### Supplementary Information

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| Name                                                                 | ICD-10 Diagnosis Code | Cases (%) | Code Position |
|----------------------------------------------------------------------|-----------------------|-----------|---------------|
| **IEM Group: Peptide, Amine and Amino Acid Metabolism Disorders**    |                       |           |               |
| Classical phenylketonuria                                           | E700                  | 124 (1.7%)| Any           |
| Other hyperphenylalaninaemias                                       | E701                  | 69 (0.9%) | Any           |
| Disorders of tyrosine metabolism                                     | E702                  | 35 (0.5%) | Any           |
| Albinism                                                             | E703                  | 71 (1.0%) | Any           |
| Other disorders of aromatic amino-acid metabolism                    | E708                  | 14 (0.2%) | Any           |
| Disorder of aromatic amino-acid metabolism, unspecified             | E709                  | 2 (<1%)   | Any           |
| Maple-syrup-urine disease                                            | E710                  | 43 (0.6%) | Any           |
| Other disorders of branched-chain amino-acid metabolism             | E711                  | 185 (2.5%)| Any           |
| Disorder of branched-chain amino-acid metabolism, unspecified       | E712                  | 6 (0.1%)  | Any           |
| Disorders of amino-acid transport                                    | E720                  | 536 (7.3%)| Any           |
| Disorders of sulfur-bearing amino-acid metabolism                   | E721                  | 802 (11.0%)| Any           |
| Disorders of urea cycle metabolism                                   | E722                  | 1449 (19.9%)| Any          |
| Disorders of lysine and hydroxylysine metabolism                    | E723                  | 62 (0.9%) | Any           |
| Disorders of ornithine metabolism                                    | E724                  | 140 (1.9%)| Any           |
| Disorders of glycine metabolism                                      | E725                  | 53 (0.7%) | Any           |
| Other specified disorders of amino-acid metabolism                  | E728                  | 64 (0.9%) | Any           |
| Disorder of amino-acid metabolism, unspecified                       | E729                  | 24 (0.3%) | Any           |
| **IEM Group: Disorders of fatty acid and ketone body metabolism**    |                       |           |               |
| Disorders of fatty-acid metabolism                                   | E713                  | 502 (6.9%)| Any           |
| **IEM Group: Disorders of carbohydrate metabolism**                                      | Code | Count (Percentage) | Ultimate Category |
|--------------------------------------------------------------------------------------|------|-------------------|-------------------|
| Glycogen storage disease                                                             | E740 | 570 (7.8%)        | Any               |
| Disorders of fructose metabolism                                                    | E741 | 686 (9.4%)        | Any               |
| Disorders of galactose metabolism                                                   | E742 | 80 (1.1%)         | Any               |
| Other disorders of intestinal carbohydrate absorption                                | E743 | 829 (11.4%)       | Any               |
| Disorders of pyruvate metabolism and gluconeogenesis                                 | E744 | 90 (1.2%)         | Any               |
| Other specified disorders of carbohydrate metabolism                                | E748 | 619 (8.5%)        | Any               |
| Disorder of carbohydrate metabolism, unspecified                                     | E749 | 60 (0.8%)         | Any               |
| Name of Group                  | ICD-10 Diagnosis Code | Code Position: Comorbidities | Code Position: Cause of Hospitalization¹ |
|-------------------------------|-----------------------|------------------------------|------------------------------------------|
| Infectious & Parasitic       | A00-B99               | Any                          | Primary                                  |
| Intestinal Infectious Disease| A00-A09               | -                            | Primary                                  |
| Bacterial Disease            | A20-A49               | -                            | Primary                                  |
| Viral Infections incl. Hepatitis and HIV | B00-B34 | -                            | Primary                                  |
| Mycoses, Protozoal and others | B35-B89              | -                            | Primary                                  |
| Other Infectious & Parasitic | A15-A19, A50-A69, B90-B99 | -                            | Primary                                  |
| Neoplasms                    | C00-D48               | Any                          | Primary                                  |
| Malignant Neoplasms          | C00-C97               | -                            | Primary                                  |
| In Situ and Benign Neoplasms | D00-D48               | -                            | Primary                                  |
| Blood & Immune System        | D50-D90               | Any                          | Primary                                  |
| Anaemias                     | D50-D64               | -                            | Primary                                  |
| Other Diseases of Blood      | D65-D77               | -                            | Primary                                  |
| Immune System                | D80-D89               | -                            | Primary                                  |
| Endocrine & Metabolic        | E00-E68, E73.1, E73.8, E73.9, E75-E90 | Any                          | Primary                                  |
| Disorders of Thyroid Gland   | E00-E07               | -                            | Primary                                  |
| Diabetes Mellitus            | E10-E14               | -                            | Primary                                  |
| Hypoglycemia                 | E15-E16               | -                            | Primary                                  |
| Other Endocrine Glands       | E20-E35               | -                            | Primary                                  |
| Nutrition Disorders          | E40-E68               | -                            | Primary                                  |
| Metabolic Disorders          | E70-E90               | -                            | Primary                                  |
| Mental & Behavioural         | F00-F99               | Any                          | Primary                                  |
| Nervous System               | G00-G99               | Any                          | Primary                                  |

¹ For the cause of hospitalization the primary discharge ICD-10 Diagnosis code was used, unless IMD was coded, in which case the secondary coded diagnosis was used.
