Death by SARS-CoV 2 - a Romanian COVID-19 multi-centre comorbidity study

Authors: Anca Pantea Stoian[1,2*]MD,PhD, Mihaela Pricop-Jeckstadt[3,4*]PhD, Adrian Pana[5*], Bogdan-Vasile Ileanu[5], Ruxandra Schitea[6*], Marius Geanta[6] MD,PhD, Doina Catrinoiu[7]MD,PhD, Andra Iulia Suceveanu[7]MD,PhD, Cristian Serafinceanu[1,2]MD,PhD, Silviu Pituru[1]MD,PhD, Catalina Poiana[1]MD,PhD, Bogdan Timar[8]MD,PhD, Cornelia Nitipir[1]MD,PhD, Simona Parvu[1]MD, Andreea Arsene[1]MD,PhD, Laura Mazilu[7]MD,PhD, Antonela Toma[4,9]PhD, Razvan Hainarosie[1,10]MD,PhD, Antonio Ceriello[11*]MD,PhD, Manfredi Rizzo[12,13*]MD,PhD, Viorel Jinga[1]MD,PhD.

[1]University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania, 37 Dionisie Lupu Str., 020021, Bucharest, Romania;

[2]National Institute of Diabetes, Nutrition and Metabolic Diseases "N. C. Paulescu", 5-7. Ion Movila Str,030167, Bucharest, Romania;

[3] Department of Applied Mathematics, University Politehnica of Bucharest, Splaiul Independentei 313, 060042, Bucharest, Romania;

[4]Center for Research and Training in Innovative Techniques of Applied Mathematics in Engineering - ~*Traian Lalescu*~ -(CiTi), University Politehnica of Bucharest, Splaiul Independentei 313, 060042, Bucharest, Romania;

[5]Center for Health Outcomes & Evaluation, Splaiul Unirii 45, 030126, Bucharest, Romania;

[6]Center for Innovation in Medicine, Bd. Theodor Pallady, no. 42J, room 1719, 032266, Bucharest, Romania;

[7]Department of Internal Medicine, Faculty of Medicine, Universitatea Ovidius University C2 Street, 900527, Constanta, Romania;

[8] "Victor Babes" University of Medicine and Pharmacy, 2 Eftimie Murgu, 300041, Timisoara, Romania;

[9]Department of Mathematical Methods and Models, University Politehnica of Bucharest, Splaiul Independentei 313, 060042, Bucharest, Romania;

[10]Prof. Dr D. Hociota" Institute of Phonoaudiology and Functional ENT Surgery, 21st Mihail Cioranu Street, 061344, Bucharest, Romania;

[11]IRCCS MultiMedica, 300 Milanese str, 20099 Sesto San Giovanni MI Milan, Italy;

[12]Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, University of South Carolina, 6311 Garners Ferry Rd, SC 29209 Columbia, SC, USA;

[13]Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, University of Palermo, 61 Piazza Marina str, 90133, Palermo, Italy.

*These authors contributed equally to the present work.

Correspondent author: Mihaela Pricop-Jeckstadt, Department of Applied Mathematics, University Politehnica of Bucharest, Splaiul Independentei 313, 060042, Center for Research and Training in Innovative Techniques of Applied Mathematics in Engineering (CiTi), University Politehnica of Bucharest, Splaiul Independentei 313, 060042, Bucharest, Romania.Email:Mihaela.Pricop@upb.ro Telephone: +04021402-9353

Supplementary Appendix

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1. Supplementary Table S1. Prevalence of distinct diseases and aggregated group of diseases, as counts and as percentage. Frequency of the male and female groups in each subpopulation with distinct diseases or aggregated group of diseases (by row, as counts and as percentage). In bold the p-values for the differences in the relative frequency per disease or per aggregated group of diseases between male and female that reached the statistical significance with respect to the one-sample proportion test.

