Multiple causes of death. Overview, applications.

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Lithuanian Social Research Centre
Teaching seminar „Causes of death: data and methods of analysis“
February 23-24, 2015 Vilnius
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EUROPEAN UNION
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The research is funded by EU structural assistance (European Social Fund) to Lithuania under the measure VP-1-3.1-ŠMM-07-K “Support to Research Activities of Scientists and Other Researchers (Global Grant)” project Nr. VP-1-3.1-ŠMM-07-K-02-067

An outlook

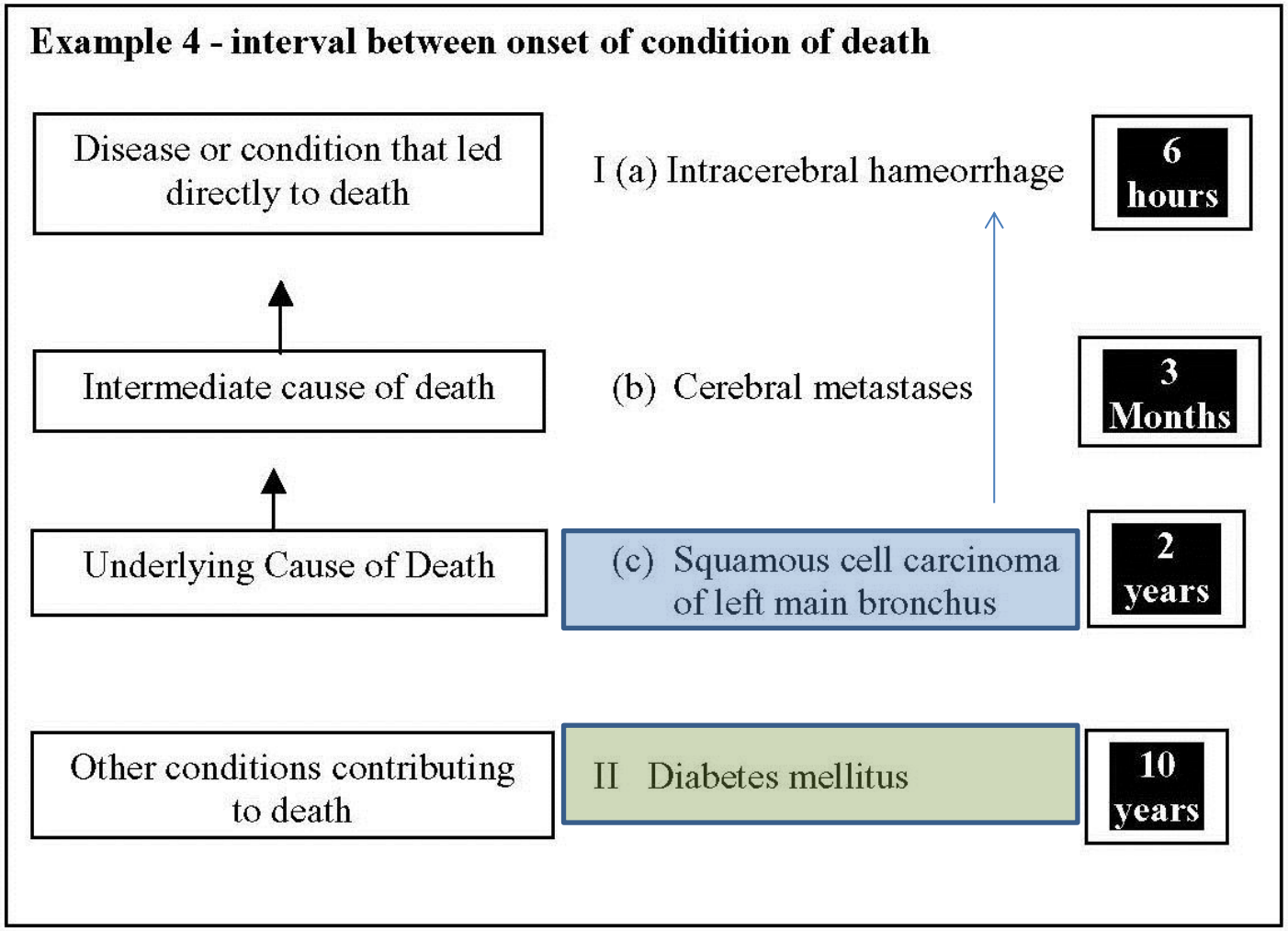
- In spite of the complexity of morbidity processes, statisticians have always sought to reduce the information to a single cause
- Statistics based on the underlying overestimate fatal diseases while masking information about broader health status
- Multiple cause-of-death data represent the most complex & unexplored source of statistical information about death

Death certificate

CAUSE OF DEATH		Approximate interval between onset and death
I		
Disease or condition	(a)	.....
*Directly leading to death**	due to (or as a consequence of)	
Antecedent causes	(b)	.....
Morbid conditions, if any,	due to (or as a consequence of)	
giving rise to the above cause,		
stating the underlying	(c)	.....
condition last	due to (or as a consequence of)	
	(d)	.....
II		
Other significant conditions	.....	.....
contributing to the death, but		
not related to the disease or	.....	.....
condition causing it		

* This means the disease, injury or complication which caused death NOT ONLY, for example, the mode of dying, such as "heart failure, asthenia", etc.

