**Adult respiratory syncytial virus (RSV) infection: defining incidence, risk factors for hospitalization and poor outcomes, a regional cohort study, 2016-2022**

**Supplementary material**

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**Table S1. ICD-9-CM and ICD-10 Coding Algorithms for Elixhauser Comorbidities**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Comorbidities** | **Group** | **Elixhauser's original ICD-9-CM** | **Elixhauser AHRQ- Web****ICD-9-CM** | **ICD-10** | **Enhanced ICD-9-CM** |
| Congestive heart failure | Cardiovascular Diseases | 398.91, 402.11,404.11, 404.13,404.93, 428.x | 402.91,404.91, | 398.91, 402.01,402.91, 404.01,404.11, 404.13,404.93, 428.x | 402.11,404.03,404.91, | I09.9, I11.0, I13.0, I13.2,I25.5, I42.0, 142.5-I42.9, I43.x, I50.x, P29.0 | 398.91, 402.01, 402.11.402.91, 404.01, 404.03,404.11, 404.13, 404.91,404.93, 425.4-425.9, 428.x |
| Cardiac arrhythmias | 426.10, | 426.11, | 426.13, |  | I44.1-I44.3, I45.6, I45.9, | 426.0, 426.13, 426.7, |
|  | 426.2-426.53, 426.6-426.8, | I47.x-I49.x, ROO.O, | 426.9, 426.10, 426.12, |
|  | 427.0, | 427.2, | 427.31, | ROO.1, ROO.8, T82.1, | 427.0-427.4, 427.6-427.9, |
|  | 427.60, | 427.9, | 785.0, | Z45.0, Z95.0 | 785.0, 996.01, 996.04, |
|  | V45.0, V53.3 |  | V45.0, V53.3 |
| Valvular disease | 093.2, 394.0-397.1, 424.0- | 093.2, 394.x-397.1, 397.9, | A52.0, I05.x-I08.x, I09.1, | 093.2, 394.x-397.x, 424.x, |
|  | 424.91, 746.3-746.6, | 424.x, 746.3-746.6, V42.2, | I09.8, I34.x-I39.x, Q23.O- | 746.3-746.6, V42.2, V43.3 |
|  | V42.2, V43.3 | V43.3 | Q23.3, Z95.2, Z95.4 |  |
| Pulmonary circulation | Pulmonary Diseases | 416.x, 417.9 | 416.x, 417.9 | I26.x, I27.x, I28.0, I28.8, | 415.0, 415.1, 416.x, 417.0, |
| Disorders |  |  |  | I28.9 | 417.8, 417.9 |
| Peripheral vascular disorders |  | 440.x, 441.2, 441.4, 441.7,441.9, 443.1- 443.9, 447.1,557.1, 557.9, V43.4 | 440.x, 441.x, 442.x, 443.1-443.9, 447.1, 557.1, 557.9, V43.4 | I70.x, I71.x, I73.1, I73.8,I73.9, I77.1, I79.0, I79.2,K55.1, K55.8, K55.9, | 093.0, 437.3, 440.x, 441.x,443.1-443.9, 447.1, 557.1557.9, V43.4 |
|  |  |  |  | Z95.8, Z95.9 |  |
| Hypertension, uncomplicated | Hypertension | 401.1, 401.9 | 401.1, 401.9, 642.0 | I10.x | 401.x |
| Hypertension, complicated | 402.10, 402.90, 404.10, | 401.0, 402.x-405.x, 642.1, | I11.x-I13.x, I15.x | 402.x-405.x |
|  |  | 404.90, 405.1, 405.9 | 642.2, 642.7, 642.9 |  |  |
| Paralysis |  | 342.0. 342.1, 342.9-344.x | 342.x-344.x, 438.2-438.5 | G04.1, G11.4, G80.1, | 334.1, 342.x, 343.x, 344.0- |