Characteristics n,%		Total n, %	Male	Female	p-value
Sample size		432 100%	282 65.3%	150 34.7%	0.0001
Diseases					
Hypertension		162 37.50%	113 69.75%	49 30.25%	0.0001
Obesity		53 12.27%	32 60.38%	21 39.62%	0.17
Diabetes	Total	153 35.42%	105 68.63%	48 31.37%	0.0001
	Diabetes mellitus, unspecified	66 15.28%	40 60.61%	26 39.39%	0.11
	Diabetes mellitus type 2	75 17.36%	56 74.67%	19 25.33%	0.0001
	Diabetes mellitus type 1	12 2.78%	9 75%	3 25%	0.15
Diseases of the circulatory system, unspecified		68 15.74%	41 60.29%	27 39.71%	0.11
Supraventricular tachyarrhythmia		25 5.79%	16 64%	9 36%	0.23
Heart failure, unspecified		30 6.94%	14 46.67%	16 53.33%	0.86
Cerebral ischaemic stroke		28 6.48%	16 57.14%	12 42.86%	0.57
Chronic kidney disease		44 10.19%	31 70.45%	13 29.55%	*0.01*
Kidney failure, unspecified		26 6.02%	17 65.38%	9 34.62%	0.17
Dependence on renal dialysis		43 9.95%	29 67.44%	14 32.56%	*0.033*
Chronic obstructive pulmonary disease		25 5.79%	18 72%	7 28%	*0.0462*
Acute ischaemic heart disease, unspecified		19 4.40%	15 78.95%	4 21.05%	*0.022*
Respiratory failure		19 4.40%	15 78.95%	4 21.05%	*0.02*
Aggregated group of diseases					
No comorbidities		13 3.01%	11 84.62%	2 15.38%	0.027
Diseases of the circulatory system		256 59.26%	168 65.62%	88 34.38%	0.0001

Endocrine, nutritional or metabolic diseases	185 42.82%	122 65.95%	63 34.05%	0.0001
Diseases of the genitourinary system	79 18.29%	54 68.35%	25 31.65%	0.002
Diseases of the respiratory system	67 15.51%	47 70.15%	20 29.85%	0.002
Diseases of the nervous system	61 14.12%	35 57.38%	26 42.62%	0.31
Diseases of the digestive system	44 10.19%	30 68.18%	14 31.982%	0.024
Neoplasms	40 9.26%	26 65%	14 35%	0.082
Mental, behavioural or neurodevelopmental disorders	36 8.33%	25 69.44%	11 30.56%	0.03
Factors influencing health status or contact with health services	54 12.50%	37 68.52%	17 31.48%	0.010
Symptoms, signs or clinical findings, not elsewhere classified	24 5.60%	13 54.17%	11 45.83%	0.84
Certain infectious or parasitic diseases	20 4.62%	15 75%	5 25%	0.044

2. Supplementary Table S2.: Study participants and severity of disease (total, male, female). In bold the differences in the relative frequency (by row) between male and female that reached the statistical significance with respect to the one-sample proportion test.

Characteristic	Total	Male	Female	p-value
Age in years mean (sd) median	67 (13.1) 68	66.4 (13) 67	68.1 (13.1) 69.5	
Disease diversity n, %	170 100%	139 82%	107 63%	
Multimorbidity mean (s.d.) median	2.583 (1.58) 2	2.58 (1.61) 2	2.59 (1.52) 2	
Multimorbidity Factor n, %				

With 0 comm	13 3%	11 85%	2 15%	*0.027*
With 1 comm	112 26%	71 63%	41 37%	*0.006*
With 2 comm	104 24%	67 64%	37 36%	*0.005*
With 3 comm	100 23%	65 65%	35 35%	*0.004*
With 4 comm	61 14%	41 67%	20 33%	*0.01*
More than 5 comm	42 10%	27 64%	15 36%	0.09
Aggregated group of diseases				
Multimorbidity mean (s.d.) median	2.109 (1.18) 2	2.14 (1.21) 2	2.05 (1.14) 2	
Multimorbidity factor n, %,				
With 0 comm	13 3%	11 85%	2 15%	*0.027*
With 1 comm	140 32%	88 63%	52 37%	*0.003*
With 2 comm	139 32%	83 60%	56 40%	*0.027*
With 3 comm	88 21%	64 73%	24 27%	0.0001
With 4 comm	38 9%	27 71%	11 29%	*0.015*
More than 5 comm	14 3%	9 64%	5 36%	0.42

CCI mean (s.d.) median	1.324 (0.95) 1	1.35 (0.98) 1	1.27 (0.89) 1	
CCI factor n, %				
mild	394 91.20%	255 65%	139 35%	0.0001
severe	38 8.80%	27 71%	11 29%	*0.015*
Prognosis				
1-year mortality mean (sd) median	0.19 (0.03) 0.15	0.24 (0.03) 0.19	0.10 (0.01) 0.08	
1-year survival probability mean (sd) median	0.81 (0.03) 0.85	0.76 (0.03) 0.81	0.90 (0.01) 0.92	

3. Supplementary Table S3. Association between gender and severity of diseases, as absolute numbers and as percentage (by column). In bold the differences in percentage that reached the statistical significance with respect to the chi-squared test.