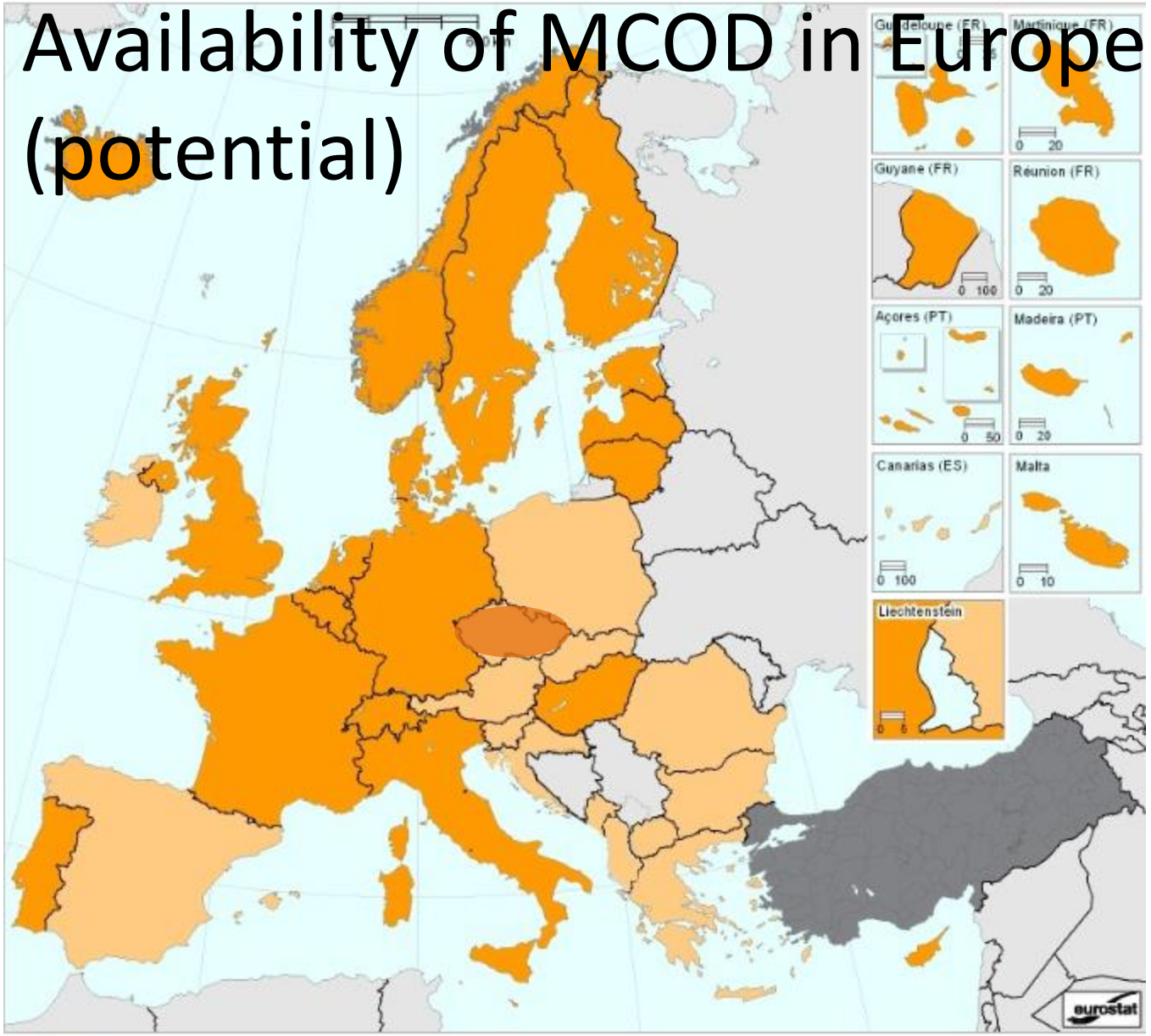
Death certificate – an example



Methodological issues

- Unavailable - not mandatory
- Unstandardized – how many causes will be kept & published? What about encoding proces?
- Unclear – when 20 multiple causes are given, which were used as a part of the morbid chain caused by the primary condition? What if the UCD is none of the MCOD?