| Name of Group                                      | ICD-10 Diagnosis Code | Code Position: Comorbidities | Code Position: Cause of Hospitalization¹ |
|---------------------------------------------------|-----------------------|------------------------------|------------------------------------------|
| Inflammatory Diseases of the Nervous System        | G00-G09               | -                            | Primary                                  |
| Degenerative and Demyelinating Diseases            | G10-G37               | -                            | Primary                                  |
| Episodic and Paroxysmal Disorders                  | G40-G47               | -                            | Primary                                  |
| Other Nervous System                               | G50-G99               | -                            | Primary                                  |
| Eye & Ear                                         | H00-H95               | Any                          | Primary                                  |
| Circulatory System                                | I00-I99               | Any                          | Primary                                  |
| Heart Disease incl. Hypertensive Disease           | I00-I52               | -                            | Primary                                  |
| Cerebrovascular Disease and Diseases of Arteries    | I60-I79               | -                            | Primary                                  |
| Diseases of Veins and Lymphatic Vessels            | I80-89                | -                            | Primary                                  |
| Respiratory System                                | J00-J99               | Any                          | Primary                                  |
| Respiratory Infections                            | J00-J22               | -                            | Primary                                  |
| Chronic Lower Respiratory Diseases                 | J40-J47               | -                            | Primary                                  |
| Other Respiratory System                          | J30-J39, J60-J99      | -                            | Primary                                  |
| Digestive System                                  | K00-K93               | Any                          | Primary                                  |
| Diseases of Appendix                              | K35-K38               | -                            | Primary                                  |
| Hernia                                            | K40-K46               | -                            | Primary                                  |
| Diseases of Intestines                            | K50-K64               | -                            | Primary                                  |
| Diseases of Liver                                 | K70-K77               | -                            | Primary                                  |
| Disorders of Gallbladder, Biliary Tract and Pancreas| K80-K87               | -                            | Primary                                  |
| Other Digestive System                            | K00-K31, K65-K67, K90-K93 | -                        | Primary                                  |
| Skin & Subcutaneous Tissue                        | L00-L99               | Any                          | Primary                                  |
| Name of Group                      | ICD-10 Diagnosis Code | Code Position: Comorbidities | Code Position: Cause of Hospitalization¹ |
|-----------------------------------|-----------------------|------------------------------|------------------------------------------|
| Musculoskeletal System            | M00-M99               | Any                          | Primary                                  |
| Arthropathies                     | M00-M25               | -                            | Primary                                  |
