

## **SUPPLEMENTAL MATERIAL**

### **Best definitions to identify multimorbid patients with high healthcare resource utilization**

### **Methods: choice of the definitions of multimorbidity.**

We assessed eight different definitions of multimorbidity: A)  $\geq 2$  distinct body system categories *and* number of health conditions; B)  $\geq 2$  distinct body system categories *and* number of chronic health conditions; C) number of distinct body system categories; D) number of CCS categories; E) number of health conditions; F) number of chronic health conditions; G) Deyo-Charlson Comorbidity Index; H) Elixhauser-Van-Walraven Comorbidity Index. Definitions A) to F) were predefined by the first and last authors, based on the different measures available using ICD codes. Moreover, we combined different measures hypothesizing that it may increase the accuracy of the definition. For this purpose, we set the cut-off at  $\geq 2$  body system categories because it is the most likely to correspond to usual definitions of multimorbidity. Initially, the number of comorbidities of the Deyo-Charlson Comorbidity Index was used in addition to definitions A) to F), because of the ease-of-use. Definition H) was added as a posthoc analysis, because unlike the Deyo-Charlson Comorbidity Index, the Elixhauser-Van-Walraven Comorbidity Index has been associated with healthcare resource utilization. The number of comorbidities of the Deyo-Charlson Comorbidity Index was then changed for the score of the Deyo-Charlson Comorbidity Index for consistency.

**Supplemental Table 1.** Performance of the different definitions of multimorbidity for the primary outcome – 30-day readmission and/or prolonged length of stay<sup>b</sup> – in the derivation (A) and validation (B) cohorts.

A)

Definition of multimorbidity	AUC (95%CI)	Cut-off favoring sensitivity <sup>c</sup>	Cut-off favoring specificity <sup>c</sup>	Se	Sp	PPV	NPV	-LR	+LR
≥2 body system categories and number of health conditions	0.65 (0.64;0.65) <sup>d</sup>	≥3		0.91	0.18	0.33	0.82	0.50	1.11
			≥9	0.61	0.61	0.40	0.78	0.65	1.54
≥2 body system categories and number of chronic health conditions	0.61 (0.61;0.61) <sup>e</sup>	≥1		0.91	0.17	0.33	0.81	0.52	1.10
			≥6	0.47	0.68	0.39	0.74	0.78	1.47
Number of distinct body system categories	0.65 (0.65;0.66) <sup>f</sup>	≥2		0.92	0.15	0.32	0.81	0.53	1.08
			≥5	0.60	0.63	0.42	0.78	0.63	1.62
Number of CCS categories	0.65 (0.65;0.66) <sup>f</sup>	≥2		0.94	0.11	0.32	0.81	0.53	1.06
			≥7	0.60	0.62	0.41	0.78	0.64	1.59
Number of health conditions	0.65 (0.65;0.65) <sup>g</sup>	≥3		0.94	0.15	0.33	0.84	0.43	1.10
			≥9	0.61	0.61	0.40	0.78	0.65	1.54
Number of chronic health conditions	0.61 (0.60;0.61) <sup>h</sup>	≥1		0.96	0.08	0.32	0.81	0.53	1.04
			≥6	0.47	0.68	0.93	0.74	0.72	1.47
Deyo-Charlson Comorbidity Index	0.62 (0.61;0.62) <sup>eh</sup>	NA <sup>n</sup>		NA	NA	NA	NA	NA	NA
			≥3	0.41	0.75	0.41	0.74	0.79	1.61
Elixhauser-Van-Walraven Comorbidity Index	0.62 (0.61;0.62) <sup>eh</sup>	0		0.94	0.08	0.31	0.73	0.83	1.01
			≥6	0.59	0.60	0.39	0.77	0.69	1.46

B)