Availability of MCOD in Europe (potential)



UC available

MCOD + UC available

Data not available

Administrative boundaries: © EuroGeographics © UN-FAO © Turkstat
Cartography: Eurostat, European Commission
Source: Eurostat metadata

What needs to be done (Pace et al. 2011):

- The IRIS implementation
- The establishment of a set of internationally agreed rules and methodologies on coding and data processing, including quality assessment
- An agreed list of indicators for dissemination
- Institutional commitment reflected in decisions and regulations
- „The coding of multiple cause using ICD10 is another powerful reason to adopt automated coding systems“ (Pavillon).

Coding related issues

- Different coding rules for underlying and multiple causes
- Example: diabetes (250.0) and coma (780.0)
- For UCD: both conditions are encoded as separate medical entities (important for the chain of events)
  - **entity axis**
- For MCOD: the preferred code is diabetic coma (250.2) (the whole record is considered)
  - **record axis**

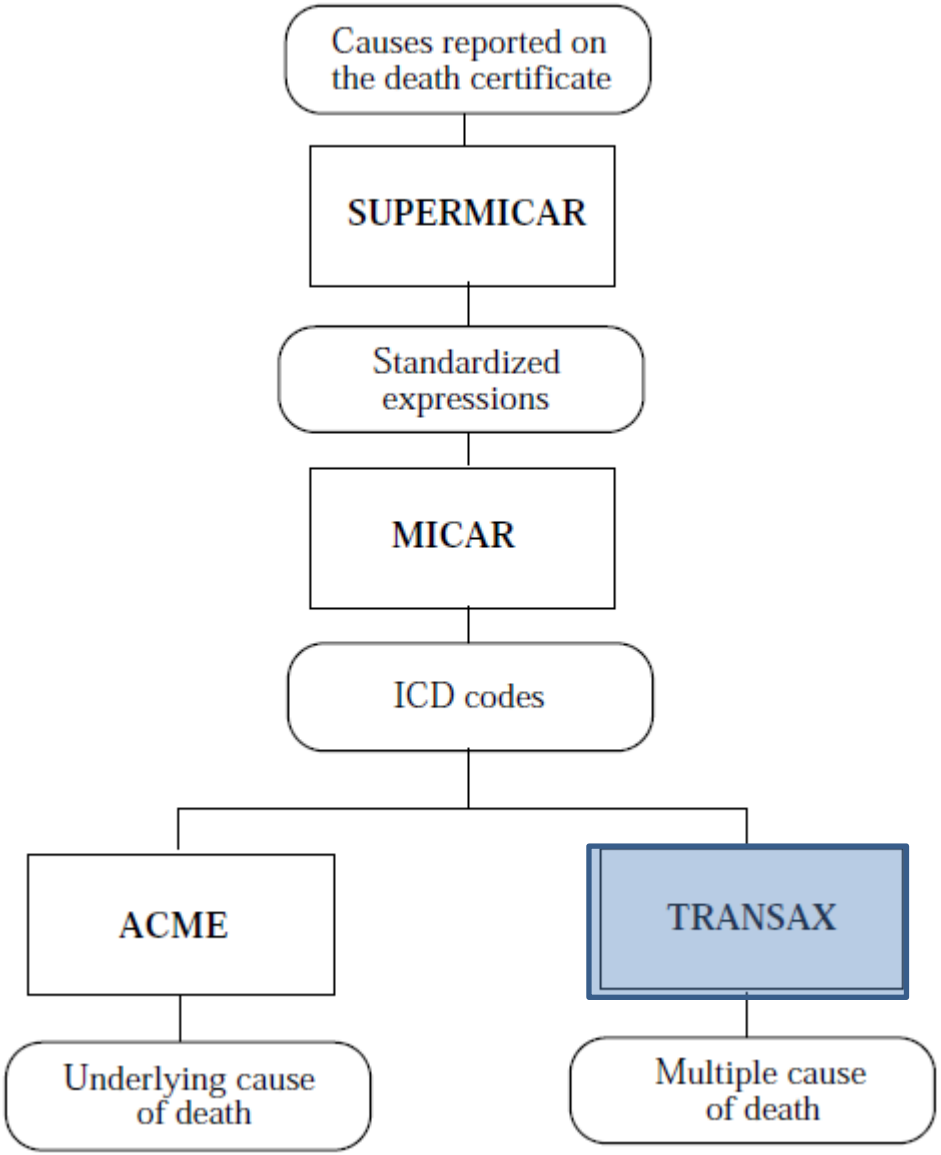
Another example

- On the same record as separate entities: cirrhosis of liver and alcoholism
  - Entity axis: 5715 (cirrhosis of liver without mention of alcohol) and 303 (alcohol dependence syndrome).
  - Record axis: 5712 (alcoholic cirrhosis of liver)

