A comparison of the mortality due to mental, behavioral and nervous disorders of France and Italy using the multiple-cause-of-death approach

Aline Désesquelles[1], Michele Antonio Salvatore[2], France Meslé[1], Viviana Egidi[2], Marilena Pappagallo[3], Luisa Frova[3], Monica Pace[3]

Though the monitoring of the mortality trends still relies on the underlying cause of the death, the multiple-cause-of-death (MCOD) approach is emerging as a promising tool in order to study the mortality profile of ageing populations. At old ages, death is indeed often the final stage of a long morbid process that involves several conditions. We use this approach to compare the mortality due to mental and behavioral disorders (ICD-10, chapter 5) and to diseases of the nervous system (ICD-10, chapter 6) of Italy and France. Our analysis is conducted for the two sexes and for two age groups (under/over the age of 80) separately.

Data and method

Data are for year 2003. They are based on the information reported on the death certificates which, in both countries, are adaptations of the model recommended by WHO. In Italy, information on the contributory causes is not available for deaths assigned to an external cause and for the infant deaths. All these cases have thus been excluded from the analysis. In addition, we excluded all deaths that occurred in the Italian provinces of Trento and Bolzano; the corresponding death certificates are coded locally and for the underlying cause only. Finally, our analysis is conducted on a total number of 507,704 deaths for France and 550,835 deaths for Italy.

The list of causes used in the present analysis is very similar to the European short list that is recommended by Eurostat for European comparisons. Our list (see appendix) comprises 15 large groups that generally correspond to the ICD-10 chapters and 66 sub-groups. The conditions belonging to the ICD-10 chapters 5 and 6 are regrouped into eight subgroups that enable to assess the specific contributions of the Alzheimer's disease, of the other dementias as well as of the chronic alcohol abuse:

- Parkinson's disease,
- Other diseases of the nervous system

1: Institut national d'études démographiques (INED)

2: Sapienza University of Rome

3 : Istituto nazionale di statistica (Istat)

- Alcoholic psychosis/chronic alcohol abuse,
- Drug dependence and toxicomania,
- Dementias (excluding Alzheimer),
- Other mental and behavioral disorders,
- Epilepsy,
- Alzheimer's disease.

All the ill-defined contributory causes of death (group #14) are excluded from the analysis.

We first calculated age- and sex- standardized mortality rates for 1) a given cause reported as the underlying cause of the death, 2) the same cause reported as multiple (underlying or contributory) cause of the death. The standard population is the WHO 2003 European population by sex and five-year age groups. The cause-specific mortality ratio (CSMR) is defined as the ratio of the second over the first of these two rates. It measures the underestimation of the role played by a given condition in the overall mortality when the analysis is performed using the underlying cause only.

We use an indicator of the frequency of the combinations of causes that can be used to compare various underlying causes within a country as well as various countries for a given underlying cause. For each country separately, we first calculated the proportions by five-year age groups 1) of a given contributory cause among all deaths assigned to a specific underlying cause, 2) of the same contributory cause among all deaths of the country. We then applied these proportions to the same deaths counts (the average number of deaths in France and Italy in 2003 by five-year age groups) in order to remove the effect of the varying age structure of deaths by underlying cause. The cause-of-death association indicator (CDAI) is defined as the ratio between these two quantities. The CDAI measures the deviation from the mean – represented by the denominator of the above formula – of the frequency of occurrence of a specific association of causes. If the CDAI is significantly over 1, then the corresponding association is more frequent than what is expected.

Results

In 2003, 20,124 deaths over the age of one (resp.24,338) have been attributed in France to a mental or behavioral disorder (resp. to a disease of the nervous system).These figures are respectively 10,093 and 18,159 in Italy. The standardized mortality rates for these two chapters are much higher in France than in Italy (table 1). For all mental and behavioral disorders, the rate is more than twice higher in France (19.6 vs. 8.9 per 100,000 in Italy). The

difference is more reduced for the diseases of the nervous system (24.1 in France vs. 17.8 per 100,000 in Italy). For most groups of causes belonging to these two chapters, the standardized mortality rates are higher in France too. As an example, the standardized mortality rates for "Alcoholic psychosis/chronic alcohol abuse" is 5.1 per 100,000 in France vs. 0.4 in Italy. The difference between the two countries is also very high for all dementias excluding Alzheimer's disease (10.8 vs. 6.9 per 100,000 in Italy) and for Alzheimer's disease (10.2 vs. 5.9 per 100,00 in Italy). We however cannot conclude from this that dementias are more prevalent in France. In particular, we cannot rule out that the diagnosis of Alzheimer's disease, which is known to be problematic, is not made exactly the same way in the two countries.

With the exception of Drug dependence/toxicomania and the group of the "other mental and behavioral disorders", the CSMR is higher in Italy than in France (table 1)[1].As a consequence, the MCOD approach leads to a more important upward revision of the mortality rates in Italy than in France. When accounting for the contributory causes, the standardized death rate for mental and behavioral disorder increases from 8.9 to 29.5 per 100,00 in Italy and from 19.6 to 57.8 per 100, 000 in France. For the diseases of the nervous system, it raises from 17.8 to 49.6 per 100,000 in Italy and from 24.1 to 52.0 per 100,000 in France. So the difference between the two countries reduces slightly but the levels remain higher in France.

Table 1 – Standardized mortality rates (per 100,000) for each cause reported as underlying cause (1) or multiple cause (2) and cause-specific standardized mortality ratio (2/1). Deaths over the age of one, France and Italy, 2003

CAUSE OF DEATH	ITALY			FRANCE		
	Underlying cause (1)	Multiple cause (2)	CSMR	Underlying cause (1)	Multiple cause (2)	CSMR
Alcoholic psychosis/chronic alcohol abuse	0,4	1,8	4,7	5,1	17,7	3,5
Drug dependence,toxicomania	0,7	0,8	1,2	0,2	0,5	2,1
Dementia (excluding Alzheimer's Disease)	6,9	21,0	3,1	10,8	20,8	1,9
Other mental and behavioral disorders	1,0	6,4	6,5	3,5	23,5	6,7
All Mental and behavioral disorders	**8,9**	**29,5**	**3,3**	**19,6**	**57,8**	**3,0**
Epilepsia	0,8	3,4	4,5	2,0	5,5	2,7
Alzheimer disease	5,9	9,5	1,6	10,2	15,6	1,5
Parkinson disease	3,2	8,5	2,6	4,4	8,2	1,9
Other diseases of the nervous system	7,9	29,0	3,7	7,5	23,5	3,1
All Diseases of the nervous system	**17,8**	**49,6**	**2,8**	**24,1**	**52,0**	**2,2**
All causes of deaths	**562**	**1370**	**2,4**	**551**	**1119**	**2,0**

Data: France: Inserm mortality database / Italy: ISTAT mortality database

[1] In a previous study on all causes of death classified in 15 groups, we found that the CSMRs in Italy always are superior or equal to the CSMRs in France.

When looking more precisely at the subgroups, we find that the CSMR is especially high for following conditions:

- Alcoholic psychosis/chronic alcohol abuse: 4.7 in Italy and 3.5 in France,
- Epilepsy: 4.5 in Italy and 2.7 in France,
- Other mental and behavioral disorders: 6.5 in Italy and 6.7 in France,
- Other diseases of the nervous system: 3.7 in Italy and 3.1 in France

The impact of the MCOD approach is moderate for Alzheimer's (1.6 in Italy and 1.5 in France) and for Parkinson's (2.6 in Italy and 1.9 in France) diseases. When reported on the death certificate, these conditions are frequently selected as the underlying cause of the death. Interestingly, the CSMR for Alzheimer's disease is almost the same in the two countries. If the Italian physicians were to more cautiously diagnose Alzheimer's disease than their French counterparts, one might expect the CSMR for that disease to be smaller in Italy. But it is also possible that doubts about the accuracy of their diagnosis lead the Italian physicians to report Alzheimer's disease as contributory cause instead of underlying cause of the death. Another possibility is that they just report the presence of dementia. This could explain that the CSMR for dementias is higher in Italy (3.1) than in France (1.9). As mentioned earlier, the standardized mortality rates for dementias is much lower in Italy than in France but the MCOD approach makes equal the situation of the two countries (21 per 100,000).