Definition of multimorbidity	AUC (95%CI)	Cut-off favoring sensitivity <sup>c</sup>	Cut-off favoring specificity <sup>c</sup>	Se	Sp	PPV	NPV	-LR	+LR
≥2 body system categories and number of health conditions	0.71 (0.71;0.71) <sup>i</sup>	≥3		0.98	0.09	0.35	0.90	0.24	1.08
			≥9	0.79	0.50	0.43	0.82	0.43	1.56
≥2 body system categories and number of chronic health conditions	0.64 (0.63;0.64) <sup>j</sup>	≥1		0.98	0.08	0.34	0.88	0.28	1.07
			≥6	0.59	0.61	0.43	0.75	0.68	1.51
Number of distinct body system categories	0.71 (0.70;0.71) <sup>k</sup>	≥2		0.98	0.07	0.34	0.89	0.26	1.05
			≥5	0.77	0.51	0.44	0.82	0.42	1.57
Number of CCS categories	0.71 (0.70;0.71) <sup>i</sup>	≥2		0.99	0.05	0.34	0.90	0.23	1.04
			≥7	0.75	0.53	0.44	0.81	0.47	1.60
Number of health conditions	0.71 (0.70;0.71) <sup>i</sup>	≥3		0.99	0.07	0.34	0.91	0.21	1.06
			≥9	0.79	0.50	0.43	0.82	0.43	1.56
Number of chronic health conditions	0.64 (0.63;0.64) <sup>l</sup>	≥1		0.99	0.04	0.34	0.89	0.25	1.03
			≥6	0.59	0.61	0.43	0.75	0.68	1.51
Deyo-Charlson Comorbidity Index	0.64 (0.64;0.65) <sup>ilm</sup>	NA <sup>n</sup>		NA	NA	NA	NA	NA	NA
			≥3	0.43	0.74	0.45	0.73	0.76	1.68
Elixhauser-Van-Walraven Comorbidity Index	0.65 (0.64;0.65) <sup>m</sup>	0		0.94	0.09	0.34	0.77	0.61	1.04
			≥6	0.65	0.59	0.44	0.77	0.60	1.57

<sup>a</sup> Abbreviations: AUC = area under the receiver operating characteristic curve; CCS = Clinical Classification Software; CI = confidence interval; LR, likelihood ratio; NPV = negative predictive value; PPV = positive predictive value; Se = sensitivity; Sp = specificity.

<sup>b</sup> A prolonged length of stay was defined as a length of stay  $\geq$  country-specific upper quartile (75%).

<sup>c</sup> The cut-off values relate to the number of items in the respective definitions of multimorbidity. We defined the lower cut-off as having a sensitivity of  $\geq 90\%$ . If several cut-offs met this criterion, we chose the cut-off with the best specificity. We defined the upper cut-off as having a specificity of  $\geq 60\%$ . If several cut-offs met this criterion, we chose the cut-off with the best sensitivity.

<sup>d-m</sup> The AUCs with different letters were statistically significantly different ( $p < 0.05$ ), according to Delong test, conducted separately in the derivation and in the validation datasets. P-values adjusted for multiple comparisons using Bonferroni correction.

<sup>n</sup> There was no cut-off with  $\geq 90\%$  sensitivity for the Deyo-Charlson Comorbidity Index, except for a score of zero, which would have resulted in one group of patients only.

**Supplemental Table 2.** Performance of the different definitions of multimorbidity for 30-day readmission in the derivation (A) and validation (B) cohorts.

A)

Definition of multimorbidity	AUC (95%CI)	Cut-off favoring sensitivity <sup>b</sup>	Cut-off favoring specificity <sup>b</sup>	Se	Sp	PPV	NPV	-LR	+LR
≥2 body system categories and number of health conditions	0.58 (0.57;0.58)	≥3		0.88	0.16	0.12	0.91	0.75	1.05
			≥9	0.55	0.56	0.14	0.91	0.80	1.25
≥2 body system categories and number of chronic health conditions	0.57 (0.57;0.58)	≥1		0.88	0.15	0.12	0.91	0.78	1.04
			≥6	0.46	0.65	0.15	0.90	0.83	1.31
Number of distinct body system categories	0.57 (0.56;0.57)	≥2		0.89	0.13	0.12	0.90	0.82	1.03
			≥5	0.53	0.57	0.14	0.90	0.82	1.23
Number of CCS categories	0.57 (0.56;0.57)	≥2		0.93	0.10	0.12	0.91	0.74	1.03
			≥7	0.53	0.57	0.14	0.90	0.82	1.23
Number of health conditions	0.58 (0.58;0.59)	≥3		0.93	0.13	0.12	0.94	0.52	1.07
			≥9	0.56	0.56	0.14	0.91	0.80	1.25
Number of chronic health conditions	0.58 (0.57;0.58)	≥1		0.96	0.07	0.12	0.93	0.61	1.03
			≥6	0.46	0.65	0.15	0.90	0.83	1.32
Deyo-Charlson Comorbidity Index	0.60 (0.59;0.61)	NA <sup>c</sup>		NA	NA	NA	NA	NA	NA
			≥3	0.42	0.71	0.16	0.90	0.82	1.46
Elixhauser-Van-Walraven Comorbidity Index	0.58 (0.57;0.58)	0		0.94	0.08	0.12	0.90	0.81	1.02
			≥6	0.56	0.56	0.14	0.91	0.79	1.26