Gender, n	Male n=282	Female n=150	
Characteristic			p-value
Diseases			
Multimorbidity Factor n, %,			0.78
With 0 comm	11 3.90%	2 1.33%	0.23
With 1 comm	71 25.18%	41 27.33%	0.71
With 2 comm	67 23.76%	37 25.67%	0.93
With 3 comm	65 23.05%	35 23.33%	1
With 4 comm	41 14.54%	20 13.33%	0.84
More than 5 comm	27 9.57%	15 10%	1
Aggregated group of diseases			
Multimorbidity mean (s.d.) median	2.14 (1.21) 2	2.05 (1.14) 2	
Multimorbidity factor n, %,			0.21
With 0 comm	11	2	0.23

	3.90%	1.33%	
With 1 comm	88 31.21%	52 34.67%	0.53
With 2 comm	83 29.43%	56 37.33%	0.12
With 3 comm	64 22.70%	24 16.00%	0.13
With 4 comm	27 9.57%	11 7.33%	0.55
More than 5 comm	9 3.19%	5 3.33%	1
CCI mean (s.d.) median - IQR	1.35 (0.98) 1 - 1	1.27 (0.89) 1 - 1	
CCI factor n, %			0.55
mild	255 90.43%	139 92.67%	0.55
severe	27 9.57%	11 7.33%	0.55
Prognosis			
1-year mortality mean (sd) median	0.24 (0.03) 0.19	0.10 (0.01) 0.08	
1-year survival probability mean (sd) median	0.76 (0.03) 0.81	0.90 (0.01) 0.92	

4. Supplementary Table S4: Association between the factor age and the severity of disease, as absolute numbers and as percentage (by column). In bold the differences in percentage that reached the statistical significance with respect to the chi-squared test

Age (stratified) n	<50 44	50-59 69	60-69 120	70-79 128	>=80 71	p-value
Characteristic						
Diseases						
Disease diversity n, %	42 24.71%	61 35.88%	100 58.83%	103 60.59%	54 31.76%	
Multimorbidity mean (s.d.) median	2.07 (1.66) 2	2.17 (1.45) 2	2.82 (1.63) 3	2.68 (1.50) 3	2.73 (1.60) 2	
Multimorbidity factor n ,%						*0.003*
With 0 comm	4 9%	4 6%	2 2%	1 1%	2 3%	*0.035*
With 1 comm	17 39%	24 35%	2 2%	27 21%	15 21%	0.058
With 2 comm	11 25%	15 22%	26 22%	32 25%	20 28%	0.86
With 3 comm	3 7%	16 23%	26 22%	43 34%	12 17%	0.003
With 4 comm	6 14%	6 9%	18 15%	16 13%	15 21%	0.30
More than 5 comm	3 7%	4 6%	19 16%	9 7%	7 10%	0.099
Aggregated Comorbidities						
Multimorbidity	1.70 (1.29)	1.77 (1.02)	2.29 (1.29)	2.26 (1.10)	2.11 (1.13)	

mean (s.d.) median	1	2	2	2	2	
Multimorbidity factor n ,%						*0.014*
With 0 comm	4 9%	4 6%	2 2%	1 1%	2 3%	*0.035*
With 1 comm	21 48%	27 39%	37 31%	35 27%	20 28%	0.079
With 2 comm	11 25%	24 35%	35 29%	41 32 %	28 39%	0.48
With 3 comm	2 5%	10 15%	25 21%	38 30%	13 18%	*0.004*
With 4 comm	5 11%	3 4%	15 13%	9 7%	6 8%	0.33
With more than 5 comm	1 2%	1 1%	6 5%	4 3%	2 3%	0.72
CCI						
Charlson comorbidity index (CCI) mean (s.d.) median	0.84 (0.94) 1	1.06 (0.78) 1	1.48 (1.05) 1	1.51 (0.89) 1	1.30 (0.87) 1	
CCI factor n ,%						0.007
Mild comorbidities	42 95.45%	69 100%	103 85.83%	113 88.28%	67 94.37%	0.007
Severe comorbidities	2 4.55%	-	17 14.17%	15 11.72%	4 5.63%	0.007
1-year prognosis						

1-year mortality rate mean	0.05	0.08	0.20	0.22	0.31	
(s.d.)	(0.01)	(0.003)	(0.03)	(0.02)	(0.03)	
median	0.03	0.07	0.16	0.19	0.29	
1-year survival probability	0.95	0.92	0.80	0.78	0.69	
Mean	(0.01)	(0.003)	(0.0275)	(0.02)	(0.03)	
(s.d.)	0.97	0.94	0.84	0.81	0.71	
median						