Figures 1 and 2 display graphically the Cause-of-death Association Indicator (CDAI) for France and Italy. After computing the standard deviation (σ) of this indicator[2], we created the five following classes: $[0;100[$, $[100;100+\sigma/4[$, $[100+\sigma/4;100+\sigma/2[$, $[100+\sigma/2;100+3\sigma/4[$ and $[100+3\sigma/4;\infty[$. The first class is a white color (weak association) while all other classes are progressively darker shades of red. The cells of the table that result from the cross-matching of every underlying and every contributory cause of death have been colored according to the value of the corresponding CDAI. Figures 1 corresponds to cases where a condition belonging to chapters 5 or 6 is reported as the underlying cause of the death, while figures 2 enables to find the underlying cause of the deaths for which a condition belonging to chapters 5 or 6 is reported as contributory cause of the death. These figures have been made for all deaths as well as for two age groups (deaths over the age of one and under the age of 80, and death at age 80 or over) and for males and females separately[3].

[2] The standard deviation has been calculated taking into account all the values of the CDAI in the two countries.
[3] See Figures A1 to A8 in the appendix

Several strong associations involving "**Alcoholic psychosis/chronic alcohol abuse**" are common to both France and Italy:

- "Alcoholic psychosis/chronic alcohol abuse"- "Ulcer of stomach, duodenum and jejunum"
- "Chronic liver disease"-"Alcoholic psychosis/chronic alcohol abuse"
- "Malignant neoplasm liver and the intrahepatic bile ducts" – "Alcoholic psychosis/chronic alcohol abuse" (over the age of 80 only)
- "Alcoholic psychosis/chronic alcohol abuse" – "Malnutrition and other nutritional deficiencies"
-"Alcoholic psychosis/chronic alcohol abuse" – "epilepsy" reflecting epileptic seizures related to alcohol abuse
- "Alcoholic psychosis/chronic alcohol abuse" and "Other Mental and behavioral disorders" (mainly "mental and behavioral disorders due to use of tobacco") that reflects the frequent concomitant use of alcohol and tobacco.

Several others are specific to France:

- "Alcoholic psychosis/chronic alcohol abuse" – "Malignant neoplasm of stomach"
- "Malignant neoplasm of lip, oral cavity, pharynx" – "Alcoholic psychosis/chronic alcohol abuse" (over the age of 80)
- "Malignant neoplasm of oesophagus" – "Alcoholic psychosis/chronic alcohol abuse" (over the age of 80)

As was expected, we find a strong association in both countries between « **Drug dependence, toxicomania** », "AIDS (HIV-disease)" and « viral hepatitis » that reflects HIV transmission among intravenous drug injectors.

In both France and Italy, **epilepsy** is frequently associated with "Lung diseases due to external agents" (mainly: "Pneumonitis due to food and vomit") and, for males and/or under the age of 80, with an external cause (e.g. "Foreign body in respiratory tract"). In both cases, regurgitation is a consequence of the epileptic seizure. Epilepsy is also frequently associated with various neoplasms. This result should be further considered in light of the medical literature on a potential secondary effect of anti-epileptic treatments on the onset of cancer.

Cases where epilepsy is both the underlying and the contributory cause of the death are not uncommon. More precisely, the contributory cause is often an unspecified "epilepsy" or "status epilepticus". In such cases, the added value of the contributory cause is of course disputable. The same applies for cases where Parkinson's disease is both the underlying and

the contributory cause (mainly: secondary Parkinson unspecified) of the death. In terms of method, this raises the question of which contributory causes must be taken account. The answer to that question is likely to be different depending on the level of classification used for the analysis.

Not surprisingly we find that dementias (excluding Alzheimer's disease) often contribute to deaths due to **Parkinson's disease**. Dementia is indeed a possible complication of Parkinson's disease. In both countries, three other groups of causes frequently contribute to the deaths attributed to **Parkinson's disease, Alzheimer's disease** or **other dementias**:

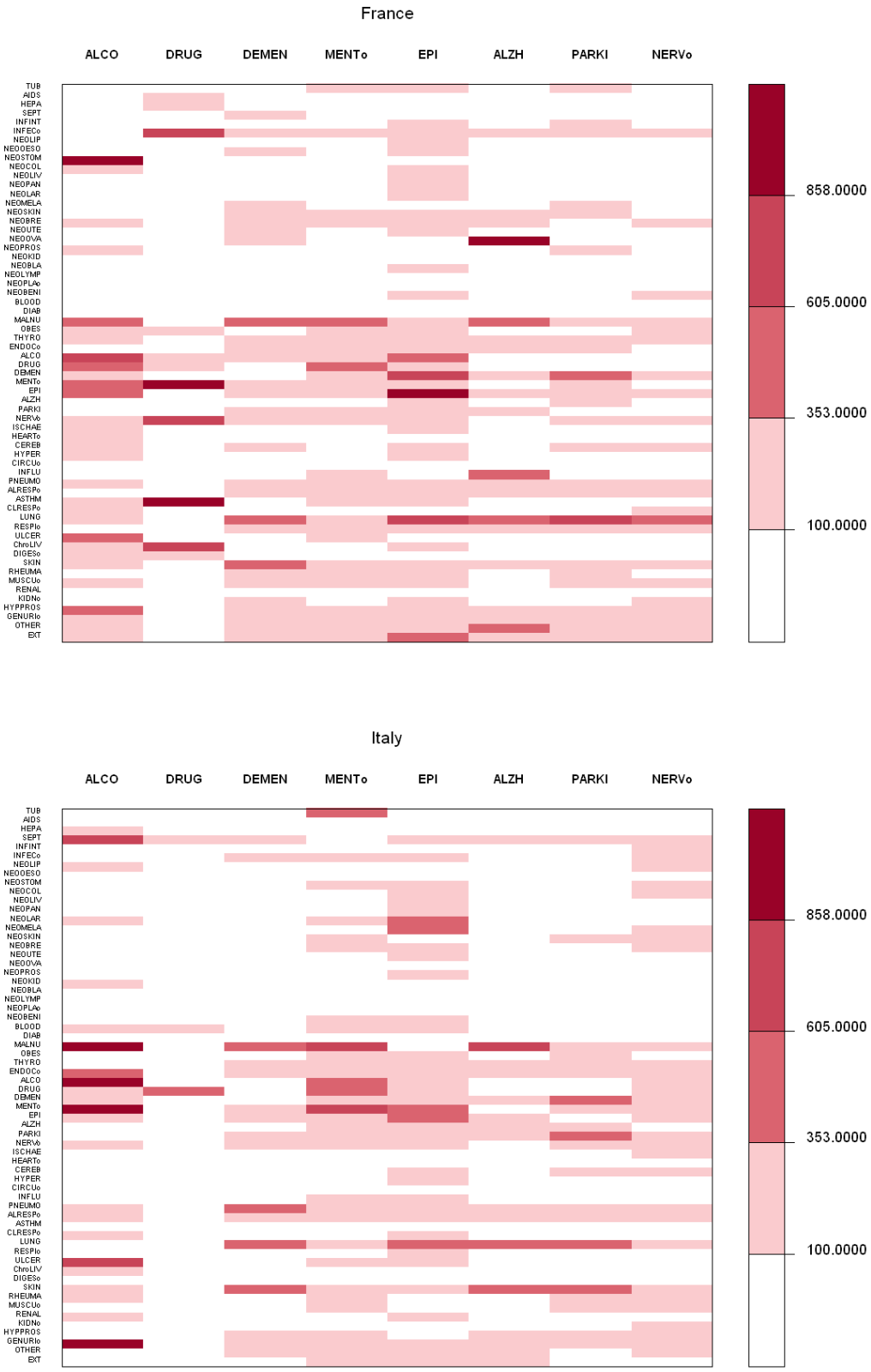
- "Malnutrition and other nutritional deficiencies ";
- "Lung diseases due to external agents » which in most cases correspond to "Pneumonitis due to food and vomit";
- "Diseases of the skin and subcutaneous tissue" (in Italy only).