B)

Definition of multimorbidity	AUC (95%CI)	Cut-off favoring sensitivity <sup>b</sup>	Cut-off favoring specificity <sup>b</sup>	Se	Sp	PPV	NPV	-LR	+LR
≥2 body system categories and number of health conditions	0.60 (0.60;0.61)	≥3		0.98	0.08	0.16	0.96	0.25	1.06
			≥9	0.73	0.43	0.18	0.90	0.63	1.28
≥2 body system categories and number of chronic health conditions	0.57 (0.57;0.58)	≥1		0.98	0.07	0.16	0.95	0.29	1.06
			≥6	0.54	0.56	0.18	0.87	0.82	1.24
Number of distinct body system categories	0.61 (0.60;0.62)	≥2		0.98	0.06	0.16	0.96	0.26	1.05
			≥5	0.73	0.44	0.19	0.90	0.62	1.30
Number of CCS categories	0.59 (0.58;0.59)	≥2		0.99	0.04	0.15	0.95	0.31	1.03
			≥7	0.68	0.46	0.18	0.89	0.71	1.25
Number of health conditions	0.60 (0.60;0.61)	≥3		0.99	0.06	0.16	0.96	0.24	1.04
			≥9	0.73	0.43	0.18	0.90	0.63	0.28
Number of chronic health conditions	0.57 (0.56;0.58)	≥1		0.99	0.03	0.15	0.94	0.35	1.02
			≥6	0.54	0.56	0.18	0.87	0.82	1.23
Deyo-Charlson Comorbidity Index	0.63 (0.62;0.63)	NA <sup>c</sup>		NA	NA	NA	NA	NA	NA
			≥3	0.43	0.71	0.21	0.88	0.81	1.46
Elixhauser-Van-Walraven Comorbidity Index	0.60 (0.59;0.61)	0		0.94	0.08	0.15	0.89	0.69	1.03
			≥6	0.63	0.53	0.19	0.89	0.69	1.35

<sup>a</sup> Abbreviations: AUC = area under the receiver operating characteristic curve; CCS = Clinical Classification Software; CI = confidence interval; LR, likelihood ratio; NPV = negative predictive value; PPV = positive predictive value; Se = sensitivity; Sp = specificity.

<sup>b</sup> The cut-off values relate to the number of items in the respective definitions of multimorbidity. We defined the lower cut-off as having a sensitivity of  $\geq 90\%$ . If several cut-offs met this criterion, we chose the cut-off with the best specificity. We defined the upper cut-off as having a specificity of  $\geq 60\%$ . If several cut-offs met this criterion, we chose the cut-off with the best sensitivity.

<sup>c</sup> There was no cut-off with  $\geq 90\%$  sensitivity for the Deyo-Charlson Comorbidity Index, except for a score of zero, which would have resulted in one group of patients only.

**Supplemental Table 3.** Performance of the different definitions of multimorbidity for prolonged length of stay<sup>b</sup> in the derivation (A) and validation (B) cohorts.