|  |  |  |  | G80.2, G81.x, G82.x, | 344.6, 344.9 |
|  |  |  |  | G83.0-G83.4, G83.9 |  |
| Other neurological disorders |  | 331.9, 332.0, 333.4, 333.5, | 330.x-331.x. 332.0, 333.4, | G10.x-G 13.x, G20.x- | 331.9, 332.0, 332.1, 333.4, |
|  |  | 334.x, 335.x, 340.x, 341.1- | 333.5, 334.x, 335.x, 340, | G22.x, G25.4, G25.5, | 333.5, 333.92, 334.x- |
|  |  | 341.9, 345.0, 345.1, 345.4, | 341.1-341.9, 345.x, 347.x, | G31.2, G31.8, G31.9, | 335.x, 336.2, 340.x, 341.x, |
|  |  | 345.5, 345.8, 345.9, 348.1, | 780.3, 784.3 | G32.x, G35.x-G37.x, | 345.x, 348.1, 348.3, 780.3, |
|  |  | 348.3, 780.3, 784.3 |  | G40.x, G41.x, G93.1, | 784.3 |
|  |  |  |  | G93.4, R47.0, R56.x |  |
| Chronic pulmonary disease |  | 490-492.8, 493.00-493.91, | 490x-492.x, 493.x, 494x- | I27.8, 127.9, J40.x-J47.x, | 416.8, 416.9, 490.x-505.x, |
|  | Pulmonary Diseases | 494.x-505.x, 506.4 | 505.x, 506.4 | J60.x-J67.x, J68.4, J70.1, | 506.4, 508.1, 508.8 |
|  |  |  |  | J70.3 |  |
| Diabetes, uncomplicated |  | 250.0-250.3 | 250.0-250.3, 648.0 | E10.0, E10.1, E10.9, | 250.0-250.3 |
|  | Diabetes |  |  | E11.0, E11.1, E11.9, |  |
|  |  |  | E12.0, E12.1, E12.9, |  |
|  |  |  | E13.0, E13.1, E13.9, |  |
|  |  |  | E14.0, E14.1, E14.9 |  |
| Diabetes, complicated | 250.4-250.7, 250.9 | 250.4-250.9, 775.1 | E10.2-E10.8, | 250.4-250.9 |
|  |  |  | E11.2-E11.8, E12.2- |  |
|  |  |  |  | E12.8, E13.2-E13.8, |  |
|  |  |  |  | E14.2-E14.8 |  |
| Hypothyroidism |  | 243-244.2, 244.8, 244.9 | 243-244.2, 244.8, 244.9 | E00.x-E03.x, E89.0 | 240.9, 243.x, 244.x, 246.1,246.8 |
| Renal failure |  | 403.11, | 403.91, | 404.12, | 403.01, 403.11, | 403.91, | I12.0, I13.1, N18.x, NI9.x, | 403.01, 403.11, 403.91, |
|  |  | 404.92, 585.x, 586.x, | 404.02, 404.03, | 404.12, | N25.0, Z49.0-Z49.2, | 404.02, 404.03, 404.12, |
|  |  | V42.0, | V45.1, | V56.0, | 404.13, 404.92, | 404.93, | Z94.0, Z199.2 | 404.13, 404.92, 404.93, |
|  |  | V56.8 | 585.x, 586.x, | V42.0, |  | 585.x, 586.x, 588.0, V42.0, |
|  |  |  | V45.1, V56.x |  |  | V45.1, V56.x |
| Liver disease |  | 070.32, 070.33, 070.54, | 070.22, 070.23, 070.32, | B18.x, I85.x, I86.4, I98.2, | 070.22, 070.23, 070.32, |
|  |  | 456.0, 456.1, 456.2, 571.0, | 070.33, 070.44, 070.54, | K70.x, K71.1, K71.3- | 070.33, 070.44, 070.54, |
|  |  | 571.2-571.9, 572.3, 572.8, | 456.0, 456.1, 456.20, | K71.5, K71.7, K72.x- | 070.6, 070.9, 456.0-456.2, |
|  |  | V42.7 | 571.0, 571.2-571.9, 572.3, | K74.x, K76.0, K76.2- | 570.x, 571.x, 572.2-572.8, |
|  |  |  | 572.8, V42.7 | K76.9. Z94.4 | 573.3, 573.4, 573.8,573.9, |
|  |  |  |  |  | V42.7 |