TRANSAX

- **TRANS**lation of **AX**is - in MCOD coding, the entity axis is converted into record (person) axis
- TRANSAX identifies the relationship between conditions mentioned on the death certificate, and then assigns an ICD code for any significant combinations (linkage). Detail and positions may be lost.
- MCOD record-axis data are not the data on which UCD was selected
- ACME – no linkage applied before selection of UCD (not to interfere with physician‘s opinion)

Fully automated coding system

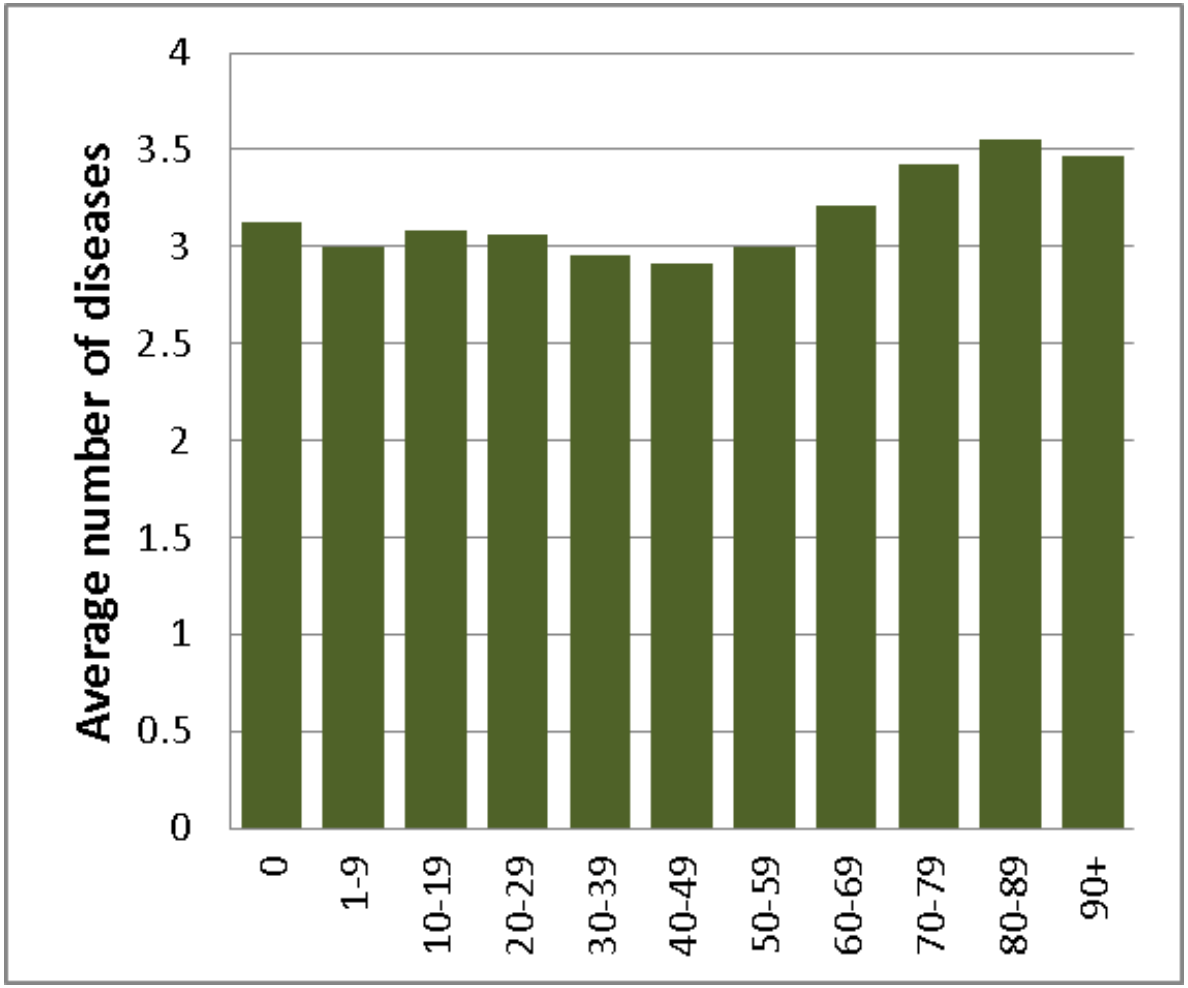


Analytical approaches

Comorbidity extent
CZ, 2011

Number of multiple causes per death certificate (%)						Average number of multiple causes per death certificate
1	2	3	4	5	6+	
8.7	21.7	26.3	20.8	13.4	9.1	3.4