Parkinson's disease and Alzheimer's disease are also found to frequently contribute to deaths attributed to a disease of the genitourinary system (e.g. hyperplasia of prostate). Clearly, all these cases reflect the circumstances surrounding the final stage of both dementia and Parkinson's disease that are often characterized by bed confinement and loss of autonomy. Old age and, to put it more precisely, frailty are also likely to play a major role in cases where the following combinations of causes - that are frequent in both countries – are reported by the physicians:

- Respiratory diseases as underlying cause (e.g influenza and pneumonia) and Alzheimer's disease as contributory cause
- Infectious diseases (mainly: septicemia) as underlying cause and Parkinson's disease as contributory cause
- Infectious diseases (mainly: septicemia) as underlying cause and Alzheimer's disease as contributory cause.

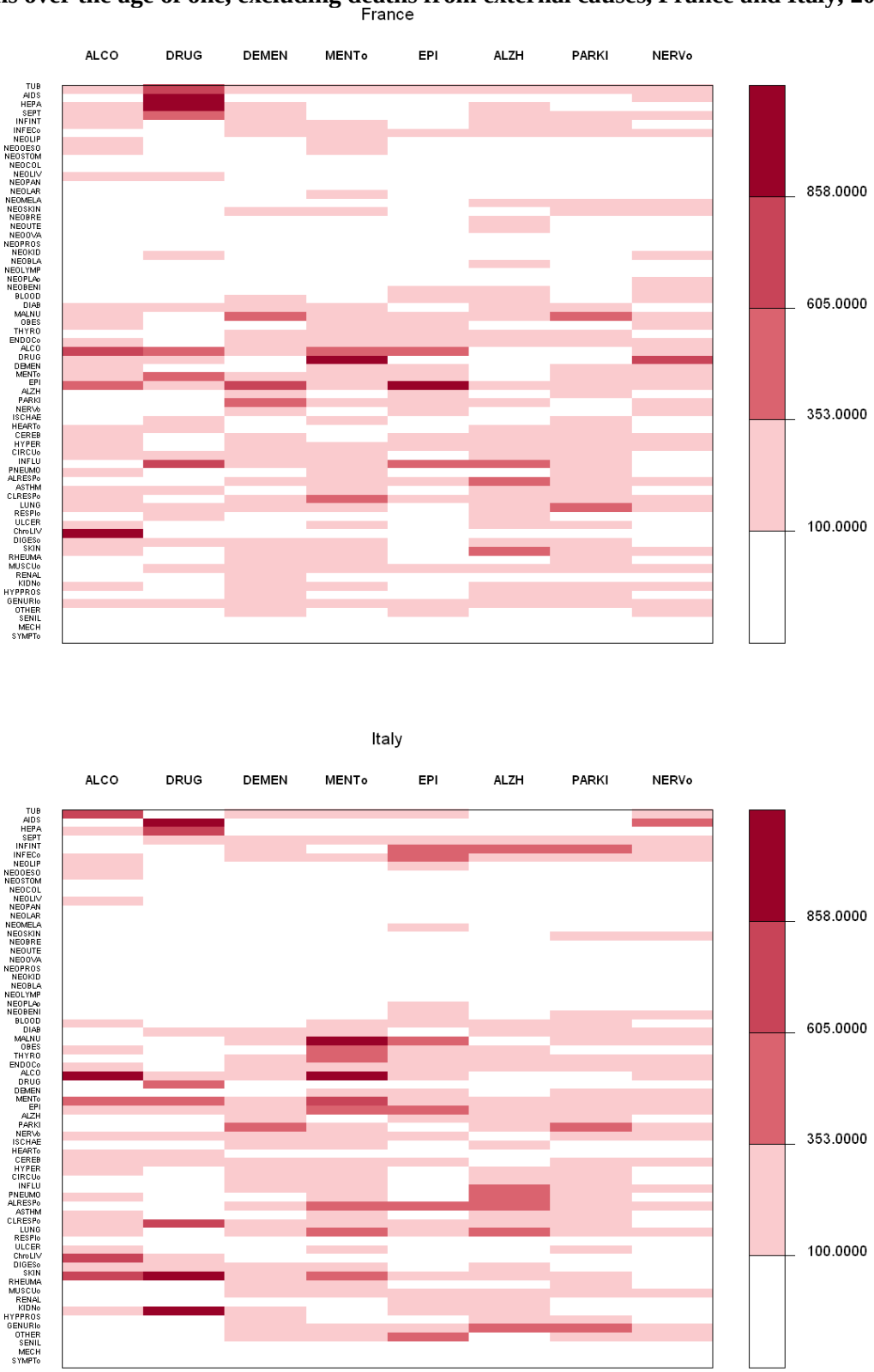
To conclude, this rapid overview suggests that most combinations of causes that we labeled as "strong" are similar in the two countries. These combinations generally find a medical explanation, which gives a lot of support to the quality of the physicians' certification. The high level of agreement between the two countries does not preclude that there are several dissimilarities; they will require in-depth examination. At this stage, the analysis of the associations of causes according to age and gender does not bring much light to the topic.

Figure 1 – CDAIs – Mental, behavioral and nervous diseases as underlying cause of the death. Deaths over the age of one, excluding deaths from external causes, France and Italy, 2003.



Horizontal axis: underlying cause Vertical axis : contributory cause.
Data: France: Inserm mortality database / Italy: ISTAT mortality database

Figure 2 – CDAIs – Mental, behavioral and nervous diseases as contributory cause of the death. Deaths over the age of one, excluding deaths from external causes, France and Italy, 2003.



Horizontal axis: contributory cause. Vertical axis: underlying cause
Data: France: Inserm mortality database / Italy: ISTAT mortality database

APPENDIX

Group #	Abb	Groups and subgroups	ICD-10 code
1		**Infectious and parasitic diseases**	
	TUB	Tuberculosis	A15-A19, B90
	AIDS	AIDS (HIV-disease)	B20-B24
	HEPA	Viral hepatitis	B15-B19, B94.2
	SEPT	Septicaemia	A40-A41
	INFINT	Intestinal infectious diseases	A00-A09
	INFECo	Other Infectious and parasitic diseases	(A00-B99) - Supra codes
2		**Neoplasms**	
	NEOLIP	Malignant neoplasm of lip, oral cavity, pharynx	C00-C14
	NEOOESO	Malignant neoplasm of oesophagus	C15
	NEOSTOM	Malignant neoplasm of stomach	C16
	NEOCOL	Malignant neoplasm of colon, rectum and anus	C18,C19, C20, C21
	NEOLIV	Malignant neoplasm liver and the intrahepatic bile ducts	C22
	NEOPAN	Malignant neoplasm of pancreas	C25
	NEOLAR	Malignant neoplasm of larynx and trachea/bronchus/lung	C32-C34
	NEOMELA	Malignant melanoma of skin	C43
	NEOSKIN	Malignant neoplasm of skin	C44
	NEOBRE	Malignant neoplasm of breast	C50
	NEOUTE	Malignant neoplasm of cervix uteri and other parts of uterus	C53, C54, C55
	NEOOVA	Malignant neoplasm of ovary	C56
	NEOPROS	Malignant neoplasm of prostate	C61
	NEOKID	Malignant neoplasm of kidney	C64
	NEOBLA	Malignant neoplasm of bladder	C67