5. Supplementary Table S5.: Co-occurrence of diseases A and B: phi parameter (all, female, male)

Disease code A	Disease code B	Phi	Phi female	Phi male
1B10	BA00	0.07	NA	0.08
5A10	BA00	0.07	NA	0.10
5A11	5B80	0.03	0.14	NA
5A11	8B11	NA	NA	0.03
5A11	BA00	0.14	0.03	0.17
5A11	BA4Z	0.08	NA	0.12
5A11	BD1Z	0.02	0.14	NA
5A11	BE2Z	0.03	NA	0.06
5A11	CA22	0.02	NA	0.02
5A11	GB61	0.07	0.17	0.03
5A11	GB6Z	NA	NA	0.02
5A11	QB42	0.01	NA	0.04
5A14	5B80	0.06	0.07	0.05
5A14	8E4Z	0.15	NA	NA
5A14	BA00	NA	0.09	NA
5A14	BE2Z	0.11	0.11	0.10
5A14	CB41	0.07	NA	0.13
5A14	GB61	0.03	NA	0.02

5A14	GB6Z	0.06	NA	NA
5B80	5A11	0.03	0.14	NA
5B80	5A14	0.06	0.07	0.05
5B80	BA00	0.06	0.09	0.05
5B80	BD1Z	0.04	NA	NA
5B80	GB61	0.09	0.15	0.06
6B60	8B11	0.41	NA	0.49
8B11	5A11	NA	NA	0.03
8B11	6B60	0.41	NA	0.49
8B11	BA00	0.15	0.16	0.14
8B11	MB53	0.26	NA	NA
8E4Z	5A14	0.15	NA	NA
8E4Z	BA00	0.05	NA	NA
BA00	1B10	0.07	NA	0.08
BA00	5A10	0.07	NA	0.10
BA00	5A11	0.14	0.03	0.17
BA00	5A14	NA	0.09	NA
BA00	5B80	0.06	0.09	0.05
BA00	8B11	0.15	0.16	0.14
BA00	8E4Z	0.05	NA	NA
BA00	BA4Z	0.04	NA	0.03
BA00	BA5Z	0.07	0.18	NA
BA00	BD10	NA	NA	0.08
BA00	BE2Z	0.07	0.19	NA
BA00	CA22	0.08	0.12	0.07
BA00	CA40	NA	NA	0.03
BA00	CB40	0.06	NA	0.04
BA00	DB9Z	0.10	NA	0.13
BA00	GB60	0.05	NA	NA
BA00	GB61	NA	0.09	NA

BA00	GB6Z	0.04	NA	0.07
BA00	QB42	NA	NA	0.03
BA4Z	5A11	0.08	NA	0.12
BA4Z	BA00	0.04	NA	0.03
BA4Z	BC81	0.14	NA	NA
BA4Z	GB61	0.08	NA	0.12
BA5Z	BA00	0.07	0.18	NA
BC81	BA4Z	0.14	NA	NA
BC81	BD10	0.20	NA	NA
BC81	BD1Z	0.13	NA	NA
BD10	BA00	NA	NA	0.08
BD10	BC81	0.20	NA	NA
BD1Z	5A11	0.02	0.14	NA
BD1Z	5B80	0.04	NA	NA
BD1Z	BC81	0.13	NA	NA
BD1Z	CA22	0.14	NA	NA
BE2Z	5A11	0.03	NA	0.06
BE2Z	5A14	0.11	0.11	0.10
BE2Z	BA00	0.07	0.19	NA
BE2Z	CB40	0.23	NA	0.20
BE2Z	GB61	0.05	0.23	NA
CA22	5A11	0.02	NA	0.02
CA22	BA00	0.08	0.12	0.07
CA22	BD1Z	0.14	NA	NA
CA40	BA00	NA	NA	0.03
CA40	CB41	0.45	NA	0.55
CB40	BA00	0.06	NA	0.04
CB40	BE2Z	0.23	NA	0.20
CB41	5A14	0.07	NA	0.13
CB41	CA40	0.45	NA	0.55