Average number of causes on certificate by age, CZ 2011



Different aims (Egidi et al. 2011)

- Evaluating the quality of certification and coding (D'Amico et al 1999; Mannino et al. 1997)
- Evaluating the "burden" of diseases (Manton, Stallard 1982; Romon et al 2008; Yu-Pei Lin, Tsung-Hsueh Lu 2012)
- Improving estimates of the effect of specific risk factors on diseases (Nelson et al. 1994; Mannino et al. 1998)
- Exploring associations between causes of death (Redelings et al. 2007)
- Testing independence of competing risks (dependent competing risks models (Chiang, 1968), cause-deleted table (Manton et al. 1976, 1979; Manton, Stallard 1990)

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Total to underlying mentions

- Total mentions – the real burden of the disease
- Total to underlying ratio: the level of underestimation
- Standardized Ratio of Multiple to Underlying cause (SRMU)
- Controlled for population structures (age, gender)

$$SRMU_i = \frac{\sum_x MCOD^i_x p^{st}{}_x}{\sum_x UCD^i_x p^{st}{}_x}$$

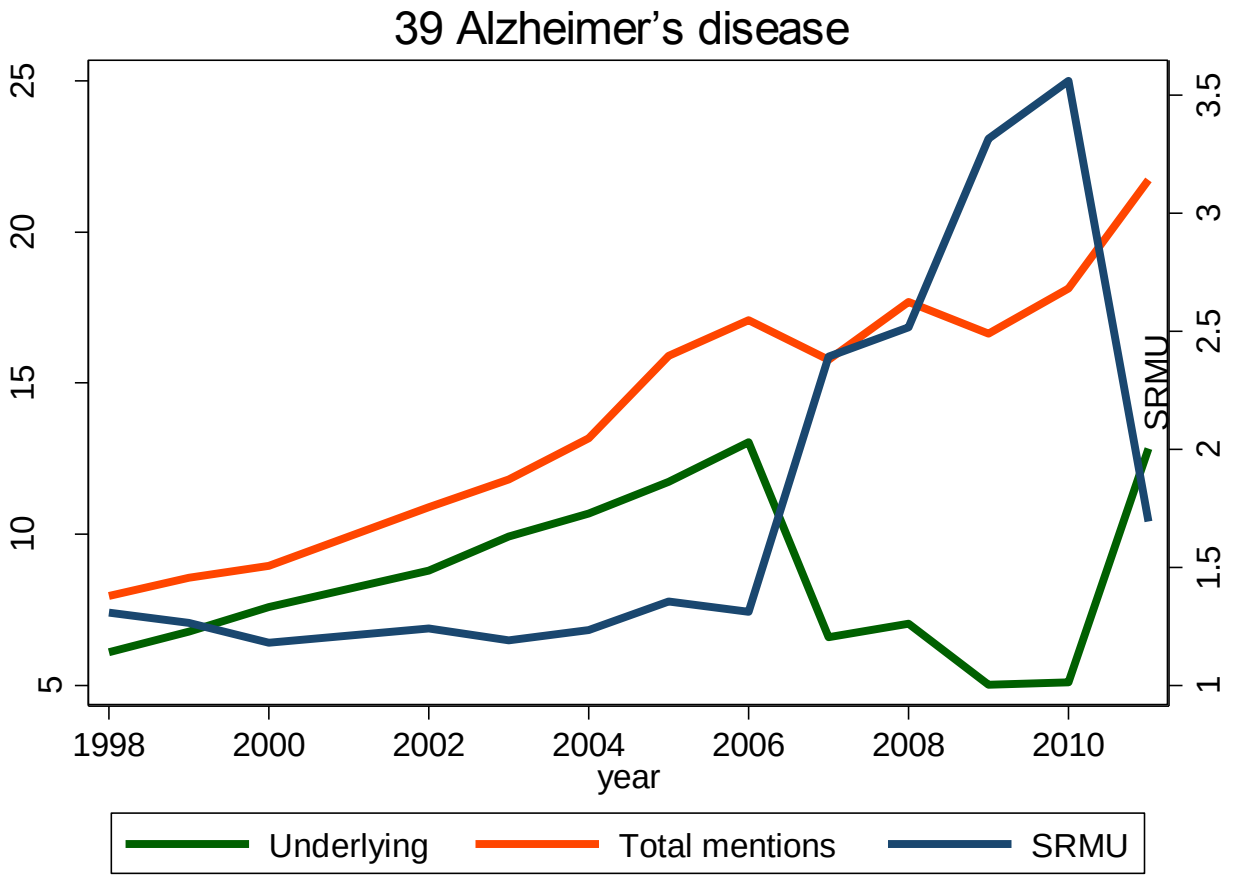
Estimating burden of disease: highest SRMU (CZ, 2011)