| Systemic Connective Tissue Disorders | M30-M36             | -                            | Primary                                  |
| Other Musculoskeletal             | M40-M99               | -                            | Primary                                  |
| Genitourinary System              | N00-N99               | Any                          | Primary                                  |
| Urinary Tract Diseases            | N00-N39               | -                            | Primary                                  |
| Disorders of Genital Organs       | N40-N99               | -                            | Primary                                  |
| Injuries                          | S00-T98               | Any                          | Primary                                  |
| Other                             | O00-R99, V01-U99      | -                            | Primary                                  |
Table S2 - Baseline characteristics among hospitalizations with IMD and controls after PSM

|                                | IMD Patients | PSM Control | SDiff, % |
|--------------------------------|--------------|-------------|----------|
| **Number of hospitalizations, n** | 7'293        | 7'293       |          |
| **Number of individual patients, n** | 4'910        | 7'228       |          |
| **Socio-demographics**          |              |             |          |
| Age, mean (SD)                  | 42.5 (27.7)  | 42.5 (27.7) | 0.000    |
| Female gender, n (%)            | 3'684 (50.5) | 3'585 (49.2) | 0.007    |
| Swiss nationality, n (%)        | 5'345 (73.3) | 5'506 (75.5) | -0.051   |
| **Comorbidities, n (%)**        |              |             |          |
| Infectious & Parasitic          | 2'144 (29.4) | 2'069 (28.4) | -0.023   |
| Neoplasms                       | 841 (11.5)   | 796 (10.9)  | -0.020   |
| Endocrine & Metabolic           | 3'833 (52.6) | 3'924 (53.8) | 0.025    |
| Mental & Behavioural            | 1'785 (24.5) | 1'538 (21.1) | -0.081   |
| Nervous System                  | 1'817 (24.9) | 1'802 (24.7) | -0.005   |
| Circulatory System              | 3'149 (43.2) | 3'226 (44.2) | 0.021    |
| Respiratory System              | 1'854 (25.4) | 1'758 (24.1) | -0.031   |
| Digestive System                | 2'588 (35.5) | 2'520 (34.6) | -0.020   |
| Musculoskeletal System          | 1'273 (17.5) | 1'371 (18.8) | 0.035    |
| Genitourinary System            | 2'508 (34.4) | 2'480 (34.0) | -0.008   |
| Injuries                        | 1'416 (19.4) | 1'270 (17.4) | -0.052   |
| Elixhauser comorbidities Index, median (IQR) | 2 (0, 3) | 1 (0, 3) | -0.007 |
| Hospital Frailty Score          |              |             | -0.072   |
| < 5 points                      | 5'305 (72.7) | 5'503 (75.5) |          |
| 5-15 points                     | 1'717 (23.5) | 1'593 (21.8) |          |
| >15 points                      | 271 (3.7)    | 197 (2.7)   |          |

Abbreviations: IMD, Inherited Metabolic Disorder; IQR, Interquartile Range; PSM, Propensity Score Matching; SD, standard deviation; SDiff, standardized difference
| Overall controls (n=462'661) | AD | FD | CD |
|-----------------------------|----|----|----|
| **In-hospital mortality**   |    |    |    |
| events, n (%)               | 1'225 (0.3) | 9 (1.4) | 15 (2.3) | 0 (0) | 2 (0.7) | 4 (0.9) | 6 (1.4) |
| adjusted RR (95% CI)        | Ref. | 8.58 (5.19 to 14.20) | 2.68 (0.67 to 10.67) | 5.21 (2.35 to 11.55) |
| RR (95% CI) after PSM       | Ref. | 2.15 (1.26 to 3.66) | 1.60 (0.42 to 6.12) | 1.38 (0.63 to 3.02) |
| **Length of hospital stay (d)** |    |    |    |
| mean (SD)                   | 4.0 (10.1) | 8.3 (20.1) | 7.7 (14.8) | 5.0 (8.1) | 5.1 (11.0) | 7.4 (15.6) | 8.9 (17.1) |
| adjusted Ref.               | Ref. | 3.65 (2.88 to 4.43) | 1.07 (0.11 to 2.26) | 4.91 (3.96 to 5.87) |
| adjusted after PSM          | Ref. | 1.01 (0.27 to 1.74) | -0.18 (-1.30 to 0.94) | 1.90 (1.00 to 2.80) |
| **ICU admission**           |    |    |    |