DB9Z	BA00	0.10	NA	0.13
GB60	BA00	0.05	NA	NA
GB61	5A11	0.07	0.17	0.03
GB61	5A14	0.03	NA	0.02
GB61	5B80	0.09	0.15	0.06
GB61	BA00	NA	0.09	NA
GB61	BA4Z	0.08	NA	0.12
GB61	BE2Z	0.05	0.23	NA
GB61	QB42	0.30	NA	0.38
GB6Z	5A11	NA	NA	0.02
GB6Z	5A14	0.06	NA	NA
GB6Z	BA00	0.04	NA	0.07
GB6Z	QB42	0.47	0.59	0.40
MB53	8B11	0.26	NA	NA
QB42	5A11	0.01	NA	0.04
QB42	BA00	NA	NA	0.03
QB42	GB61	0.30	NA	0.38
QB42	GB6Z	0.47	0.59	0.40

6. Supplementary Table S6 -part 1. Spatial distribution of diseases as counts and relative frequency (prop)

County	Counts	Prop	BA00	BA00 prop	5B80	5B80 prop	5A14	5A14 prop	5A10	5A10 prop	5A11	5A11 prop	BE2Z	BE2Z prop	BC81	BC8 prop
AB	4	0.01	3	0.02	2	0.04	0	0	1	0.08	1	0.01	0	0	0	0
AG	5	0.01	2	0.01	0	0	0	0	0	0	1	0.01	0	0	1	0.04
AR	44	0.10	20	0.12	8	0.15	2	0.03	0	0	12	0.16	0	0	4	0.16
B	32	0.07	14	0.09	3	0.06	5	0.07	0	0	6	0.08	9	0.14	2	0.08
BC	9	0.02	4	0.03	1	0.02	1	0.02	0	0	2	0.03	0	0	3	0.12
BH	4	0.01	3	0.02	0	0	1	0.02	0	0	1	0.01	1	0.02	1	0.04

BN	10	0.02	7	0.04	0	0	0	0	2	0.17	4	0.05	1	0.02	2	0.08
BT	17	0.04	4	0.03	1	0.02	4	0.06	0	0	7	0.09	6	0.09	0	0
BV	12	0.03	2	0.01	3	0.07	0	0	1	0.08	6	0.08	0	0	0	0
CJ	4	0.01	2	0.01	0	0	3	0.05	0	0	0	0	1	0.02	0	0
CS	2	0.05	1	0.01	1	0.02	0	0	0	0	0	0	1	0.02	0	0
CT	8	0.02	4	0.03	2	0.04	3	0.05	0	0	1	0.01	1	0.02	0	0
CV	4	0.01	0	0	1	0.02	0	0	0	0	0	0	0	0	0	0
DB	4	0.01	1	0.01	0	0	0	0	1	0.08	0	0	0	0	0	0
DJ	1	0.01	0	0	1	0.02	1	0.02	1	0.08	0	0	0	0	0	0
GJ	2	0.05	0	0	1	0.02	0	0	0	0	0	0	0	0	0	0
GL	23	0.05	8	0.05	2	0.04	6	0.09	0	0	2	0.03	2	0.03	2	0.08
GR	3	0.01	1	0.01	0	0	0	0	0	0	1	0.01	0	0	0	0
HN	41	0.09	14	0.09	1	0.02	4	0.06	0	0	1	0.01	2	0.03	3	0.12
IF	8	0.02	2	0.01	2	0.04	5	0.08	0	0	2	0.03	2	0.03	0	0
IL	8	0.02	5	0.03	2	0.04	1	0.015	1	0.08	2	0.03	1	0.02	0	0
IS	7	0.02	4	0.03	0	0	2	0.03	0	0	0	0	0	0	0	0
MH	7	0.02	3	0.02	2	0.04	1	0.02	0	0	2	0.03	1	0.02	0	0
MM	1	0.01	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MS	23	0.05	10	0.06	8	0.15	6	0.09	0	0	3	0.04	9	0.14	0	0
NT	17	0.04	3	0.02	1	0.02	3	0.05	0	0	1	0.01	0	0	0	0
PH	1	0.01	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SB	14	0.03	7	0.04	1	0.02	1	0.02	0	0	0	0	7	0.11	0	0
SJ	3	0.01	2	0.01	0	0	0	0	0	0	1	0.01	0	0	0	0
SM	5	0.01	1	0.01	0	0	1	0.02	1	0.08	0	0	0	0	0	0
SV	67	0.16	18	0.11	4	0.08	7	0.11	1	0.08	8	0.11	12	0.18	5	0.2
TL	3	0.01	1	0.01	1	0.02	1	0.02	0	0	1	0.01	1	0.02	0	0
TM	24	0.06	12	0.07	3	0.06	4	0.06	2	0.17	7	0.09	4	0.06	1	0.04
VL	1	0.01	0	0	1	0.02	0	0	1	0.08	0	0	0	0	0	0
VN	12	0.03	4	0.03	0	0	3	0.05	0	0	3	0.04	5	0.08	1	0.04
VS	2	0.01	0	0	1	0.02	1	0.02	0	0	0	0	0	0	0	0