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| **Continued** |
| **Comorbidities** | **Group** | **Elixhauser's original****ICD-9-CM** | **Elixhauser AHRQ-Web****ICD-9-CM** | **ICD-10** | **Enhanced ICD-9-CM** |
| Peptic ulcer disease excluding bleeding |  | 531.70, 531.90, 532.70,532.90, 533.70, 533.90,534.70, 534.90, V12.71 | 531.41, 531.51, 531.61,531.7, 531.91, 532.41,532.51, 532.61, 532.7,532.91, 533.41, 533.51,533.61, 533.7, 533.91,534.41, 534.51, 534.61,534.7, 534.91 | K25.7, K25.9, K26.7, K26.9,K27.7, K27.9, K28.7, K28.9 | 531.7, 531.9, 532.7, 532.9,533.7, 533.9, 534.7, 534.9 |
| AIDS/H1V |  | 042.x-044.x | 042.x-044.x | B20.x-B22.x, B24.x | 042.x-044.x |
| Lymphoma |  | 200.x-202.3x, 202.5-203.0,203.8, 238.6, 273.3,V10.71, V10.72, V10.79 | 200.x-202.3, 202.5-203.0,203.8, 238.6, 273.3 | C81.x-C85.x, C88.x, C96.x, C90.0, C90.2 | 200.x-202.x, 203.0, 238.6 |
| Metastatic cancer | Solid Tumor | 196.x-199.x | 196.x-199.x | C77.x-C80.x | 196.x-199.x |
| Solid tumor without metastasis | 140.x-172.x, 174.x, 175.x,179.x-195.x, V10.x | 140.x-172.x, 174.x, 175.x,179.x-195.x | C00.x-C26.x, C30.x-C34.x,C37.x-C41.x, C43.x, C45.x-C58.x,C60.x-C76.x, C97.x | 140.x-172.x,174.x-195.x |
| Rheumatoid arthritis/ collagen vascular diseases |  | 701.0, 710.x, 714.x, 720.x,725.x | 701.0, 710.x, 714.x, 720.x,725.x | L94.0, L94.1, L94.3, M05.x,M06.x, M08.x, M12.0, M12.3, M30.x,M31.0-M31.3,M32.x-M35.x,M45.x, M46.1, M46.8,M46.9 | 446.x, 701.0, 710.0-710.4,710.8, 710.9, 711.2, 714.x,719.3, 720.x, 725.x, 728.5,728.89, 729.30 |
| Coagulopathy |  | 286.x, 287.1, 287.3-287.5 | 286.x, 287.1, 287.3-287.5 | D65-D68.x, D69.1,D69.3-D69.6 | 286.x, 287.1, 287.3-287.5 |
| Obesity |  | 278.0 | 278.0 | E66.x | 278.0 |
| Weight loss |  | 260.x-263.x | 260.x-263.x, 783.2 | E40.x-E46.x, R63.4, R64 | 260.x-263.x, 783.2, 799.4 |
| Fluid and electrolytedisorders |  | 276.x | 276.x | E22.2, E86.x, E87.x | 253.6, 276.x |
| Blood loss anemia |  | 280.0 | 280.0, 648.2 | D50.0 | 280.0 |
| Deficiency anemia |  | 280.1-281.9, 285.9 | 280.1-281.9, 285.2, 285.9 | D50.8, D50.9, D51.x-D53.x | 280.1-280.9, 281.x |
| Alcohol abuse |  | 291.1, 291.2, 291.5-291.9,303.9, 305.0, V113 | 291.0-291.3, 291.5, 291.8,291.9, 303.x, 305.0 | F10, E52, G62.1, I42.6, K29.2, K70.0, K70.3,K70.9, T51.x, Z50.2, Z71.4, Z72.1 | 265.2, 291.1-291.3,291.5-291.9, 303.0,303.9, 305.0, 357.5,425.5, 535.3,571.0-571.3, 980.x,V11.3 |
| Drug abuse |  | 292.0, 292.82-292.89, 292.9,304.0, 305.2, 305.9 | 292.0, 292.82-292.89,292.9, 304.x,305.2-305.9, 648.3 | F11.x-F16.x, F18.x, F19.x, Z71.5. Z72.2 | 292.x, 304.x, 305.2-305.9, V65.42 |
| Psychoses |  | 295.x-298.x, 299.1 | 295.x-298.x, 299.1 | F20.x, F22.x-F25.x, F28.x,F29.x, F30.2, F31.2, F31.5 | 293.8, 295.x, 296.04, 296.14,296.44, 296.54, 297.x,298.x |
| Depression |  | 300.4, 301.12, 309.0, 309.1,311 | 300.4, 301.12, 309.0, 309.1,311 | F20.4, F31.3-F31.5, F32.x,F33.x, F34.1, F41.2, F43.2 | 296.2, 296.3, 296.5, 300.4,309.x, 311 |

**Source:**

Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining Comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care.* 2005 Nov; 43(11): 1130-9.