A)

Definition of multimorbidity	AUC (95%CI)	Cut-off favoring sensitivity <sup>c</sup>	Cut-off favoring specificity <sup>c</sup>	Se	Sp	PPV	NPV	-LR	+LR
≥2 body system categories and number of health conditions	0.66 (0.66;0.67)	≥3		0.92	0.18	0.24	0.89	0.44	1.12
			≥9	0.64	0.59	0.31	0.85	0.61	1.58
≥2 body system categories and number of chronic health conditions	0.61 (0.61;0.62)	≥1		0.92	0.16	0.24	0.88	0.46	1.10
			≥6	0.48	0.67	0.29	0.82	0.78	1.45
Number of distinct body system categories	0.67 (0.67;0.68)	≥2		0.93	0.14	0.24	0.88	0.46	1.09
			≥5	0.65	0.62	0.32	0.86	0.58	1.68
Number of CCS categories	0.67 (0.67;0.68)	≥2		0.95	0.11	0.23	1.87	0.51	1.06
			≥7	0.64	0.61	0.32	0.86	0.58	1.66
Number of health conditions	0.66 (0.66;0.67)	≥3		0.94	0.14	0.24	0.89	0.43	1.09
			≥9	0.64	0.59	0.31	0.85	0.61	1.58
Number of chronic health conditions	0.61 (0.60;0.61)	≥1		0.96	0.07	0.23	0.87	0.54	1.04
			≥6	0.48	0.67	0.29	0.82	0.78	1.44
Deyo-Charlson Comorbidity Index	0.60 (0.60; 0.61)	NA <sup>d</sup>		NA	NA	NA	NA	NA	NA
			≥3	0.41	0.73	0.30	0.81	0.80	1.53
Elixhauser-Van-Walraven Comorbidity Index	0.62 (0.61;0.62)	0		0.94	0.08	0.22	0.81	0.84	1.01
			≥6	0.60	0.59	0.29	0.84	0.68	1.46

B)

Definition of multimorbidity	AUC (95%CI)	Cut-off favoring sensitivity <sup>c</sup>	Cut-off favoring specificity <sup>c</sup>	Se	Sp	PPV	NPV	-LR	+LR
≥2 body system categories and number of health conditions	0.75 (0.74;0.75)	≥3		0.98	0.08	0.23	0.93	0.25	1.07
			≥9	0.84	0.47	0.31	0.91	0.34	1.59
≥2 body system categories and number of chronic health conditions	0.66 (0.65;0.66)	≥1		0.98	0.08	0.23	0.92	0.30	1.06
			≥6	0.63	0.60	0.30	0.85	0.62	1.57
Number of distinct body system categories	0.74 (0.73;0.74)	≥2		0.98	0.06	0.23	0.93	0.28	1.05
			≥5	0.82	0.48	0.31	0.91	0.37	1.59
Number of CCS categories	0.76 (0.75;0.76)	≥2		0.99	0.04	0.22	0.95	0.20	1.04
			≥7	0.82	0.51	0.32	0.91	0.35	1.68
Number of health conditions	0.75 (0.74;0.75)	≥3		0.99	0.06	0.23	0.95	0.21	1.05
			≥9	0.84	0.47	0.31	0.91	0.34	1.59
Number of chronic health conditions	0.66 (0.65;0.66)	≥1		0.99	0.03	0.22	0.94	0.22	1.03
			≥6	0.63	0.60	0.30	0.85	0.62	1.57
Deyo-Charlson Comorbidity Index	0.62 (0.62;0.63)	NA <sup>d</sup>		NA	NA	NA	NA	NA	NA
			≥3	0.44	0.72	0.91	0.82	0.76	1.61
Elixhauser-Van-Walraven Comorbidity Index	0.65 (0.65;0.66)	0		0.95	0.09	0.22	0.86	0.59	1.04
			≥6	0.67	0.56	0.30	0.86	0.59	1.52

<sup>a</sup> Abbreviations: AUC = area under the receiver operating characteristic curve; CCS = Clinical Classification Software; CI = confidence interval; LR, likelihood ratio; NPV = negative predictive value; PPV = positive predictive value; Se = sensitivity; Sp = specificity.

