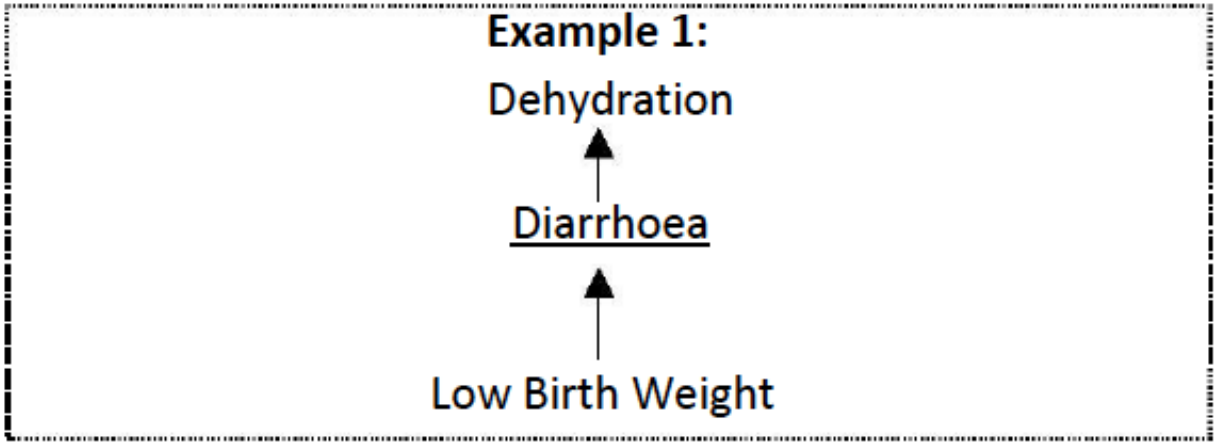
Contributory CODs (also called co-morbidities) are diseases or conditions that are independent of the causal chain of events, but which may contribute indirectly to the final event of death. For example, if a person dies of a stroke but had diabetes in the past, then diabetes may have contributed to this condition. Similarly, if a neonate dies of diarrhoea and also has low birth weight, then low birth weight may be a contributory COD. Use your best clinical judgement to assign only the underlying condition as the COD, and where possible, write in the contributory COD and modes of death as keywords.

Examples

- **Diabetes and renal failure (N17-19).** Generally code renal failure (N17-N19), even if it was diabetes that led to the series of events that resulted in renal death. Your keywords should include *diabetes*.
- **Diabetes and cardiovascular disease (I21-24, I63-64).** Generally code cardiovascular disease. Your keywords should include *diabetes.* You may code diabetes (E10-E14) as a cause of death in cases who died of hypoglycaemia/hyperglycemias, or diabetic keto-acidosis.
- **Malnutrition/low birth weight (LBW) (E46) and diarrhoeal (A09) or measles (B05) death.** Generally code the infectious COD, and note *malnutrition/LBW* as keywords.
- **Anaemia (D60-64).** Generally code the patho-physiological COD (e.g. malaria), and note *anaemia* as a keyword.
- **Essential hypertension (I10) or hypertensive heart disease (I11)** should not be coded as a COD. Instead code the conditions that hypertensive heart disease leads to, such as congestive heart failure (I50), myocardial infarction (I21-I25), or stroke (I60-I69).

