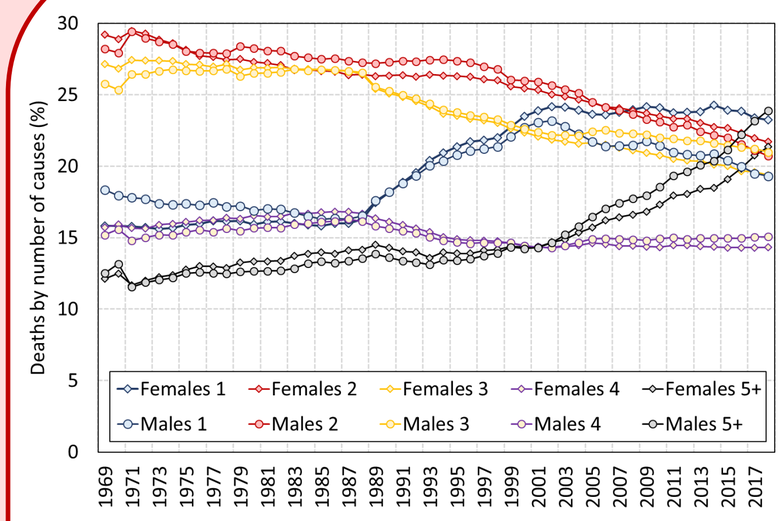
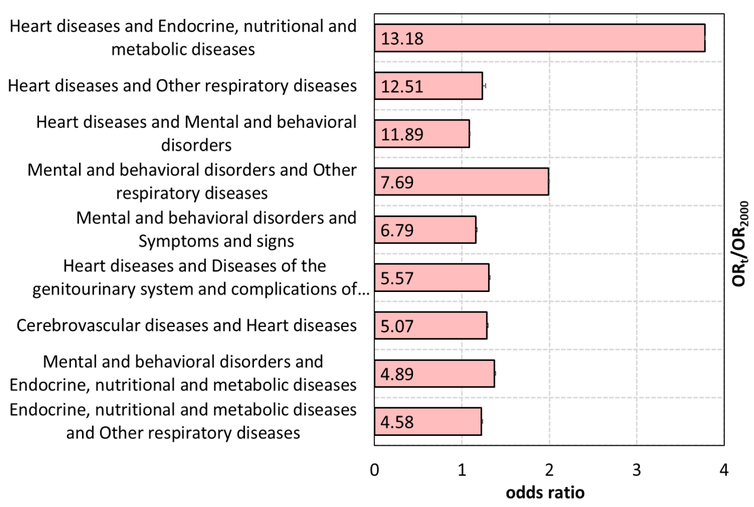
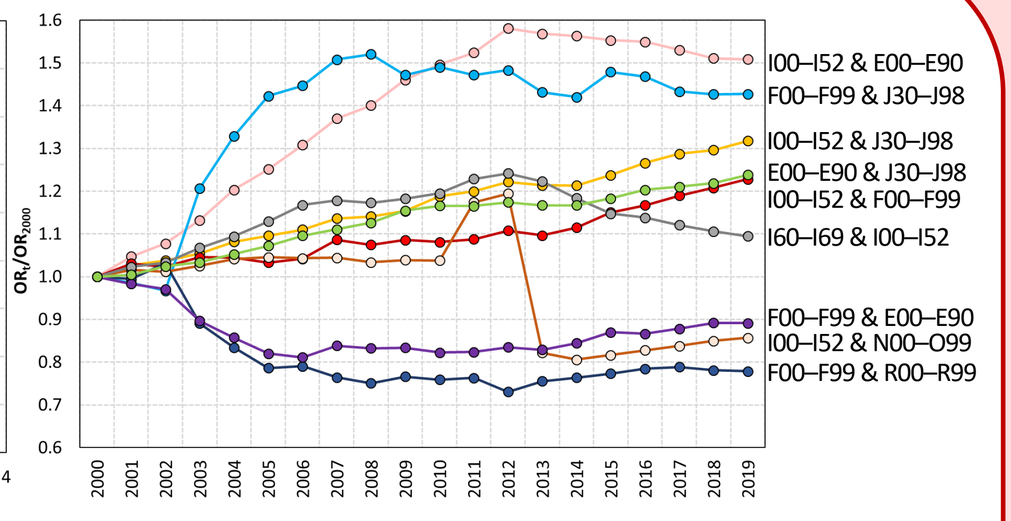