	NEOLYMP	Malignant neoplasm of lymph./haematopoietic tissue	C81-C96
	NEOPLAo	Other malignant neoplasms	(C00-C99) – Supra codes
	NEOBENI	Benign neoplasms, in situ neoplasms and neoplasms of uncertain or unknown behavior	D00-D09, D10-D36, D37-D48
3	**BLOOD**	**Diseases of the blood(-forming organs), immunol.disorders**	D50-D89
4		**Endocrine, nutritional and metabolic diseases**	
	DIAB	Diabetes mellitus	E10-E14
	MALNU	Malnutrition and other nutritional deficiencies	E40-E64
	OBES	Obesity	E65-E68
	THYRO	Disorders of thyroid gland	E00-E07
	ENDOCo	Other Endocrine, nutritional and metabolic diseases	(E00-E90) - Supra codes
5		**Mental and behavioral disorders**	
	ALCO	Alcoholic psychosis/chronic alcohol abuse	F10, G31.2
	DRUG	Drug dependence, toxicomania	F11-F16, F18-F19
	DEMEN	Dementias (excluding Alzheimer)	F01, F03, G31.0, G31.8, G31.9
	MENTo	Other Mental and behavioral disorders	(F00-F99) - Supra F codes
6		**Diseases of the nervous system**	
	EPI	Epilepsy	G40-G41
	ALZH	Alzheimer's disease	G30
	PARKI	Parkinson's disease	G20, G21
	NERVo	Other Diseases of the nervous system	(G00-G98) – (G31.0, G31.2, G31.8, G31.9)– Supra codes
7		**Diseases of the circulatory system**	
	ISCHAE	Ischaemic heart diseases	I20-I25

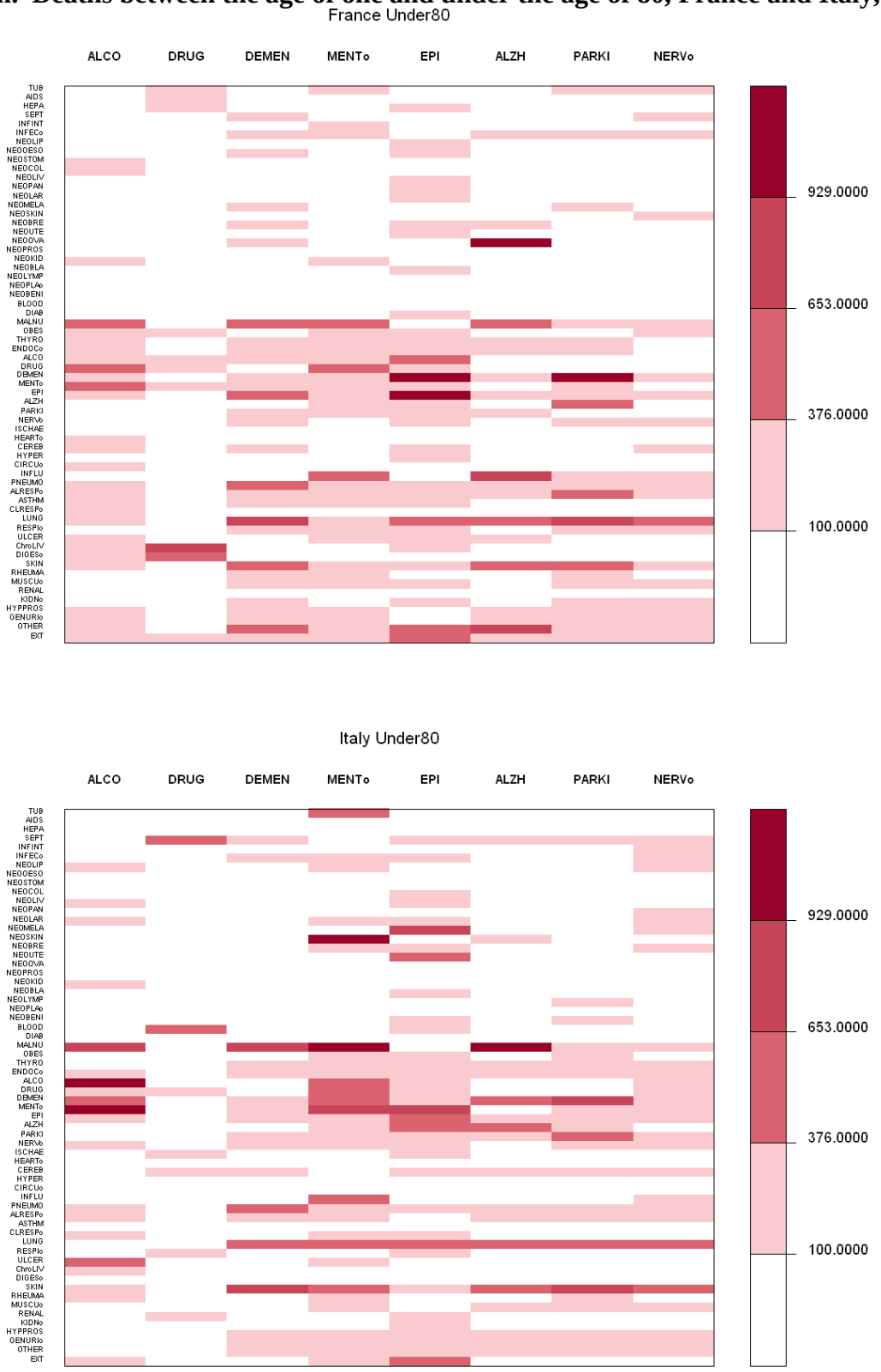
	HEARTo	Other heart diseases	I30-I33, I39-I45, I47-I48, I49.1-I52, I00-I09
	CEREB	Cerebrovascular diseases	I60-I69
	HYPER	Hypertensive diseases	I10-I15
	CIRCUo	Other Diseases of the circulatory system	(I00-I99) – (I46, I49.0, I95.9, I99) – Supra codes
8		**Diseases of the respiratory system**	
	INFLU	Influenza	J10-J11
	PNEUMO	Pneumonia	J12-J18
	ALRESPo	Other acute lower respiratory diseases	J00-J09, J19-J22
	ASTHM	Asthma	J45-J46
	CLRESPo	Other Chronic lower respiratory diseases	J40-J44
	LUNG	Lung diseases due to external agents	J60-J70
	RESPIo	Other Diseases of the respiratory system	(J00-J99) (J96.0, J96.9) –Supra codes
9		**Diseases of the digestive system**	
	ULCER	Ulcer of stomach, duodenum and jejunum	K25-K28
	ChroLIV	Chronic liver disease	K70, K73-K74
	DIGESo	Other Diseases of the digestive system	(K00-K93) – Supra codes
10	**SKIN**	**Diseases of the skin and subcutaneous tissue**	L00-L99
11		**Diseases of the musculoskeletal system/connective tissue**	
	RHEUMA	Rheumatoid arthritis and osteoarthrosis	M05-M06, M15-M19
	MUSCUo	Other Diseases of the musculoskeletal system/connective tissue	(M00-M99) – Supra codes
12		**Diseases of the genitourinary system**	
	RENAL	Renal Failure	N17-N19
	KIDNo	Other Diseases of kidney and ureter	N00-N16