Table S2: Mean incidence rates for hospitalization of adults with Respiratory syncytial virus (RSV) and influenza (FLU), 2016-2022

|  |  |  |
| --- | --- | --- |
| Age group, years | RSV incidence/100,000 population, median (IQR) | FLU incidence/100,000 population, median (IQR) |
| 20-24 | 2.5 (1.3-2.7) | 40.0 (22-52.8) |
| 25-29 | 2.9 (1.4-2.9) | 36.6 (23.8-49.5) |
| 30-34 | 3.3 (3.1-4.8) | 35.7 (34.7-46.8) |
| 35-44 | 5.3 (1.8-5.7) | 23.3 (22.4-45.5) |
| 45-54 | 12.5 (8.3-13.4) | 62 (33.2-64.7) |
| 55-64 | 19 (14.3-29.7) | 117.2 (74.6-118.7) |
| 65-74 | 63.9 (36.3-78.3) | 217.1 (148.3-236.5) |
| ≥75 | 199 (79.2-202.5) | 411.8 (387-565.4) |

Abbreviations: RSV, respiratory syncytial virus; FLU, influenza; IQR, interquartile range

Table S3: Characteristics of Clalit Health Services' Insured Population in the Southern District and hospitalized patients with respiratory syncytial virus infection and influenza at Soroka University Medical Center, 2017-2021

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | CHS insured population | Hospitalized patients with influenza | Hospitalized patients with RSV |
| N |  | 1,858,742 | 1,462 | 411 |
| Male sex, N (%) |  | 885,058 (47.6%) | 695 (47.5%) | 168 (40.9%) |
| Jewish ethnicity, n (%) |  | 1,365,545 (73.5%) | 1,012 (69.2%) | 311 (75.7%) |
| Season, n (%) | 2017/18 | 353,398 (19%) | 533 (36.5%) | 118 (28.7%) |
|  | 2018/19 | 362,058 (19.5%) | 364 (24.9%) | 111 (27%) |
|  | 2019/20 | 370,644 (19.9%) | 313 (21.4%) | 106 (25.8%) |
|  | 2020/21 | 380,702 (20.5%) | 0 (0%) | 18 (4.4%) |
|  | 2021/22 | 391,940 (21.1%) | 252 (17.2%) | 58 (14.1%) |
| Comorbidity, n (%) | any | 759,091 (40.8%) | 1,224 (83.7%) | 377 (91.7%) |
|  | Cardiovascular disease | 203,094 (10.9%) | 638 (43.6%) | 222 (54%) |
|  | Pulmonary disease | 258,772 (13.9%) | 660 (45.1%) | 227 (55.2%) |
|  | Hypertension | 386,191 (20.8%) | 880 (60.2%) | 309 (75.2%) |
|  | Diabetes mellitus | 164,377 (8.8%) | 510 (34.9%) | 173 (42.1%) |
|  | Renal failure | 80,398 (4.3%) | 350 (23.9%) | 135 (32.8%) |
|  | Liver disease | 142,203 (7.7%) | 232 (15.9%) | 58 (14.1%) |
|  | Lymphoma | 14,928 (0.8%) | 49 (3.4%) | 15 (3.6%) |
|  | Solid tumor | 89,279 (4.8%) | 200 (13.7%) | 62 (15.1%) |
|  | Rheumatological disease | 76,555 (4.1%) | 135 (9.2%) | 45 (10.9%) |

Table S4: Comparative demographic and clinical profile of influenza and respiratory syncytial virus cases, SUMC and AAUH, 2017-2022