6. Supplementary Table S6 -part 2. Spatial distribution of diseases as counts and relative frequency

BC81	BC81prop	BD1Z	BD1Zprop	8B11	8B11prop	GB61	GB61prop	QB42	QB42prop	GB6Z	GB6Zprop	CB41	CB41prop	CA22	CA22prop	FC	FCprop
0	0	0	0	0	0	2	0.05	1	0.02	0	0	2	0.11	0	0	0	0
1	0.04	2	0.07	1	0.04	1	0.02	1	0.02	0	0	0	0	1	0.04	0	0
4	0.16	4	0.14	1	0.04	2	0.05	3	0.07	2	0.08	4	0.211	2	0.08	1	0.08
2	0.08	2	0.07	0	0	8	0.186	11	0.26	5	0.19	0	0	1	0.04	0	0
3	0.12	2	0.07	0	0	0	0	0	0	0	0	2	0.105	1	0.04	0	0
1	0.04	0	0	0	0	0	0	0	0	0	0	1	0.05	1	0.04	0	0
2	0.08	0	0	1	0.036	1	0.023	0	0	0	0	1	0.053	2	0.08	0	0
0	0	1	0.03	1	0.036	1	0.023	1	0.023	0	0	0	0	1	0.04	0	0
0	0	2	0.07	0	0	0	0	0	0	0	0	2	0.11	1	0.04	1	0.08
0	0	1	0.03	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0.04	0	0
0	0	0	0	1	0.04	0	0	0	0	1	0.04	1	0.05	0	0	0	0
0	0	2	0.07	0	0	0	0	0	0	0	0	1	0.05	0	0	0	0
0	0	1	0.03	1	0.04	0	0	3	0.07	2	0.08	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0.04	0	0
2	0.08	1	0.03	3	0.11	2	0.05	1	0.02	1	0.04	0	0	1	0.04	0	0
0	0	0	0	0	0	1	0.02	1	0.023	0	0	0	0	0	0	0	0
3	0.12	4	0.14	8	0.29	0	0	0	0	1	0.04	1	0.05	5	0.21	2	0.15
0	0	0	0	1	0.04	4	0.09	1	0.02	1	0.04	0	0	0	0	0	0

0	0	0	0	0	0	1	0.02	1	0.02	2	0.08	0	0	0	0	1	0.08
0	0	1	0.03	0	0	1	0.02	0	0	0	0	1	0.05	1	0.04	0	0
0	0	0	0	0	0	1	0.02	1	0.02	1	0.04	1	0.05	0	0	1	0.08
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	2	0.05	1	0.023	3	0.12	0	0	1	0.04	0	0
0	0	0	0	1	0.04	2	0.05	3	0.07	0	0	1	0.05	0	0	1	0.08
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	3	0.07	1	0.02	1	0.04	0	0	0	0	1	0.08
0	0	0	0	1	0.036	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	1	0.02	1	0.04	0	0	0	0	0	0
5	0.2	3	0.10	7	0.25	7	0.16	7	0.16	1	0.04	0	0	3	0.13	5	0.39
0	0	0	0	0	0	1	0.02	0	0	0	0	0	0	0	0	0	0
1	0.04	1	0.03	1	0.04	2	0.05	2	0.05	2	0.08	1	0.05	1	0.04	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	0.04	1	0.03	0	0	1	0.023	3	0.07	2	0.08	0	0	0	0	0	0
0	0	1	0.03	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend Supplementary Table S6

8B11 Cerebral ischaemic stroke

BA5Z Chronic ischaemic heart disease, unspecified

MB53 Hemiplegia

QB42 Dependence on renal dialysis

BA00 Essential hypertension

GB61 Chronic kidney disease

6B60 Dissociative neurological symptom disorder

GB60 Acute kidney failure

5A10 Diabetes mellitus type 1

CA40 Pneumonia

1B10 Tuberculosis of the respiratory system

CB41 Respiratory failure

5B80 Overweight or localised adiposity

GB6Z Kidney failure, unspecified

BD1Z Heart failure, unspecified

CB40 Certain diseases of the respiratory system

CA22 Chronic obstructive pulmonary disease

BE2Z Diseases of the circulatory system, unspecified

8E4Z Other disorders of the nervous system, unspecified

BA4Z Acute ischaemic heart disease, unspecified

BC81 Supraventricular tachyarrhythmia

5A11 Diabetes mellitus type 2

BD10 Congestive heart failure

DB9Z Diseases of liver, unspecified

5A14 Diabetes mellitus, type unspecified

7. Supplementary Table S7 -part 1. Spatial distribution of aggregated groups of diseases as counts and relative frequency (prop)