	HYPPROS	Hyperplasia of prostate	N40
	GENURIo	Other Diseases of the genitourinary system	(N00-N99) – Supra codes
13		**Other diseases**	
	PREGN PERINAT MALFORM EYE EAR SIDS	Complications of pregnancy, childbirth and puerperium Certain conditions originating in the perinatal period Congenital malformations and chromosomal abnormalities Diseases of the eye and adnexia Diseases of the ear and mastoid process SIDS	O00-O99 (P00-P96)- P28.5 Q00-Q99 H00- H59 H60- H95 R95
14	**OTHER**	**Symptoms, signs, abnormal findings and ill-defined causes**	
	SENIL	Senility	R54
	MECHA	Mechanisms of the death °	I46, I49.0, R09.2, R40.2, R57
	SYMPTo	Other Symptoms, signs, abnormal findings and ill-defined causes °°	(R00-R94), (R96-R99), I95.9, I99, J96.0, J96.9, P.28.5, U00 - Supra R codes
15	**EXT**	**External causes**	S, T, V, W, X Y codes

°) Cardiac arrest (I46.0), Ventricular fibrillation (I49.0), Respiratory arrest (R09.2), Coma (R40.2), Shock (R57)

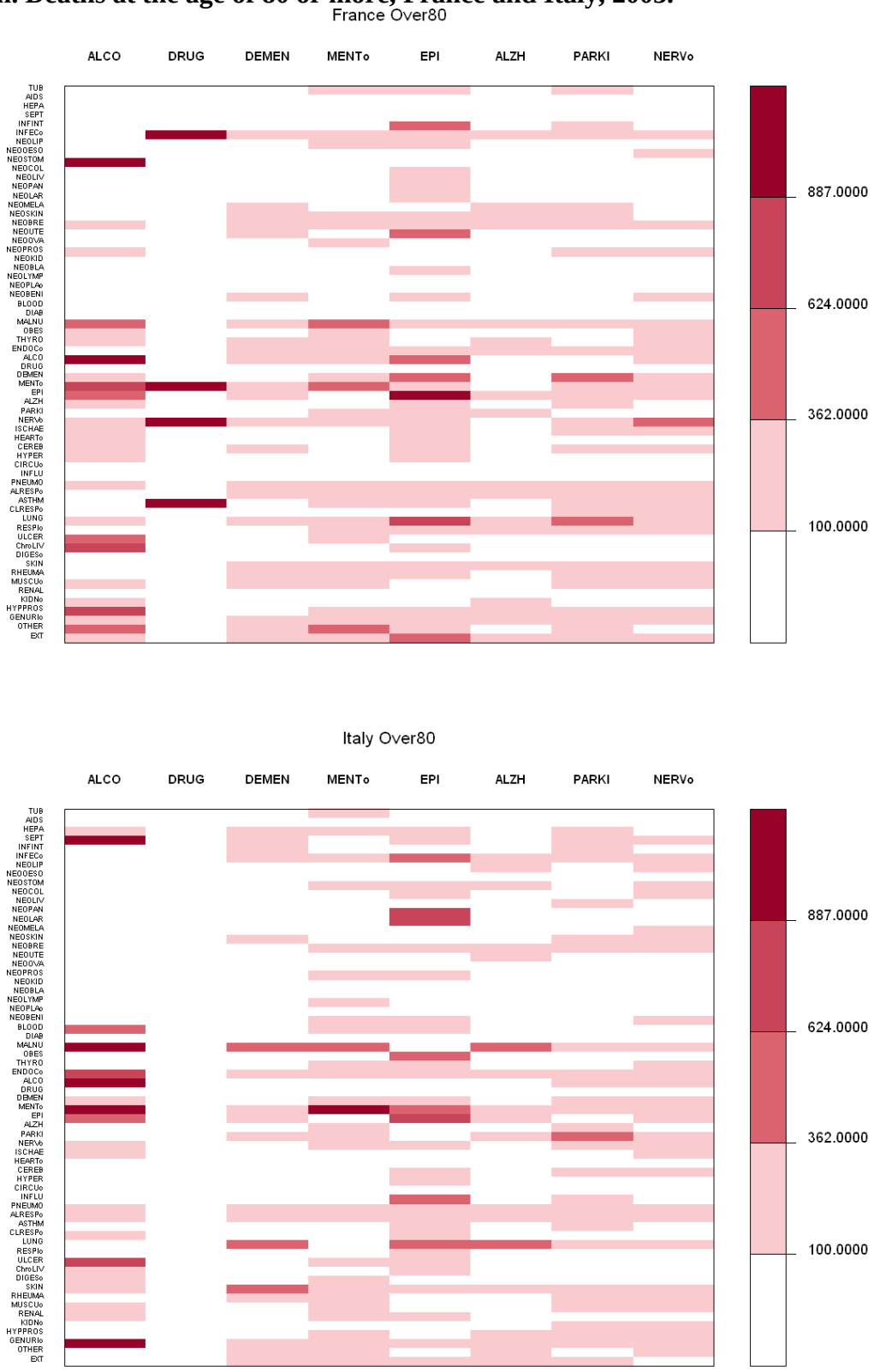
°°) Hypotension (I95.9), Other unspecified disorders of circulatory system (I99), Acute respiratory failure (J96.0), Respiratory failure unspecified (J96.9), Respiratory failure of newborn P(.28.5)

Figure A1 – CDAIs – Mental, behavioral and nervous diseases as underlying cause of the death. Deaths between the age of one and under the age of 80, France and Italy, 2003.



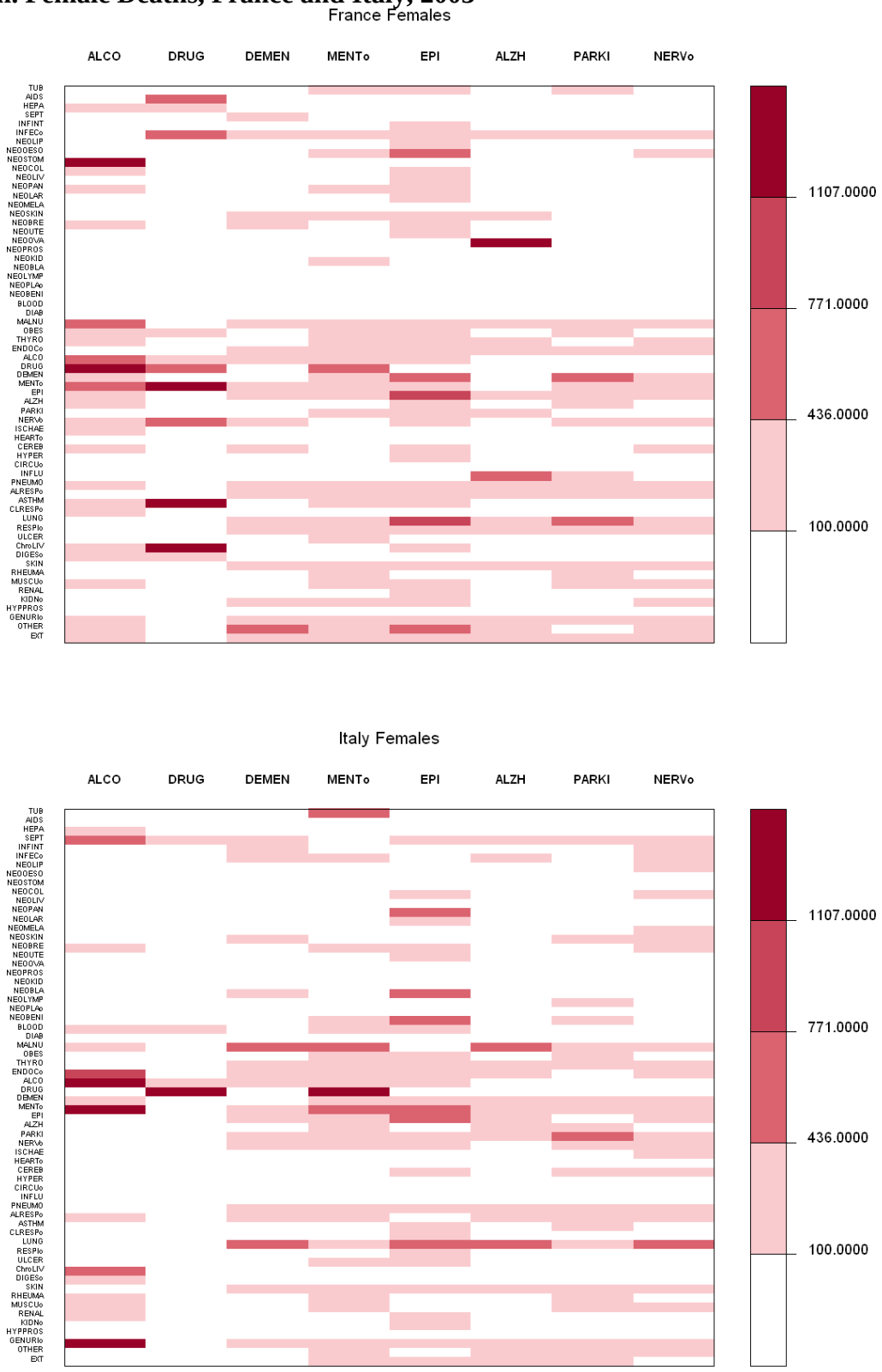
Horizontal axis: underlying cause Vertical axis: contributory cause.
Data: France: Inserm mortality database / Italy: ISTAT mortality database