| events, n (%)               | 70'963 (15.3) | 155 (23.5) | 149 (22.6) | 56 (19.9) | 37 (13.1) | 113 (26.0) | 138 (31.7) |
| adjusted Ref.               | Ref. | 1.47 (1.28 to 1.70) | 0.86 (0.63 to 1.16) | 2.07 (1.80 to 2.37) |
| adjusted after PSM          | Ref. | 1.00 (0.85 to 1.17) | 0.71 (0.52 to 0.97) | 1.38 (1.17 to 1.62) |
| **Length of ICU stay (d)** |    |    |    |
| events, n (%)               | 17'990 (3.9) | 65 (9.9) | 45 (6.8) | 18 (6.4) | 13 (4.6) | 49 (11.3) | 68 (15.6) |
| adjusted Ref.               | Ref. | 1.75 (1.32 to 2.33) | 1.19 (0.70 to 2.02) | 4.02 (3.23 to 5.00) |
| adjusted after PSM          | Ref. | 0.67 (0.50 to 0.91) | 0.73 (0.43 to 1.25) | 1.67 (1.29 to 2.17) |
| **30-day readmission**      |    |    |    |
| events, n (%)               | 27'392 (5.9) | 69 (10.6) | 124 (19.2) | 15 (5.3) | 31 (11.1) | 32 (7.4) | 74 (17.3) |
| adjusted Ref.               | Ref. | 3.24 (2.76 to 3.80) | 1.87 (1.34 to 2.60) | 2.91 (2.36 to 3.58) |
| adjusted after PSM          | Ref. | 2.37 (2.03 to 2.77) | 1.80 (1.36 to 2.40) | 2.34 (1.92 to 2.84) |
| **1-year readmission**      |    |    |    |
| events, n (%)               | 79'579 (17.3) | 176 (27.0) | 350 (54.3) | 57 (20.2) | 133 (47.5) | 104 (24.1) | 228 (53.2) |
| adjusted Ref.               | Ref. | 3.15 (2.93 to 3.38) | 2.75 (2.43 to 3.12) | 3.08 (2.82 to 3.37) |
| adjusted after PSM          | Ref. | 2.63 (2.42 to 2.85) | 2.52 (2.22 to 2.85) | 2.71 (2.46 to 2.99) |
| **2-year readmission**      |    |    |    |
| events, n (%)               | 94'679 (20.5) | 200 (30.7) | 376 (58.6) | 66 (23.4) | 155 (55.4) | 114 (26.5) | 250 (58.3) |
| adjusted Ref.               | Ref. | 2.86 (2.68 to 3.05) | 2.70 (2.43 to 2.80) | 2.84 (2.62 to 3.08) |
| adjusted after PSM          | Ref. | 2.44 (2.26 to 2.63) | 2.49 (2.24 to 2.78) | 2.58 (2.36 to 2.81) |

**Abbreviations:** AD, disorders of peptide, amine and amino acid metabolism; CD, disorders of carbohydrate metabolism; Cf., Regression Coefficient; CI, confidence interval; FD, disorders of fatty acid and ketone body metabolism mellitus; ICU, Intensive Care Unit; IMD, Inherited Metabolic Disorder; PS, Propensity Score; PSM, Propensity Score Matching; PY, person-years; Ref., Reference; RR, Risk Ratio.
Table S3B - Hospital associated outcomes in IMDs from 10–19-year old’s, by groups of IMDs with overall, adjusted and propensity score matched control

|                         | Overall controls (n=379'511) | AD | FD | CD |
|-------------------------|------------------------------|----|----|----|
|                         | PSM controls (n=343)         | IMD cases (n=343) | PSM controls (n=79) | IMD cases (n=79) | PSM controls (n=285) | IMD cases (n=285) |
| In-hospital mortality   |                              |     |    |    |
| unadjusted RR (95% CI)  |                              |     |    |    |
| adjusted RR (95% CI)    |                              |     |    |    |
| RR (95% CI) after PSM   |                              |     |    |    |
| events, n (%)           | 469 (0.1)                    | 4 (1.2) | 8 (2.3) | 0 (0) | 1 (1.3) | 2 (0.7) | 2 (0.7) |
| mean (SD)               | 3.6 (16.9)                   | 4.7 (8.6) | 6.5 (12.2) | 5.8 (10.6) | 9.0 (17.1) | 7.1 (10.7) | 8.9 (16.3) |
| unadjusted Cf. (95% CI) |                              |     |    |    |
| adjusted Cf. (95% CI)   |                              |     |    |    |
| Cf. (95% CI) after PSM  |                              |     |    |    |
| events, n (%)           | 34'905 (9.2)                 | 60 (17.5) | 82 (23.9) | 15 (19.0) | 12 (15.2) | 63 (22.1) | 68 (23.9) |
| mean (SD)               | 1.2 (4.5)                    | 2.1 (5.6) | 4.5 (13.2) | 2.3 (4.6) | 7.8 (6.8) | 2.9 (5.2) | 4.1 (13.3) |
| unadjusted RR (95% CI)  |                              |     |    |    |
| adjusted RR (95% CI)    |                              |     |    |    |
| RR (95% CI) after PSM   |                              |     |    |    |