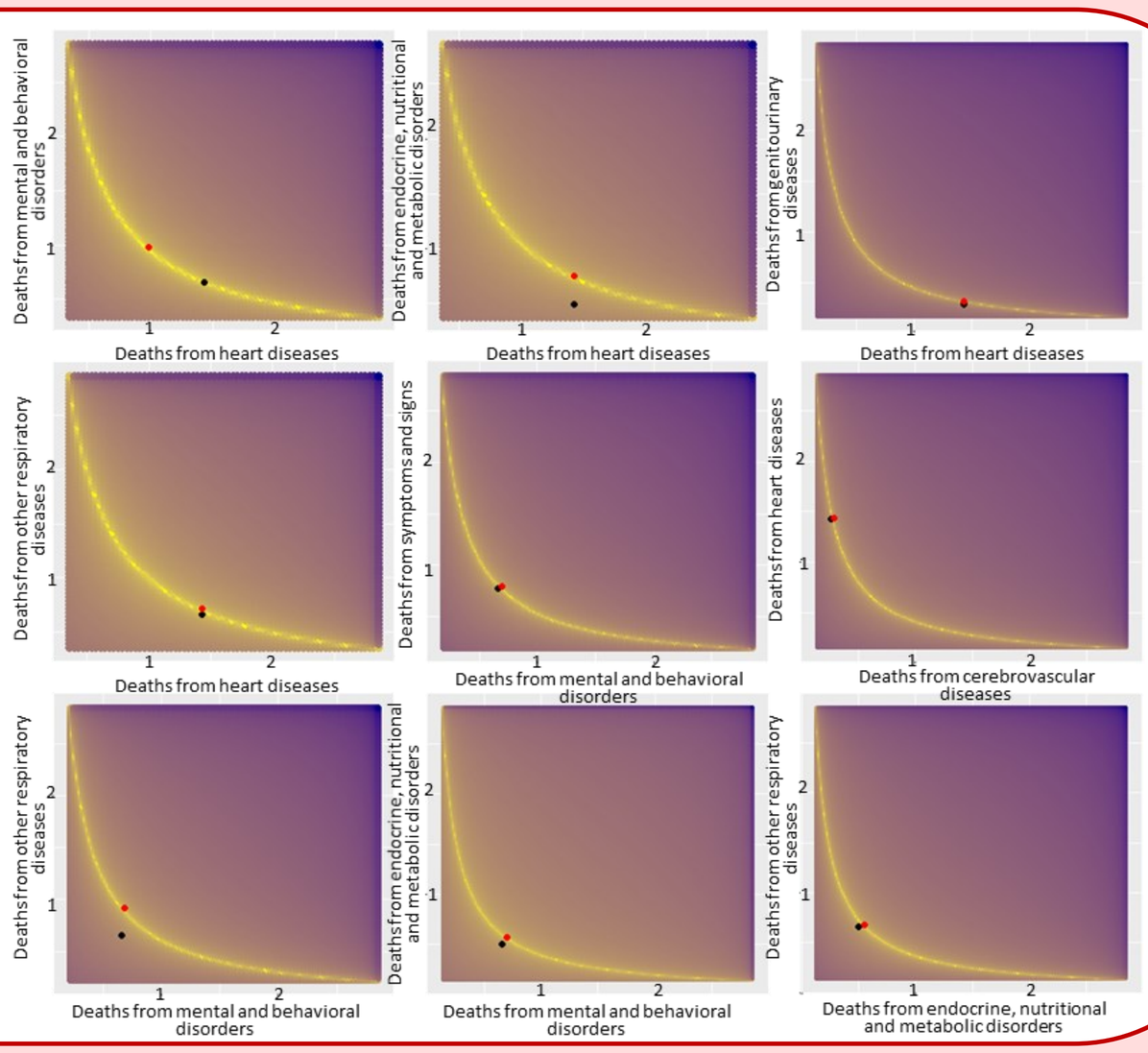




Causes of death seldom operate independently from one another. In the USA, the long-term trends in the distribution of deaths by the number of causes indicate a gradual increase in deaths occurring with five causes or more already since the 1970s. In 2019, one in ten individuals died due to a combination of heart disease with endocrine, nutritional, and metabolic diseases (13%), as well as with other respiratory diseases (13%) and mental and behavioral disorders (12%). Since 2000, the association between these pairs of causes of death has strengthened, mirroring the trend observed in other leading pairs of causes of death. In the context of these trends, the question arises:

What if Causes of Death were Independent?

This contribution aims to assess the impact of distortions in significant associations between causes of death on the overall structure of dependencies among causes of death. We present a curve depicting all possible scenarios of independence between diseases by optimizing the marginal distributions in contingency tables (on the right). Subsequently, we choose the independence that can be achieved with minimal intervention in the contingency table and examine the potential impact of establishing such a relationship between diseases *i* and *j* on the connections between *i* and all other diseases except *j*, as well as between *j* and all other diseases except *i*. As illustrated in Figure on the right, for each pair of leading causes of death, the combinations of marginal distributions that do not exhibit a significant relationship between diseases *i* and *j* tend to cluster around the yellow line. This line follows the characteristic shape of a *1/x*-hyperbola. In the same figure, we observe two dots at each panel: (i) the black one representing the original combination of D_i and D_j resulting in dependance between diseases *i* and *j*, and (ii) the red one indicating the optimal scenario of independence. By optimal, we mean the result achieved by relocating the minimum number of deaths within the contingency table.