Other mental and behavioural disorders	29.1
Disorders of thyroid gland	20.4
Rheumatoid arthritis and osteoarthrosis	20.1
Obesity	14.4
Diseases of the blood(-forming organs) & immunol.disorders	14.3
Hyperplasia of prostate	12.9
Pneumonia	12.1
Diseases of the skin and subcutaneous tissue	11.9
Hypertensive diseases	10.9
Other endocrine, nutritional and metabolic diseases	10.7
Septicaemia	10.3
Renal Failure	9.9
Drug dependence, toxicomania	9.6
Malnutrition and other nutritional deficiencies	9.2
Other diseases of the nervous system	8.7
Other diseases of the respiratory system	8.4
Other diseases of the genitourinary system	7.4
Other diseases of the musculoskeletal system/connective	7.2
Other acute lower respiratory diseases	7.2

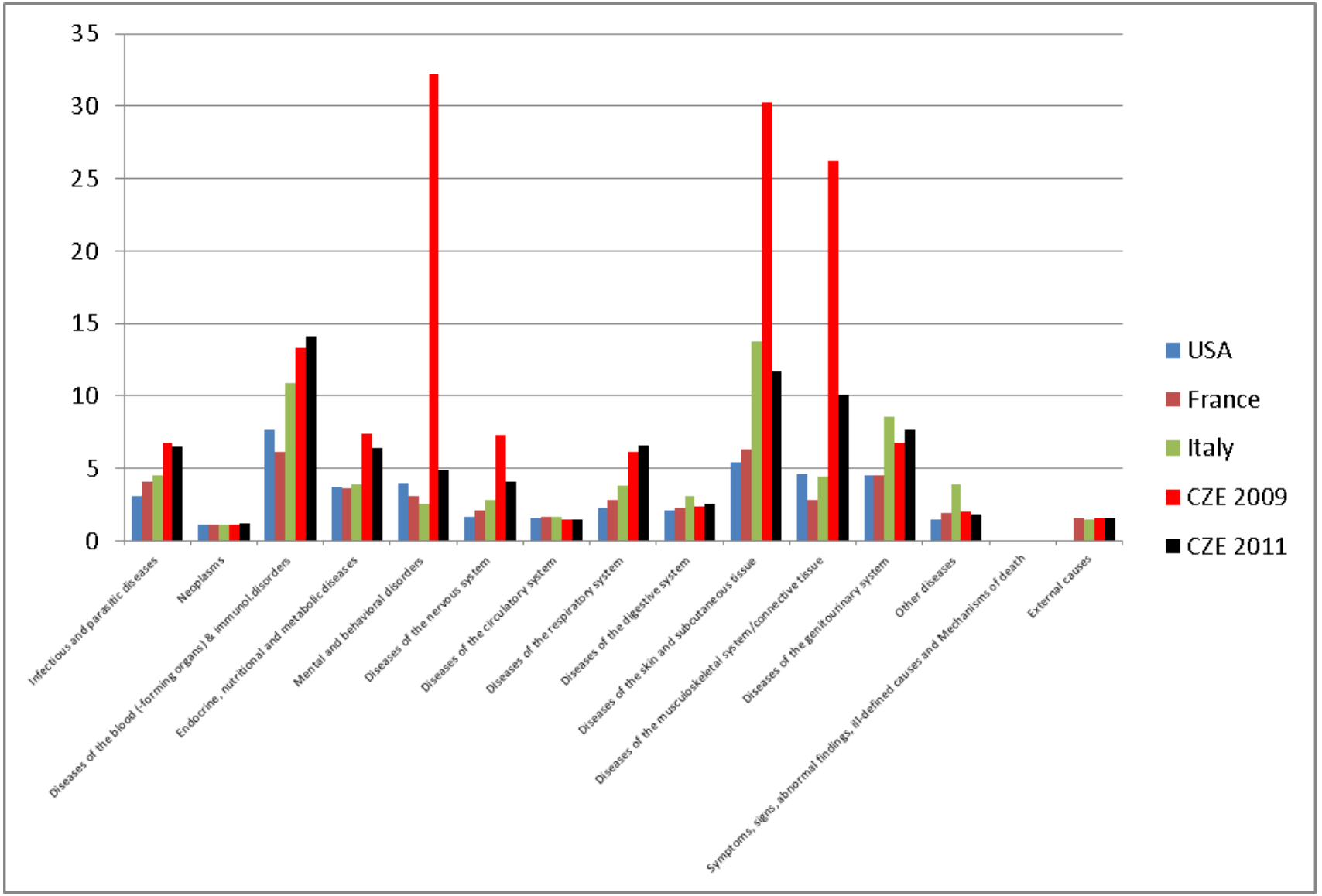
Lowest SRMU (CZ, 2011)