Figure A2 – CDAIs – Mental, behavioral and nervous diseases as underlying cause of the death. Deaths at the age of 80 or more, France and Italy, 2003.



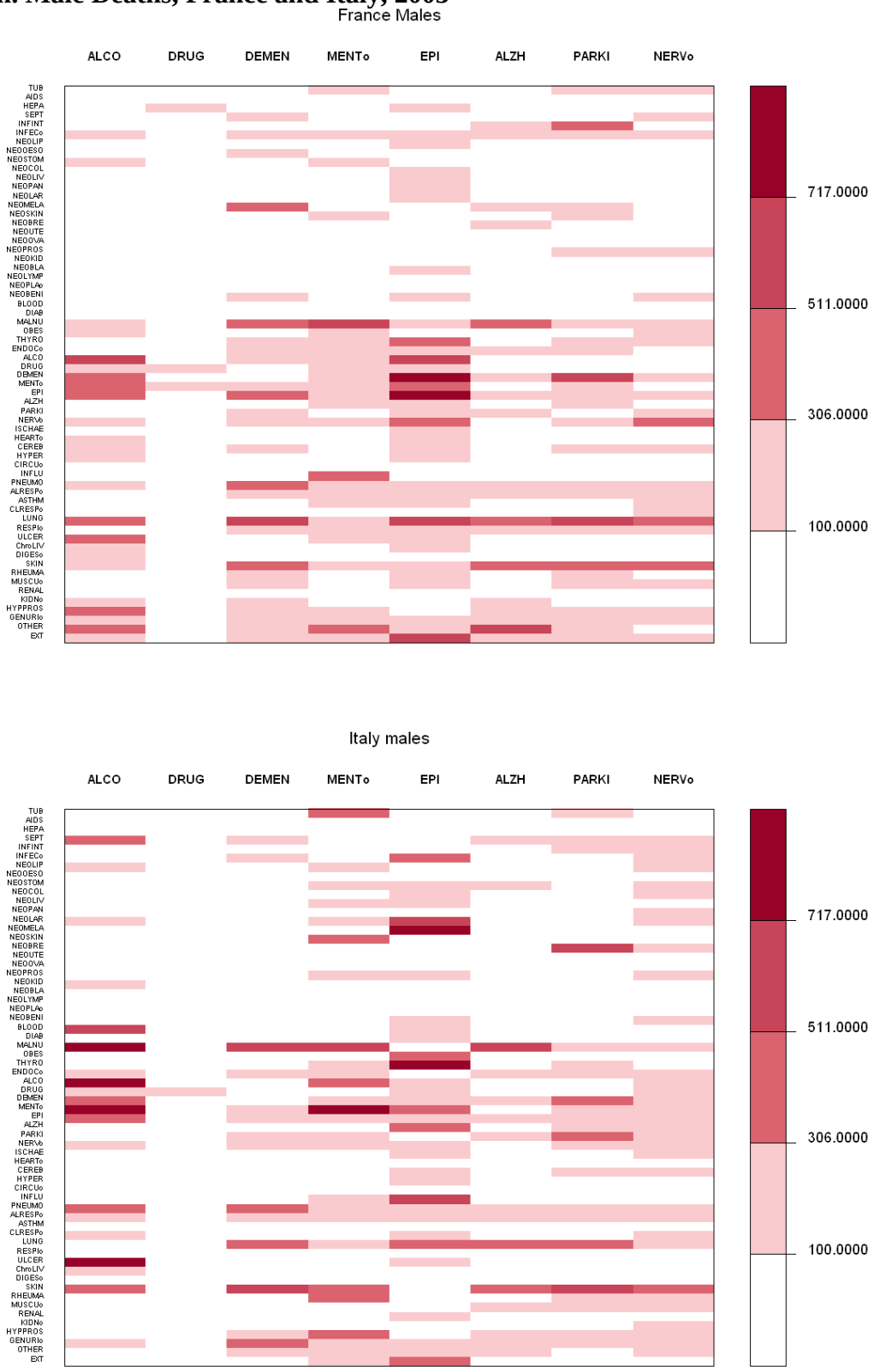
Horizontal axis: underlying cause Vertical axis: contributory cause.
Data: France: Inserm mortality database / Italy: ISTAT mortality database

Figure A3 – CDAIs – Mental, behavioral and nervous diseases as underlying cause of the death. Female Deaths, France and Italy, 2003