| events, n (%)           | 3'836 (1.0)                  | 19 (5.5) | 23 (6.7) | 4 (5.1) | 5 (6.3) | 19 (6.7) | 19 (6.7) |
| mean (SD)               | 4.47 (4.35)                  | 6.47 (9.61) | 6.10 (2.61) | 14.26 | 6.43 (4.16) | 9.94 |
| unadjusted Cf. (95% CI) |                              |     |    |    |
| adjusted Cf. (95% CI)   |                              |     |    |    |
| Cf. (95% CI) after PSM  |                              |     |    |    |
| events, n (%)           | 17'258 (4.6)                 | 26 (7.7) | 68 (20.3) | 4 (5.1) | 5 (6.4) | 24 (8.5) | 30 (10.6) |
| mean (SD)               | 4.46 (3.60)                  | 4.46 (5.51) | 1.41 (0.60) | 3.29 | 2.33 (1.66) | 3.27 |
| unadjusted RR (95% CI)  |                              |     |    |    |
| adjusted RR (95% CI)    |                              |     |    |    |
| RR (95% CI) after PSM   |                              |     |    |    |
| events, n (%)           | 62'417 (16.5)                | 67 (19.8) | 177 (52.8) | 19 (24.1) | 34 (43.6) | 69 (24.4) | 120 (42.4) |
| mean (SD)               | 3.21 (2.90)                  | 3.21 (3.55) | 2.65 (2.06) | 3.41 | 2.58 (2.25) | 2.95 |
| unadjusted RR (95% CI)  |                              |     |    |    |
| adjusted RR (95% CI)    |                              |     |    |    |
| RR (95% CI) after PSM   |                              |     |    |    |
| events, n (%)           | 83'414 (22.0)                | 93 (27.4) | 193 (57.6) | 23 (29.1) | 41 (52.6) | 88 (31.1) | 143 (50.5) |
| mean (SD)               | 2.62 (2.39)                  | 2.62 (2.87) | 2.39 (1.93) | 2.95 | 2.30 (2.05) | 2.58 |
| unadjusted RR (95% CI)  |                              |     |    |    |
| adjusted RR (95% CI)    |                              |     |    |    |
| RR (95% CI) after PSM   |                              |     |    |    |
| Length of hospital stay (d) |                              |     |    |    |
| unadjusted Cf. (95% CI) |                              |     |    |    |
| adjusted Cf. (95% CI)   |                              |     |    |    |
| Cf. (95% CI) after PSM  |                              |     |    |    |
| Length of ICU stay (d)  |                              |     |    |    |
| unadjusted Cf. (95% CI) |                              |     |    |    |
| adjusted Cf. (95% CI)   |                              |     |    |    |
| Cf. (95% CI) after PSM  |                              |     |    |    |
| Mechanical ventilation  |                              |     |    |    |
| unadjusted RR (95% CI)  |                              |     |    |    |
| adjusted RR (95% CI)    |                              |     |    |    |
| RR (95% CI) after PSM   |                              |     |    |    |
| 30-day readmission      |                              |     |    |    |
| unadjusted RR (95% CI)  |                              |     |    |    |
| adjusted RR (95% CI)    |                              |     |    |    |
| RR (95% CI) after PSM   |                              |     |    |    |
| 1-year readmission      |                              |     |    |    |
| unadjusted RR (95% CI)  |                              |     |    |    |
| adjusted RR (95% CI)    |                              |     |    |    |
| RR (95% CI) after PSM   |                              |     |    |    |
| 2-year readmission      |                              |     |    |    |
| unadjusted RR (95% CI)  |                              |     |    |    |
| adjusted RR (95% CI)    |                              |     |    |    |
| RR (95% CI) after PSM   |                              |     |    |    |

**Abbreviations:** AD, disorders of peptide, amine and amino acid metabolism; CD, disorders of carbohydrate metabolism; Cf., Regression Coefficient; CI, confidence interval; FD, disorders of fatty acid and ketone body metabolism mellitus; ICU, Intensive Care Unit; IMD, Inherited Metabolic Disorder; PS, Propensity Score; PSM, Propensity Score Matching; PY, person-years; Ref., Reference; RR, Risk Ratio.