County	Counts	Prop	11	11 prop	5	5 prop	24	24 prop	16	16 prop	2	2 prop	12	12 prop	21	21 prop	1	1 prop
AB	4	0.01	4	0.02	3	0.02	1	0.02	2	0.03	0	0	2	0.03	0	0	2	0.1
AG	5	0.01	4	0.02	1	0.01	1	0.02	1	0.01	0	0	2	0.03	2	0.08	0	0
AR	44	0.10	26	0.10	19	0.10	3	0.06	5	0.06	4	0.1	10	0.15	4	0.17	2	0.1
B	32	0.07	21	0.08	14	0.08	13	0.241	13	0.165	4	0.1	4	0.06	0	0	2	0.1
BC	9	0.02	6	0.02	4	0.02	0	0	3	0.04	1	0.03	2	0.03	0	0	0	0
BH	4	0.01	3	0.01	2	0.01	0	0	0	0	0	0	2	0.03	1	0.04	0	0
BN	10	0.02	9	0.04	6	0.03	0	0	2	0.03	1	0.03	4	0.06	1	0.04	0	0
BT	17	0.04	8	0.03	12	0.07	1	0.02	2	0.03	3	0.08	2	0.03	1	0.04	0	0
BV	12	0.03	7	0.03	8	0.04	0	0	0	0	1	0.03	2	0.03	1	0.04	1	0.05
CJ	4	0.01	4	0.02	3	0.02	0	0	1	0.01	1	0.03	1	0.02	0	0	1	0.05
CS	2	0.01	2	0.01	1	0.01	1	0.02	0	0	0	0	1	0.02	0	0	1	0.05
CT	8	0.02	4	0.02	6	0.03	1	0.02	1	0.01	0	0	2	0.03	1	0.04	1	0.05
CV	4	0.01	2	0.01	1	0.01	1	0.02	0	0	0	0	1	0.02	1	0.04	0	0
DB	4	0.01	2	0.01	1	0.01	3	0.06	2	0.03	0	0	0	0	0	0	2	0.1
DJ	1	0.01	0	0	1	0.01	0	0	0	0	0	0	0	0	0	0	0	0
GJ	2	0.01	1	0.01	1	0.01	0	0	0	0	0	0	1	0.02	1	0.04	0	0
GL	23	0.05	13	0.	10	0.05	1	0.02	3	0.04	0	0	1	0.02	1	0.04	1	0.05
GR	3	0.01	2	0.01	1	0.01	1	0.02	1	0.01	0	0	0	0	0	0	0	0
HN	41	0.09	22	0.09	6	0.03	1	0.02	2	0.03	12	0.3	6	0.09	4	0.17	0	0
IF	8	0.02	4	0.02	7	0.05	1	0.02	5	0.06	1	0.03	0	0	0	0	0	0
IL	8	0.02	5	0.02	6	0.03	1	0.02	4	0.05	0	0	0	0	0	0	1	0.05
IS	7	0.02	4	0.02	2	0.01	0	0	1	0.01	1	0.03	1	0.02	0	0	1	0.05
MH	7	0.02	3	0.01	4	0.02	1	0.02	3	0.04	0	0	2	0.03	0	0	2	0.1
MM	1	0.01	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MS	23	0.05	14	0.06	14	0.08	1	0.02	5	0.06	0	0	2	0.03	0	0	0	0

NT	17	0.04	5	0.02	4	0.02	3	0.06	2	0.03	4	0.1	1	0.02	1	0.04	0	0
PH	1	0.01	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SB	14	0.03	11	0.04	2	0.01	2	0.04	4	0.05	1	0.03	1	0.02	0	0	1	0.05
SJ	3	0.01	2	0.01	1	0.01	0	0	0	0	0	0	2	0.03	0	0	0	0
SM	5	0.01	2	0.01	2	0.01	1	0.02	1	0.01	1	0.03	0	0	1	0.04	0	0
SV	67	0.16	36	0.14	19	0.10	10	0.19	8	0.101	3	0.075	8	0.12	4	0.17	1	0.05
TL	3	0.01	2	0.01	2	0.01	0	0	1	0.01	0	0	0	0	0	0	0	0
TM	24	0.06	18	0.07	14	0.08	2	0.04	4	0.05	2	0.05	4	0.06	0	0	1	0.05
VL	1	0.01	0	0	1	0.01	0	0	0	0	0	0	0	0	0	0	0	0
VN	12	0.03	9	0.04	6	0.03	3	0.06	3	0.04	0	0	3	0.05	0	0	0	0
VS	2	0.01	1	0.01	1	0.01	1	0.02	0	0	0	0	0	0	0	0	0	0