What impact do these distortions have on relations with other causes of death? Table below right displays adjusted odds ratios (OR), between diseases in the rows of the table, with the first disease being dissolved in the pair specified in the column headings. Similarly, Table below left presents the same information but in relation to the second disease in the column headings. In both tables, adjusted ORs that significantly differ from the original values are highlighted in pink. Additionally, in brackets, we provide the ratio between the adjusted and original OR. By adjusted OR we mean OR that are calculated under the assumption of independence between leading causes of death.

Neighbouring disease of i

	Cause of death pair (i_j) being dissolved (minimum relocation scenario)								
	Endocrine, nutritional and metabolic diseases and Other respiratory diseases	Mental and behavioral disorders and Other respiratory diseases	Mental and behavioral disorders and Symptoms and signs	Mental and behavioral disorders and Endocrine, nutritional and metabolic diseases	Heart diseases and Other respiratory diseases	Heart diseases and Diseases of the genitourinary system and complications of pregnancy, childbirth and puerperium	Heart diseases and Endocrine, nutritional and metabolic diseases	Heart diseases and Mental and behavioral disorders	Cerebrovascular diseases and Heart diseases
A00–B99	1.15 (0.88)	0.67 (0.96)	0.64 (0.92)	0.64 (0.92)	0.7 (1.00)	0.7 (0.99)	0.7 (1.00)	1.42 (2.03)	0.51 (0.88)
C00–D48	0.50 (0.87)	0.78 (0.95)	0.74 (0.91)	0.74 (0.91)	0.3 (1.00)	0.3 (0.99)	0.3 (1.00)	0.69 (2.30)	0.26 (0.88)
D50–D89	2.08 (0.88)	0.91 (0.96)	0.88 (0.92)	0.88 (0.92)	1.45 (1.00)	1.44 (0.99)	1.45 (1.00)	2.82 (1.95)	0.93 (0.88)
E00–E90	()	1.31 (0.95)	1.25 (0.91)	()	3.8 (1.00)	3.78 (0.99)	()	8.81 (2.32)	1.12 (0.86)
F00–F99	1.18 (0.85)	()	()	()	1.09 (1.00)	1.08 (0.99)	1.09 (1.00)	()	0.90 (0.86)
G00–G44, G47–H95	1.05 (0.87)	0.65 (0.95)	0.63 (0.92)	0.63 (0.92)	0.74 (1.00)	0.74 (0.99)	0.74 (1.00)	1.55 (2.09)	0.96 (0.87)
I00–I52	2.60 (0.68)	1.00 (0.92)	0.93 (0.86)	0.93 (0.86)	()	()	()	()	()
G45, I60–I69	1.15 (0.88)	1.00 (0.95)	0.96 (0.92)	0.96 (0.92)	1.29 (1.00)	1.28 (0.99)	1.29 (1.00)	2.64 (2.05)	()
I70–I99	1.58 (0.88)	1.23 (0.96)	1.19 (0.92)	1.19 (0.92)	2.18 (1.00)	2.17 (0.99)	2.18 (1.00)	4.30 (1.97)	1.31 (0.88)
J00–J22, U04	0.87 (0.88)	0.8 (0.96)	0.78 (0.92)	0.78 (0.92)	0.79 (1.00)	0.79 (0.99)	0.79 (1.00)	1.56 (1.97)	0.62 (0.88)
J30–J98	()	()	1.79 (0.90)	1.79 (0.90)	()	1.23 (0.99)	1.24 (1.00)	2.96 (2.38)	0.68 (0.86)
K00–K93	1.22 (0.88)	0.72 (0.96)	0.70 (0.92)	0.7 (0.92)	0.71 (1.00)	0.71 (0.99)	0.71 (1.00)	1.44 (2.02)	0.42 (0.88)
L00–M99	2.37 (0.88)	1.27 (0.96)	1.22 (0.92)	1.22 (0.92)	1.47 (1.00)	1.47 (0.99)	1.47 (1.00)	2.87 (1.94)	0.91 (0.88)
N00–O99	1.27 (0.88)	0.74 (0.95)	0.72 (0.92)	0.72 (0.92)	1.32 (1.00)	()	1.32 (1.00)	2.72 (2.06)	0.63 (0.88)
P00–Q99, R95	0.36 (0.89)	0.20 (0.96)	0.19 (0.93)	0.19 (0.93)	0.27 (1.00)	0.27 (0.99)	0.27 (1.00)	0.52 (1.91)	0.38 (0.89)
R00–R99	0.82 (0.85)	1.10 (0.94)	()	1.05 (0.90)	0.64 (1.00)	0.64 (0.99)	0.64 (1.00)	1.57 (2.43)	0.66 (0.86)