Accidental falls	1.4
Malignant neoplasm of cervix uteri and other parts of uterus	1.3
Malignant melanoma of skin	1.3
Malignant neoplasm of eye, brain and other parts of central	1.3
Malignant neoplasm of small intestine, colon, rectum and anus,	1.3
Malignant neoplasm of lymph./haematopoietic tissue	1.3
Malignant neoplasm of liver, the intrahepatic bile ducts,	1.2
Malignant neoplasm of lip, oral cavity, pharynx	1.2
Malignant neoplasm of stomach	1.2
Malignant neoplasm of oesophagus	1.2
Malignant neoplasm of ovary	1.2
Accidental poisoning	1.2
Malignant neoplasm of larynx and trachea/bronchus/lung	1.1
Transport accidents	1.1
Suicide/intentional self-harm	1.1
Malignant neoplasm of pancreas	1.1
AIDS (HIV-disease)	1.0

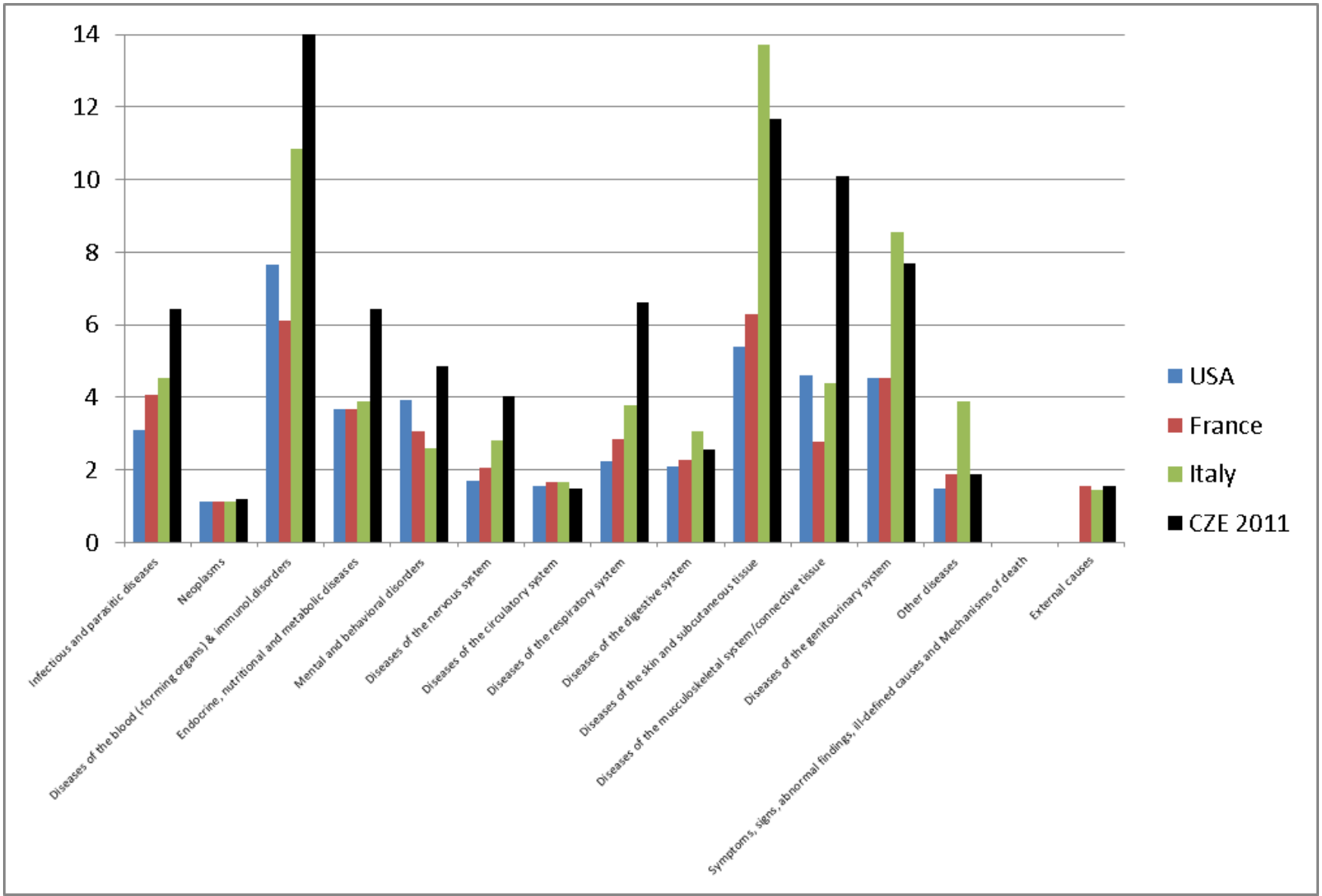
Evaluate coding practices (CZ, 1998-2011)