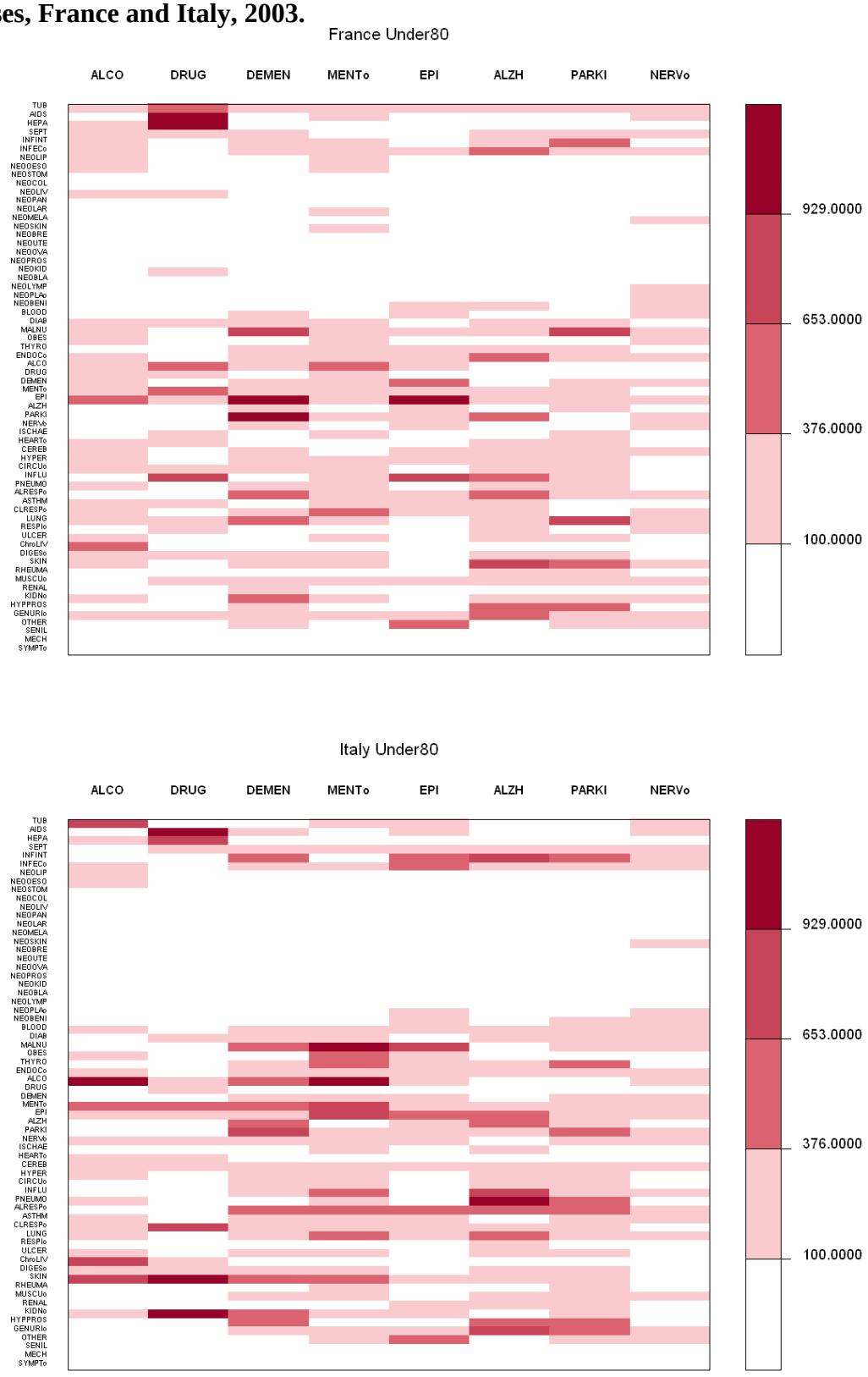
Horizontal axis: underlying cause Vertical axis: contributory cause.
Data: France: Inserm mortality database / Italy: ISTAT mortality database

Figure A4 – CDAIs – Mental, behavioral and nervous diseases as underlying cause of the death. Male Deaths, France and Italy, 2003



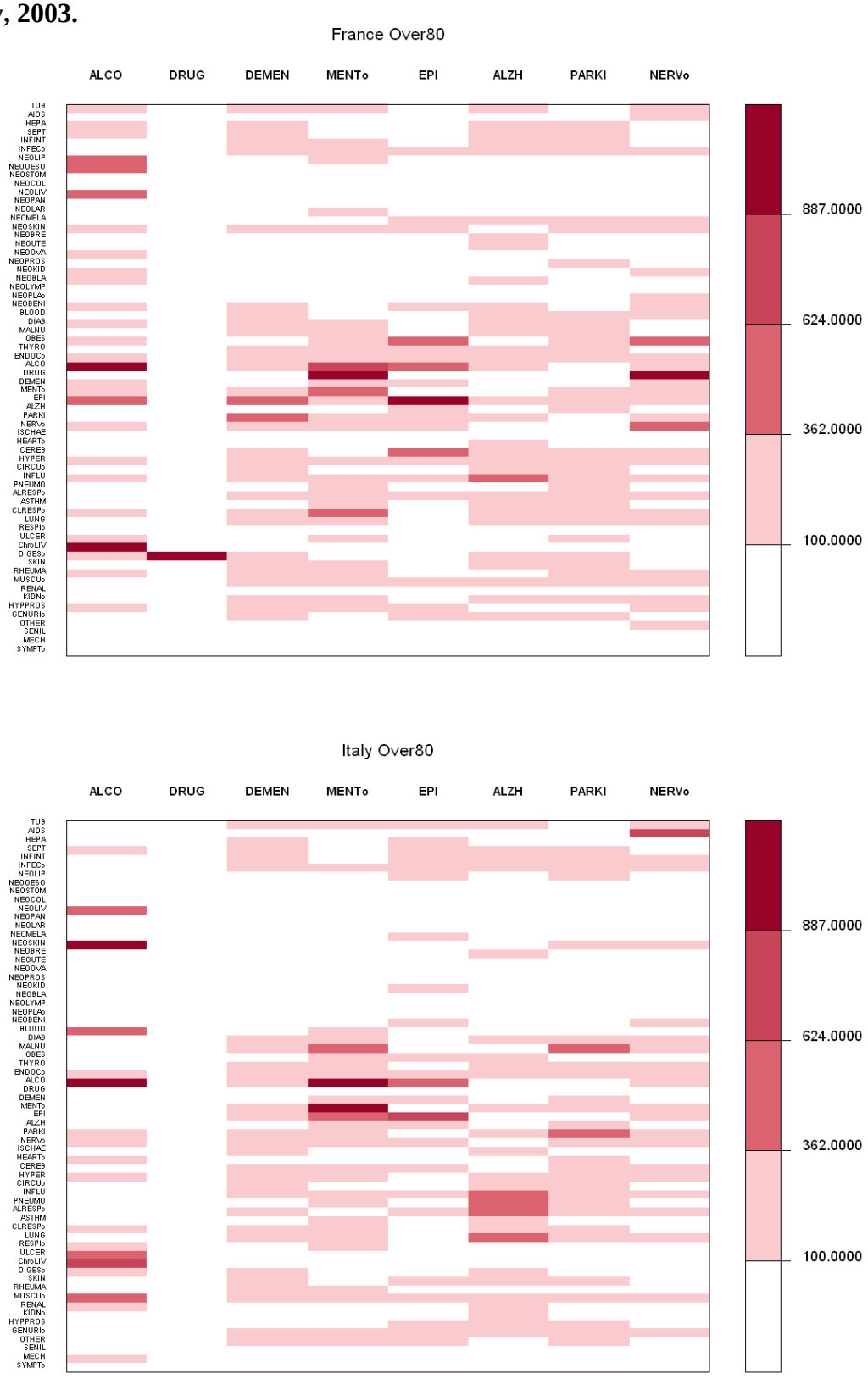
Horizontal axis: underlying cause Vertical axis: contributory cause.
Data: France: Inserm mortality database / Italy: ISTAT mortality database

Figure A5 – CDAIs – Mental, behavioral and nervous diseases as contributory cause of the death. Deaths between the age of one and under the age of 80, excluding deaths from external causes, France and Italy, 2003.