7. Supplementary Table S7 -part 2. Spatial distribution of aggregated groups of diseases as counts and relative frequency (prop)

County	6	6 prop	8	8 prop	13	13 prop	0	0 prop
AB	0	0	0	0	0	0	0	0
AG	1	0.03	1	0.02	2	0.05	0	0
AR	1	0.03	4	0.07	3	0.07	1	0.08
B	2	0.06	4	0.07	1	0.02	0	0
BC	1	0.03	0	0	1	0.02	0	0
BH	0	0	1	0.02	0	0	0	0
BN	1	0.03	1	0.02	0	0	0	0
BT	0	0	2	0.03	0	0	0	0
BV	2	0.06	2	0.03	4	0.09	1	0.08
CJ	1	0.03	1	0.02	2	0.05	0	0
CS	1	0.03	0	0	0	0	0	0
CT	0	0	1	0.02	1	0.02	0	0
CV	0	0	0	0	0	0	0	0

DB	0	0	1	0.02	1	0.02	0	0
DJ	0	0	0	0	0	0	0	0
GJ	0	0	0	0	0	0	0	0
GL	7	0.19	8	0.13	2	0.05	0	0
GR	0	0	0	0	1	0.02	0	0
HN	6	0.17	9	0.15	3	0.07	2	0.15
IF	0	0	3	0.05	1	0.02	0	0
IL	0	0	0	0	0	0	1	0.08
IS	1	0.03	0	0	2	0.05	0	0
MH	0	0	1	0.02	2	0.05	1	0.08
MM	0	0	1	0.02	0	0	0	0
MS	1	0.03	1	0.02	4	0.09	0	0
NT	0	0	2	0.03	4	0.09	1	0.08
PH	0	0	0	0	1	0.02	0	0
SB	0	0	3	0.05	2	0.05	1	0.08
SJ	1	0.03	1	0.02	0	0	0	0
SM	1	0.03	0	0	0	0	0	0
SV	7	0.19	11	0.18	3	0.07	5	0.39
TL	0	0	0	0	0	0	0	0
TM	1	0.03	2	0.03	2	0.05	0	0
VL	0	0	0	0	0	0	0	0
VN	1	0.03	1	0.02	2	0.05	0	0
VS	0	0	0	0	0	0	0	0

Legend Supplementary Table S7

0	No comorbidities
11	Diseases of the circulatory system
5	Endocrine, nutritional or metabolic diseases
16	Diseases of the genitourinary system
12	Diseases of the respiratory system
8	Diseases of the nervous system
13	Diseases of the digestive system
2	Neoplasms
6	Mental, behavioural or neurodevelopmental disorders
24	Factors influencing health status or contact with health services
21	Symptoms, signs or clinical findings, not elsewhere classified
1	Certain infectious or parasitic disease

8. Section 8: Death risk and survival probability

Starting from the 1-year crude death risk for the general Romanian population in 2020 calculated by the United Nations [1], we estimated the Romanian gender-specific baseline crude death rates as 89 (female) respectively 177 (male) per 1000 people by considering the gender ratio of the death rates from the World Bank statistics for 2017 [2]. Hence, we overestimated the death rate for the group under 50 and at the baseline (50), and we retrospectively computed the point prediction of the individual death risk for each patient from our study. The 1-year survival probability is one minus the death rate. The empirical mean, median and standard deviation of both risks were computed starting from a beta model for the distribution of probabilities. [3,4] The forecast quality and accuracy of extrapolation for a Romanian study need to be further investigated.[3]

References

1. Macrotrends (https://www.macrotrends.net/countries/ROU/).
2. Trading Economics (https://tradingeconomics.com/romania/death-rate-crude-per-1-000-people-wb-data.html).
3. Henderson, R., Keiding, N. Individual survival time prediction using statistical models. *Journal of medical ethics* 31,703-6 (2006).
4. Ferrari, S., Cribari-Neto, F. Beta Regression for Modelling Rates and Proportions. *Journal of Applied Statistics* 31(7), 799-815 (2004).