Evaluating international comparability



Without CZ 2009



CDAI (cause-of-death association indicator)

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

where ${}_u d_{c,x}$ = number of deaths observed at age x with underlying cause u and contributing cause c;

${}_u d_{c,x}$ = the number of deaths observed at age x with cause u as the underlying cause;

$d_{c,x}$ = the total number of deaths observed at age x with cause c as the contributing cause (regardless of the underlying cause);

d_x = the total number of deaths observed at age x (regardless of the underlying cause);

$\bar{d}_x$ = the standard number of deaths at age x (based on the 2009 WHO life table for high-income countries).

Associations between diseases, CZ 2011

UCD	MCD													
	INF	NEO	BLOOD	ENDOC	MENT	NERV	CIRC	RESP	DIGES	SKIN	MUSC	GENIT	OTHER	EXT
INF	366	62	122	127	96	97	87	89	275	308	145	209	137	46
NEO	83	296	205	99	48	66	85	95	123	33	79	98	80	25
BLOOD	293	63	683	110	45	123	86	87	138	53	157	143	31	30
ENDOC	237	53	125	153	100	81	107	107	93	250	117	234	20	42
MENT	126	30	60	122	317	125	96	179	69	322	137	89	0	59
NERV	123	43	73	98	453	220	80	155	61	245	142	104	146	59
CIRC	61	52	62	107	97	121	114	92	65	95	100	88	119	43
RESP	164	58	67	95	122	113	97	164	73	72	102	100	124	34
DIGES	359	61	170	90	81	62	82	83	547	34	34	129	98	40
SKIN	1275	10	69	155	167	67	89	74	81	445	202	153	0	11
MUSC	491	28	308	121	10	55	75	141	48	53	845	178	177	97
GENIT	511	54	183	111	79	39	97	85	96	140	96	402	108	37
OTHER	114	40	48	88	36	122	79	74	16	0	64	218	627	123
ILLDEF	69	71	25	63	129	151	100	56	54	128	179	48	165	82
EXT	77	37	67	64	107	105	71	112	46	181	69	58	29	1107

MultiCause Network (Désesquelles, 2014

- An international network devoted to the MCOD approach
- To foster analysis based on MCOD data
- To develop common standards and make cross-country comparisons
- Scientific meeting every two-years : Paris (2012), Rome (2014), Prague (2016)

MultiCause results

- Désesquelles, A., Salvatore, M.A., Frova, L., Pace, M., Pappagallo, M., Meslé, M., & Egidi, V. (2010). Revisiting the mortality of France and Italy with the multiple-cause-of-death approach. *Demographic research*, 23(28): 71-806.

- Désesquelles, A., Salvatore, M.A., Pappagallo, M., Frova, L., Pace, M., Meslé, F., & Egidi, V. (2012). Analysing Multiple Causes of Death: Which Methods For Which Data? An Application to the Cancer-Related Mortality in France and Italy. *European Journal of Population*, 28.

- Désesquelles A., Demuru E., Egidi V., Frova L., Meslé F., Pappagallo M., Salvatore M.A. (2014). «Cause-specific mortality analysis: is the underlying cause of death sufficient?. *Quetelet Journal*, 1 (2): 119-135

- Désesquelles A., Demuru E., Salvatore M.A., Pappagallo M., Frova L., Pace M., Meslé F., Egidi V. (2014). Mortality from Alzheimer's disease, Parkinson's disease and dementias in France and Italy: a comparison using the multiple cause-of-death approach, *Journal of Aging and Health*, 26 (2): 283 - 315.

- Pechholdová M., (2014). Multiple causes of death in the Czech Republic: an exploratory analysis, Demografie, 56(4):335–346.

Summary

- A bit more issues than with UCD data
- Two types of MCOD data: entity-axis and record-axis
- Automated coding improves comparability
- Need to enhance standardization procedures (collection, analysis)
- The results are valuable and innovative

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