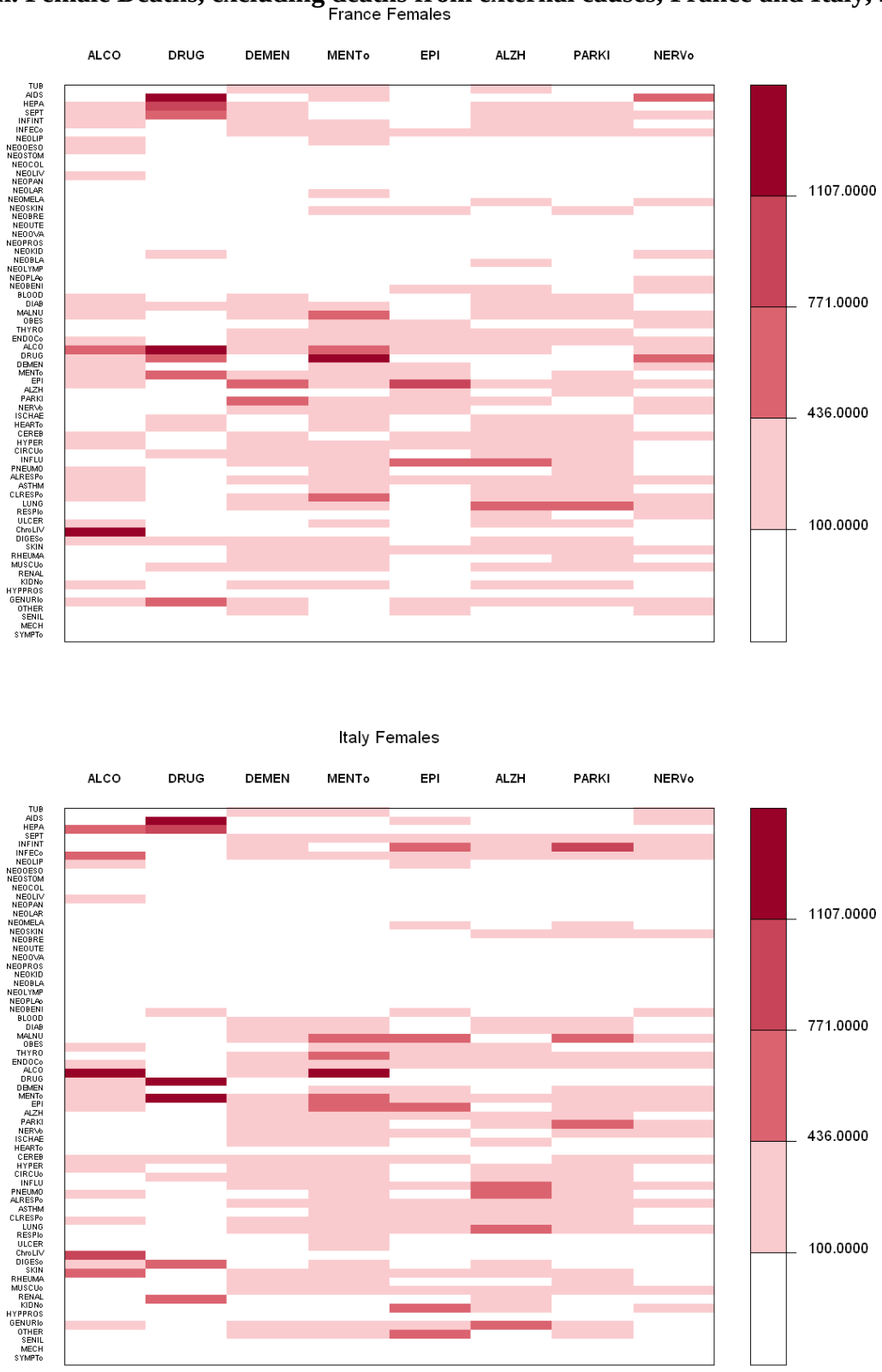
Horizontal axis: contributory cause. Vertical axis: underlying cause
Data: France: Inserm mortality database / Italy: ISTAT mortality database

Figure A6 – CDAIs – Mental, behavioral and nervous diseases as contributory cause of the death. Deaths at the age of 80 or more, excluding deaths from external causes, France and Italy, 2003.



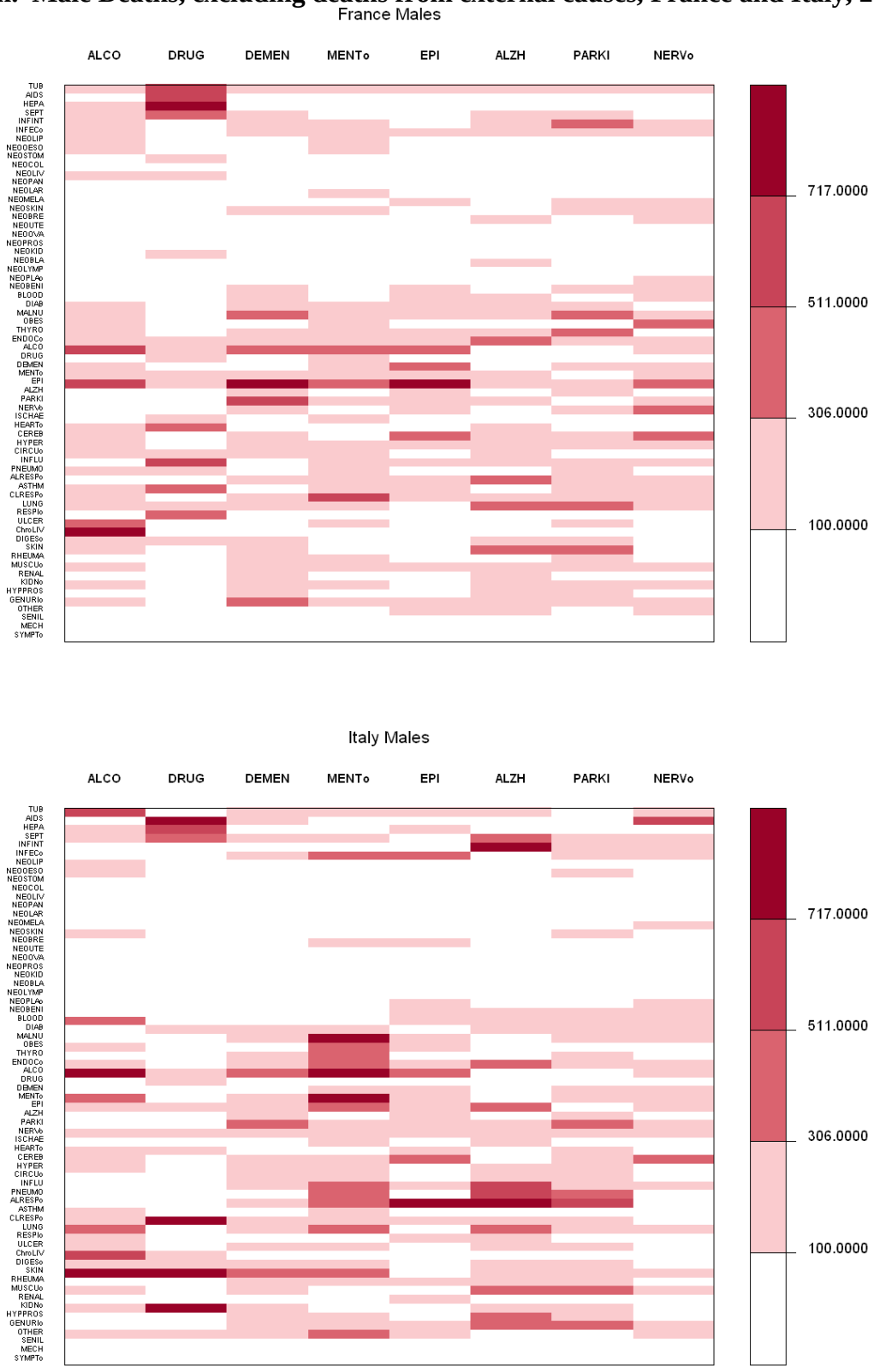
Horizontal axis: contributory cause. Vertical axis: underlying cause
Data: France: Inserm mortality database / Italy: ISTAT mortality database

Figure A7 – CDAIs – Mental, behavioral and nervous diseases as contributory cause of the death. Female Deaths, excluding deaths from external causes, France and Italy, 2003



Horizontal axis : contributory cause. Vertical axis : underlying cause
Data: France: Inserm mortality database / Italy: ISTAT mortality database

Figure A8 – CDAIs – Mental, behavioral and nervous diseases as contributory cause of the death. Male Deaths, excluding deaths from external causes, France and Italy, 2003



Horizontal axis: contributory cause. Vertical axis: underlying cause
Data: France: Inserm mortality database / Italy: ISTAT mortality database