| Table S3C – Hospital associated outcomes in IMDs from 20–39-year old’s, by groups of IMDs with overall, adjusted and propensity score matched control |
|-------------------------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| | Overall controls (n=2'015'176) | AD | FD | CD |
| | | PSM controls (n=574) | IMD cases (n=574) | PSM controls (n=47) | IMD cases (n=47) | PSM controls (n=507) | IMD cases (n=507) |
| In-hospital mortality | | | | | | |
| events, n (%) | 2'649 (0.1) | 5 (0.9) | 10 (1.7) | 0 (0) | 2 (4.3) | 4 (0.8) | 0 (0) |
| unadjusted RR (95% CI) | | | | | | |
| Ref. | 13.25 (7.16 to 24.53) | Ref. | 32.38 (8.34 to 125.71) | N/A | N/A |
| adjusted RR (95% CI) | | | | | | |
| Ref. | 1.84 (0.97 to 3.48) | Ref. | 12.38 (3.33 to 46.07) | N/A | N/A |
| RR (95% CI) after PSM | | | | | | |
| Ref. | 2.00 (0.69 to 5.81) | Ref. | N/A | Ref. | N/A |
| Length of hospital stay (d) | | | | | | |
| mean (SD) | 3.8 (12.2) | 6.5 (10.5) | 9.6 (23.9) | 4.0 (3.1) | 6.4 (8.2) | 6.0 (8.6) | 7.6 (14.8) |
| unadjusted Cf. (95% CI) | | | | | | |
| Ref. | 5.83 (4.04 to 8.63) | Ref. | 2.67 (0.81 to 6.15) | 3.85 (2.79 to 5.41) | 7.85 (4.91 to 12.38) |
| adjusted Cf. (95% CI) | | | | | | |
| Ref. | 4.07 (3.08 to 5.06) | Ref. | 1.62 (1.83 to 5.08) | 2.05 (0.99 to 3.10) | |
| Cf. (95% CI) after PSM | | | | | | |
| Ref. | 3.08 (0.94 to 5.22) | Ref. | 2.40 (0.14 to 4.94) | Ref. | 1.60 (0.11 to 3.09) |
| ICU admission | | | | | | |
| events, n (%) | 138'270 (6.9) | 110 (19.2) | 153 (26.7) | 8 (17.0) | 13 (27.7) | 84 (16.6) | 103 (20.3) |
| unadjusted RR (95% CI) | | | | | | |
| Ref. | 3.88 (3.39 to 4.45) | Ref. | 4.03 (2.54 to 6.40) | 2.96 (2.49 to 3.52) | |
| adjusted RR (95% CI) | | | | | | |
| Ref. | 1.81 (1.52 to 2.16) | Ref. | 2.13 (1.23 to 3.69) | 1.43 (1.17 to 1.75) | |
| RR (95% CI) after PSM | | | | | | |
| Ref. | 1.39 (1.12 to 1.73) | Ref. | 1.63 (0.74 to 3.55) | 1.23 (0.95 to 1.59) | |
| Length of ICU stay (d) | | | | | | |
| mean (SD) | 1.0 (4.3) | 3.0 (5.6) | 8.8 (27.9) | 1.0 (1.2) | 1.7 (2.6) | 2.1 (4.0) | 1.9 (3.8) |
| unadjusted Cf. (95% CI) | | | | | | |
| Ref. | 10.74 (9.40 to 12.08) | Ref. | 0.68 (4.33 to 5.69) | 1.36 (0.50 to 3.21) | |
| adjusted Cf. (95% CI) | | | | | | |
| Ref. | 7.81 (6.56 to 9.06) | Ref. | -2.79 (-7.45 to 1.88) | -0.40 (-2.13 to 1.32) | |
| Cf. (95% CI) after PSM | | | | | | |
| Ref. | 7.86 (-0.55 to 16.26) | Ref. | 1.48 (-1.58 to 4.54) | Ref. | 0.24 (-1.65 to 2.12) |