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Parameter |  | FLU | RSV | P value |
| N |  | 1821 | 520 |  |
| Age, years, median (IQR) |  | 68.4 (52.3-79.4) | 73.6 (62.6-81.8) | <0.001 |
| Male sex, n (%) |  | 861 (47.3%) | 207 (39.8%) | 0.003 |
| Jewish, n (%) |  | 1226 (67.3%) | 389 (74.8%) | 0.001 |
| Socioeconomic score, n (%) | Very high | 49 (2.7%) | 15 (2.9%) | 0.049 |
|  | High | 224 (12.3%) | 69 (13.3%) |  |
|  | Medium | 410 (22.5%) | 132 (25.4%) |  |
|  | Low | 459 (25.2%) | 151 (29%) |  |
|  | Very low | 367 (20.2%) | 82 (15.8%) |  |
|  | No data  | 312 (17.1%) | 71 (13.7%) |  |
| Comorbidities, n (%) | Any | 1511 (83%) | 475 (91.3%) | <0.001 |
|  | Cariovascular disease | 767 (42.1%) | 284 (54.6%) | <0.001 |
|  | Pulmonary disease | 824 (45.2%) | 284 (54.6%) | <0.001 |
|  | Hypertension | 1086 (59.6%) | 390 (75%) | <0.001 |
|  | Diabetes mellitus  | 629 (34.5%) | 227 (43.7%) | <0.001 |
|  | Chronic renal failure | 423 (23.2%) | 167 (32.1%) | <0.001 |
|  | Liver disease | 296 (16.3%) | 81 (15.6%) | 0.762 |
|  | Lymphoma | 58 (3.2%) | 23 (4.4%) | 0.220 |
|  | Rheumatological disease | 174 (9.6%) | 61 (11.7%) | 0.170 |

Abbreviations: SUMC, Soroka University Medical Center; AAUH, Assuta Ashdod University Hospital

Table S5. Risk Factors Associated with Hospitalization due to Influenza and Respiratory Syncytial Virus, Adjusted for Age

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | RSV |  | Influenza |  |
| Comorbidity | Relative risk (95% CI) | P | Relative risk (95% CI) | P |
| Cardiovascular diseases | 3.3 (2.6-4.2) | <0.001 | 2.7 (2.4-3) | <0.001 |
| Chronic pulmonary diseases | 4.2 (3.4-5.2) | <0.001 | 3.2 (2.9-3.6) | <0.001 |
| Hypertension | 2.9 (2.2-3.8) | <0.001 | 1.8 (1.5-2) | <0.001 |
| Diabetes mellitus | 2.4 (1.9-3) | <0.001 | 2.1 (1.9-2.4) | <0.001 |
| Chronic renal failure | 2.9 (2.3-3.7) | <0.001 | 2.3 (2.-2.6) | <0.001 |
| Lymphoma | 2.2 (1.3-3.6) | 0.004 | 2.2 (1.7-3) | <0.001 |
| Rheumatologic diseases | 1.2 (0.9-1.7) | 0.172 | 1.2 (1-1.4) | 0.082 |
| Solid tumor | 1.1 (0.8-1.4) | 0.628 | 1.2 (1-1.36) | 0.065 |
| Liver disease | 1.1 (0.8-1.4) | 0.681 | 1.3 (1.1-1.5) | <0.001 |

Table S6: Multivariable analysis evaluating risk factors for poor outcomes among hospitalized patients with RSV

|  |  |  |
| --- | --- | --- |
| **Parameter** | **Relative risk (95% CI)** | **P** |
| Age (per year) | 1.01 (0.998-1.02) | 0.115 |
| Cardiovascular diseases | 0.85 (0.56-1.27) | 0.419 |
| Pulmonary diseases | 1.17 (0.79-1.73) | 0.878 |
| Diabetes mellitus | 1.34 (0.95-1.88) | 0.092 |
| **Renal Failure** | **1.81 (1.23-2.66)** | **0.003** |
| **Neutrophil count <1000/μL** | **2.53 (1.19-5.35)** | **0.016** |
| **Neutrophil count >4000/μL** | **1.66 (1.81-2.34)** | **0.004** |
| **Lymphocyte count<500** | **2.03 (1.37-3.0)** | **<0.001** |