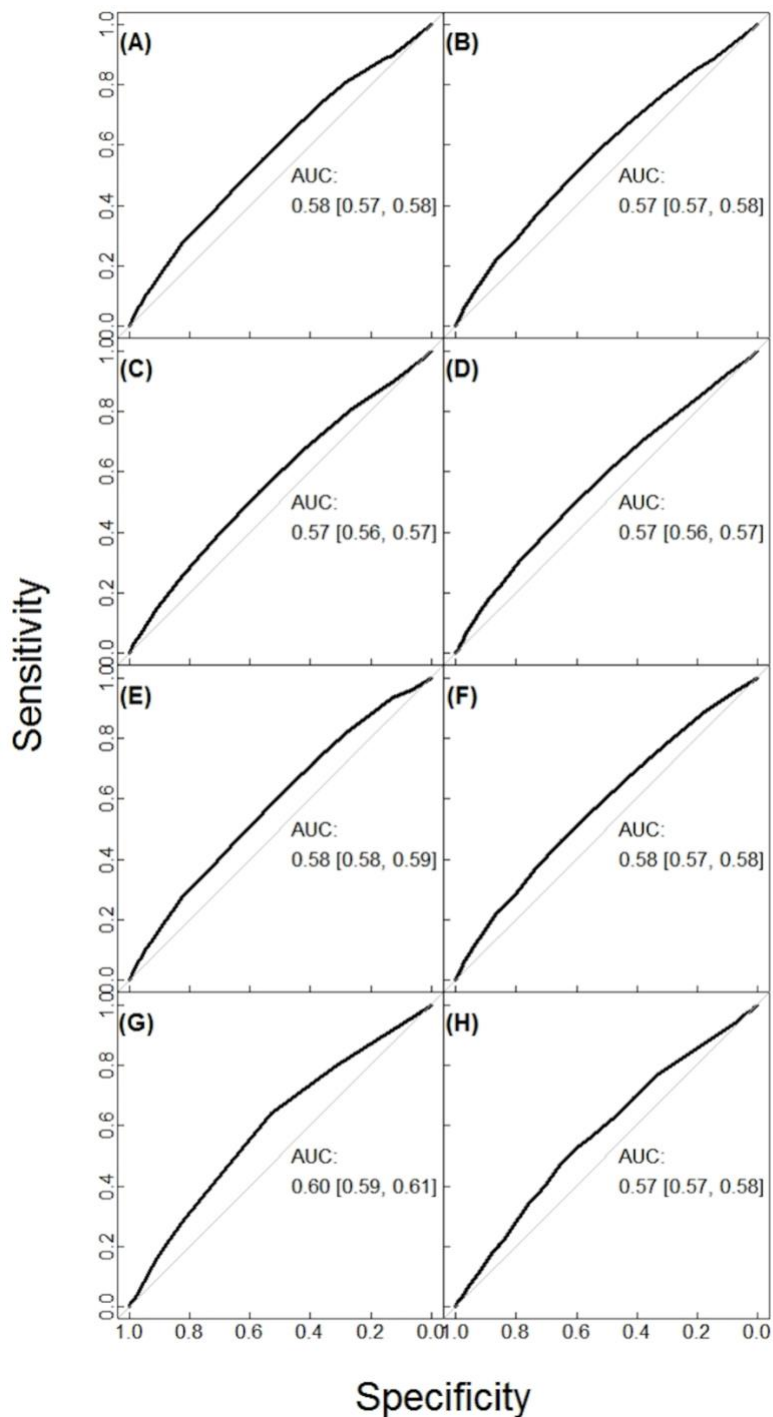
<sup>b</sup> A prolonged length of stay was defined as a length of stay  $\geq$  country-specific upper quartile (75%).

<sup>c</sup> The cut-off values relate to the number of items in the respective definitions of multimorbidity. We defined the lower cut-off as having a sensitivity of  $\geq 90\%$ . If several cut-offs met this criterion, we chose the cut-off with the best specificity. We defined the upper cut-off as having a specificity of  $\geq 60\%$ . If several cut-offs met this criterion, we chose the cut-off with the best sensitivity.

<sup>d</sup> There was no cut-off with  $\geq 90\%$  sensitivity for the Deyo-Charlson Comorbidity Index, except for a score of zero, which would have resulted in one group of patients only.



**Supplemental Figure 1.** AUCs of the different definitions of multimorbidity to predict any 30-day readmission in the derivation cohort.