| Mechanical ventilation | | | | | | |
| events, n (%) | 13'455 (0.7) | 32 (5.6) | 47 (8.2) | 2 (4.3) | 2 (4.3) | 10 (2.0) | 28 (5.5) |
| unadjusted RR (95% CI) | | | | | | |
| Ref. | 12.26 (9.32 to 16.14) | Ref. | 6.37 (1.64 to 24.74) | 8.27 (5.77 to 11.86) | |
| adjusted RR (95% CI) | | | | | | |
| Ref. | 1.73 (1.24 to 2.43) | Ref. | 0.92 (0.22 to 3.90) | 2.07 (1.43 to 2.99) | |
| RR (95% CI) after PSM | | | | | | |
| Ref. | 1.47 (0.95 to 2.27) | Ref. | 1.00 (0.15 to 6.81) | Ref. | 2.80 (1.37 to 5.70) |
| 30-day readmission | | | | | | |
| events, n (%) | 91'076 (4.5) | 48 (8.4) | 68 (12.1) | 1 (2.1) | 5 (11.1) | 38 (7.6) | 46 (9.1) |
| unadjusted RR (95% CI) | | | | | | |
| Ref. | 2.66 (2.13 to 3.33) | Ref. | 2.46 (1.08 to 5.61) | 2.00 (1.52 to 2.64) | |
| adjusted RR (95% CI) | | | | | | |
| Ref. | 1.61 (1.27 to 2.04) | Ref. | 2.13 (0.94 to 4.85) | 1.30 (0.98 to 1.73) | |
| RR (95% CI) after PSM | | | | | | |
| Ref. | 1.43 (1.01 to 2.03) | Ref. | 5.22 (0.63 to 42.98) | Ref. | 1.20 (0.80 to 1.81) |
| 1-year readmission | | | | | | |
| events, n (%) | 314'116 (15.6) | 133 (23.4) | 233 (41.3) | 10 (21.3) | 13 (28.9) | 131 (26.0) | 178 (35.1) |
| unadjusted RR (95% CI) | | | | | | |
| Ref. | 2.65 (2.40 to 2.92) | Ref. | 1.85 (1.17 to 2.93) | 2.25 (2.00 to 2.53) | |
| adjusted RR (95% CI) | | | | | | |
| Ref. | 1.92 (1.70 to 2.17) | Ref. | 1.57 (0.97 to 2.56) | 1.52 (1.32 to 1.75) | |
| RR (95% CI) after PSM | | | | | | |
| Ref. | 1.77 (1.48 to 2.11) | Ref. | 1.36 (0.66 to 2.78) | 1.35 (1.12 to 1.63) | |
| 2-year readmission | | | | | | |
| events, n (%) | 461'957 (23.0) | 166 (29.2) | 257 (45.6) | 14 (29.8) | 17 (37.8) | 168 (33.4) | 214 (42.2) |
| unadjusted RR (95% CI) | | | | | | |
| Ref. | 1.99 (1.81 to 2.17) | Ref. | 1.65 (1.13 to 2.39) | 1.84 (1.62 to 2.04) | |
| adjusted RR (95% CI) | | | | | | |
| Ref. | 1.62 (1.46 to 1.80) | Ref. | 1.67 (1.15 to 2.42) | 1.40 (1.24 to 1.58) | |
| RR (95% CI) after PSM | | | | | | |
| Ref. | 1.56 (1.34 to 1.83) | Ref. | 1.27 (0.71 to 2.26) | Ref. | 1.26 (1.08 to 1.48) |

Abbreviations: AD, disorders of peptide, amine and amino acid metabolism; CD, disorders of carbohydrate metabolism; Cf., Regression Coefficient; CI, confidence interval; FD, disorders of fatty acid and ketone body metabolism mellitus; ICU, Intensive Care Unit; IMD, Inherited Metabolic Disorder; PSM, Propensity Score; PSM, Propensity Score Matching; PY, person-years; Ref., Reference; RR, Risk Ratio.