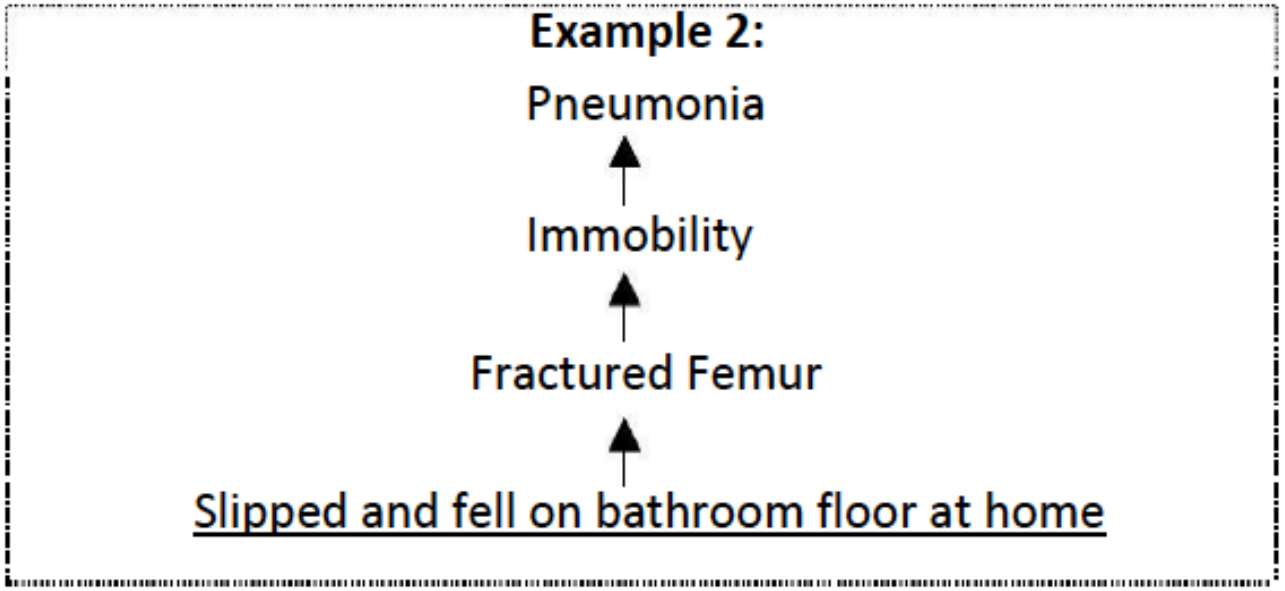
Case studies for assigning COD

Example 1: A 13 days' old law birth weight girl not having feeds, developed loose motions and fever, did not respond to treatment, eyes sunken, died in 2 days.



Underlying cause of death: A09 - diarrhoea and gastroenteritis of presumed infectious origin

Example 2: An 80 years old female slipped and fell on bathroom floor at home and got fractured her femur. She was bed-laden, developed pneumonia, and died.



Underlying cause of death: W01 - fall on same level from slipping, tripping, and stumbling

The "6 STEPS" (MDS guidelines)

Carefully read past history & narrative

↓

Highlight cardinal symptoms & negative evidence
Highlight keywords and input any notes

↓

Think of chronological sequence. Adhere to cardinal symptoms & negative evidence. Do not imagine facts which are not in the record

↓

Assign underlying COD by selecting an ICD code

↓

Confirm your ICD selection against clinical guidelines and reconsider the ICD code using any suggested differential diagnoses

↓

Select certainty of diagnosis & quality of narrative

You are encouraged to attempt assigning, wherever possible, specific disease codes, rather than ill-defined conditions such as senility, abdominal pain, fever, etc. In uncertain cases, try to assign the ICD-10 chapter diagnosis rather than a general R54 or R99 code.

For example, for a diagnosis of pneumonia:

Ideal choice	2nd best choice	3rd best choice
J18	J99	R99

Generally, DO NOT CODE the following risk factors:

- **ADULTS: Diabetes, Hypertension, Smoking, Alcoholism**
- **CHILDREN: Malnutrition**
- **NEWBORNS: Low birth weight**

ICD-10 based diagnoses

Verbal autopsy code	Verbal autopsy title	ICD-10 code (to ICD)	ICD-10 codes (from ICD)
VAs-01 Infectious and parasitic diseases			
VAs-01.01	Sepsis	A41	A40-A41
VAs-01.02	Acute respiratory infection, including pneumonia	J22/J18	J00-J22
VAs-01.03	HIV/AIDS related death	B24	B20-B24
VAs-01.04	Diarrheal diseases	A09	A00-A09
VAs-01.05	Malaria	B54	B50-B54
VAs-01.06	Measles	B05	B05
VAs-01.07	Meningitis and encephalitis	G03;G04	A39; G00-G05

- **A six page long document, with ALL major causes that are required**


cism
centro de
investigação
em saúde de
manhiça