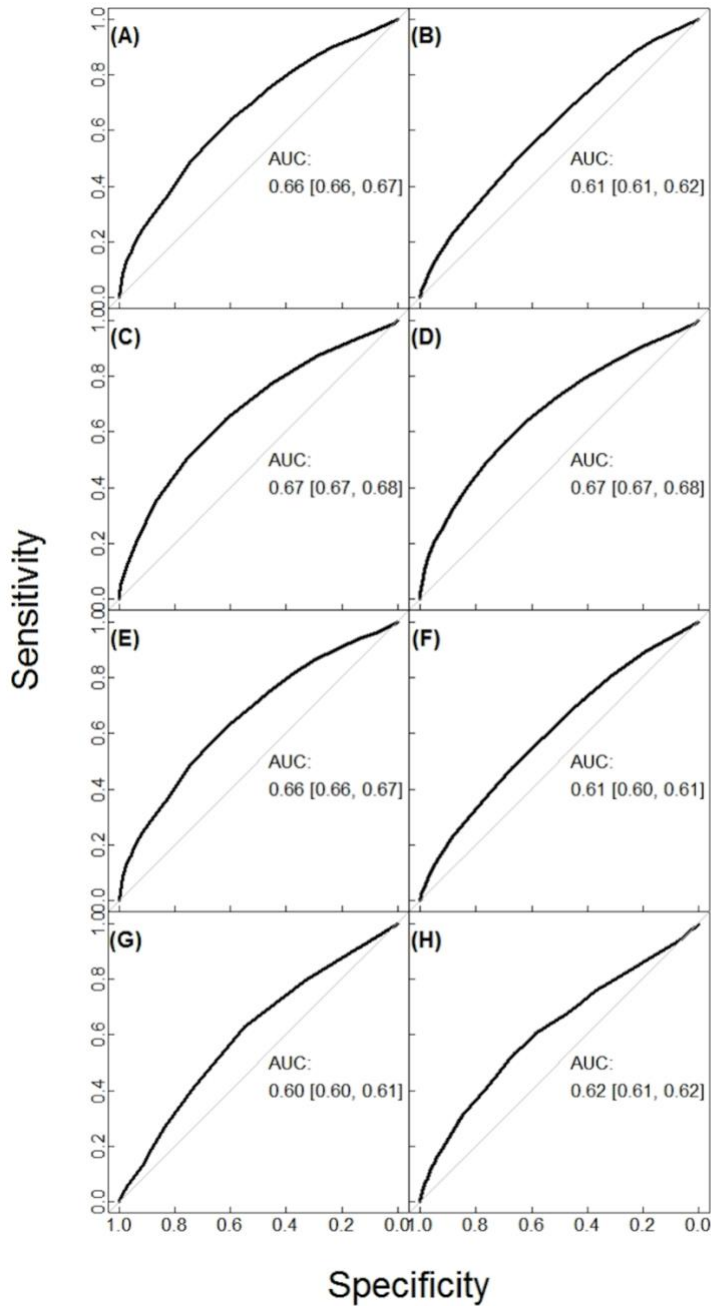


**Legend:** A)  $\geq 2$  distinct body system categories and number of health conditions; B)  $\geq 2$  distinct body system categories and number of chronic health conditions; C) number of distinct body system categories; D) number of CCS categories; E) number of health conditions; F) number of chronic health conditions; G) Deyo-Charlson Comorbidity Index; H) Elixhauser-Van-Walraven Comorbidity Index.

<sup>a</sup> Abbreviations: AUC = area under the receiver operating characteristic curve; CCS = Clinical Classification Software.

Aubert

**Supplemental Figure 2.** AUCs of the different definitions of multimorbidity to predict a prolonged length of stay <sup>a</sup> in the derivation cohort.



**Legend:** A) ≥2 distinct body system categories and number of health conditions; B) ≥2 distinct body system categories and number of chronic health conditions; C) number of distinct body system categories; D) number of CCS categories; E) number of health conditions; F) number of chronic health conditions; G) Deyo-Charlson Comorbidity Index; H) Elixhauser-Van-Walraven Comorbidity Index.

<sup>a</sup> Abbreviations: AUC = area under the receiver operating characteristic curve; CCS = Clinical Classification Software.

<sup>b</sup> A prolonged length of stay was defined as a stay longer than or equal to country-specific upper (75%) quartile.