Neighbouring disease of j

	Cause of death pair (i_j) being dissolved (minimum relocation scenario)								
	Endocrine, nutritional and metabolic diseases and Other respiratory diseases	Mental and behavioral disorders and Other respiratory diseases	Mental and behavioral disorders and Symptoms and signs	Mental and behavioral disorders and Endocrine, nutritional and metabolic diseases	Heart diseases and Other respiratory diseases	Heart diseases and Diseases of the genitourinary system and complications of pregnancy, childbirth and puerperium	Heart diseases and Endocrine, nutritional and metabolic diseases	Heart diseases and Mental and behavioral disorders	Cerebrovascular diseases and Heart diseases
A00–B99	1.78 (0.96)	1.11 (0.96)	1.11 (0.96)	1.08 (0.96)	1.65 (0.96)	4.04 (0.96)	0.73 (0.96)	0.38 (0.96)	0.70 (0.96)
C00–D48	0.69 (0.95)	0.41 (0.56)	0.36 (0.96)	0.47 (0.82)	0.64 (0.88)	0.53 (0.86)	0.31 (0.53)	0.40 (0.49)	0.30 (0.99)
D50–D89	1.50 (0.96)	0.97 (0.62)	1.55 (0.97)	1.98 (0.84)	1.41 (0.90)	2.82 (0.87)	1.36 (0.58)	0.54 (0.56)	1.44 (0.99)
E00–E90	()	0.70 (0.57)	0.92 (0.96)	()	1.08 (0.88)	1.23 (0.85)	()	0.70 (0.51)	3.77 (0.99)
F00–F99	1.89 (0.95)	()	()	()	1.73 (0.86)	0.66 (0.85)	0.70 (0.51)	()	1.08 (0.99)
G00–G44, G47–H95	0.84 (0.96)	0.52 (0.60)	0.92 (0.96)	0.99 (0.82)	0.78 (0.89)	0.76 (0.87)	0.66 (0.55)	0.37 (0.54)	0.74 (0.99)
I00–I52	1.15 (0.92)	0.51 (0.41)	0.61 (0.94)	2.26 (0.59)	()	()	()	()	()
G45, I60–I69	0.76 (0.96)	0.48 (0.61)	0.74 (0.96)	1.08 (0.83)	0.71 (0.89)	0.63 (0.87)	0.73 (0.56)	0.57 (0.54)	()
I70–I99	0.99 (0.96)	0.64 (0.62)	1.07 (0.97)	1.50 (0.84)	0.93 (0.90)	1.54 (0.87)	1.03 (0.58)	0.72 (0.56)	2.17 (0.99)
J00–J22, U04	2.37 (0.96)	1.51 (0.61)	0.96 (0.97)	0.82 (0.84)	2.21 (0.89)	1.86 (0.87)	0.57 (0.58)	0.47 (0.56)	0.79 (0.99)
J30–J98	()	()	0.94 (0.96)	0.98 (0.80)	()	1.29 (0.84)	0.63 (0.51)	0.93 (0.47)	1.23 (0.99)
K00–K93	1.02 (0.96)	0.65 (0.61)	1.14 (0.96)	1.15 (0.83)	0.95 (0.89)	2.03 (0.86)	0.78 (0.56)	0.42 (0.55)	0.71 (0.99)
L00–M99	1.30 (0.96)	0.84 (0.62)	1.54 (0.97)	2.25 (0.84)	1.22 (0.90)	1.88 (0.87)	1.55 (0.58)	0.74 (0.56)	1.47 (0.99)
N00–O99	1.48 (0.96)	0.92 (0.60)	1.09 (0.96)	1.20 (0.83)	1.37 (0.89)	()	0.81 (0.56)	0.42 (0.54)	1.31 (0.99)
P00–Q99, R95	0.49 (0.96)	0.32 (0.63)	0.66 (0.97)	0.35 (0.85)	0.46 (0.90)	0.60 (0.88)	0.24 (0.59)	0.12 (0.57)	0.27 (0.99)
R00–R99	0.93 (0.95)	0.53 (0.54)	()	0.77 (0.80)	0.85 (0.87)	0.95 (0.84)	0.49 (0.50)	0.55 (0.47)	0.64 (0.99)

Data source: Center for Disease Control and Prevention, available online: https://www.cdc.gov/nchs/data_access/vitalstatsonline.htm#Mortality_Multiple

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