Table S3D – Hospital associated outcomes in IMDs from 40–59-year-old’s, by groups of IMDs with overall, adjusted and propensity score matched control

|                      | Overall controls (n=2341845) | AD | FD | CD |
|----------------------|--------------------------------|----|----|----|
|                      | PSM controls (n=785)          | PSM controls (n=785) | IMD cases (n=785) | PSM controls (n=39) | IMD cases (n=39) | PSM controls (n=655) | IMD cases (n=655) |
| **In-hospital mortality** | events, n (%)                | 20884 (0.9) | 29 (3.7) | 80 (10.2) | 1 (2.6) | 0 (0) | 11 (1.7) | 6 (0.9) |
| unadjusted RR (95% CI) | Ref.                          | 11.43 (9.28 to 14.07) | N/A | 2.72 (2.15 to 3.45) | N/A | 0.48 (0.22 to 0.95) | Ref. |
| adjusted RR (95% CI)  | Ref.                          | 2.76 (1.83 to 4.17) | N/A | Ref. | N/A | Ref. | 0.55 (0.20 to 1.47) |
| RR (95% CI) after PSM |                               |                               |                               |                               |                               |                               |                               |
| **Length of hospital stay (d)** | mean (SD)                  | 4.7 (8.8) | 11.1 (16.4) | 14.2 (21.7) | 13.1 (22.5) | 10.3 (17.0) | 7.4 (12.8) | 8.1 (11.3) |
| unadjusted Cl. (95% CI) | Ref.                          | 9.50 (8.88 to 10.12) | 5.63 (2.86 to 8.41) | 3.40 (2.73 to 4.08) | 3.40 (2.73 to 4.08) | 3.40 (2.73 to 4.08) | 3.40 (2.73 to 4.08) |
| adjusted Cl. (95% CI)  | Ref.                          | 4.36 (3.78 to 4.94) | 0.74 (1.86 to 3.33) | 0.90 (0.26 to 1.53) | 0.90 (0.26 to 1.53) | 0.90 (0.26 to 1.53) | 0.90 (0.26 to 1.53) |
| Cl. (95% CI) after PSM | Ref.                          | 3.08 (1.17 to 4.98) | -2.79 (-1.80 to 6.22) | Ref. | N/A | Ref. | 0.69 (-0.26 to 2.00) |
| **ICU admission** | mean (SD)                  | 1.7 (4.6) | 6.5 (11.9) | 8.1 (12.9) | 6.0 (9.3) | 2.9 (2.2) | 4.7 (13.0) | 3.1 (9.1) |
| unadjusted Cl. (95% CI) | Ref.                          | 6.64 (5.92 to 7.37) | 0.04 (-5.89 to 3.97) | 2.05 (0.84 to 3.27) | 2.05 (0.84 to 3.27) | 2.05 (0.84 to 3.27) | 2.05 (0.84 to 3.27) |
| adjusted Cl. (95% CI)  | Ref.                          | 3.08 (2.43 to 3.73) | -2.69 (-6.19 to 0.81) | Ref. | N/A | Ref. | 1.18 (0.09 to 2.26) |
| Cl. (95% CI) after PSM | Ref.                          | 1.72 (-0.71 to 4.16) | -5.67 (-13.14 to 1.79) | Ref. | N/A | Ref. | -1.40 (-5.21 to 2.40) |
| **Length of ICU stay (d)** | mean (SD)                  | 11.46 (10.20 to 13.12) | 0 (0) | 37 (5.7) | 29 (4.3) | 2.09 (1.45 to 3.00) | 0.83 (0.58 to 1.19) |
| unadjusted Cl. (95% CI) | Ref.                          | 2.68 (2.27 to 3.15) | N/A | Ref. | N/A | Ref. | 0.76 (0.47 to 1.22) |
| adjusted Cl. (95% CI)  | Ref.                          | 1.68 (1.35 to 2.07) | N/A | N/A | Ref. | 0.76 (0.47 to 1.22) | 0.76 (0.47 to 1.22) |
| Cl. (95% CI) after PSM | Ref.                          | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| **Mechanical ventilation** | mean (SD)                  | 144461 (6.2) | 77 (10.2) | 96 (13.6) | 1 (2.6) | 3 (7.7) | 53 (8.2) | 76 (11.7) |
| unadjusted RR (95% CI) | Ref.                          | 2.19 (1.82 to 2.64) | 1.24 (0.62 to 2.67) | 1.88 (1.52 to 2.32) | 1.88 (1.52 to 2.32) | 1.88 (1.52 to 2.32) | 1.88 (1.52 to 2.32) |
| adjusted RR (95% CI)  | Ref.                          | 1.20 (0.99 to 1.47) | 0.80 (0.27 to 2.39) | 1.42 (1.15 to 1.76) | 1.42 (1.15 to 1.76) | 1.42 (1.15 to 1.76) | 1.42 (1.15 to 1.76) |
| RR (95% CI) after PSM | Ref.                          | 1.34 (1.01 to 1.77) | 2.92 (0.32 to 26.86) | Ref. | N/A | Ref. | 1.42 (1.02 to 1.99) |
| **30-day readmission** | mean (SD)                  | 546852 (23.5) | 239 (31.6) | 234 (38.9) | 11 (29.0) | 14 (35.9) | 181 (28.1) | 231 (35.6) |
| unadjusted RR (95% CI) | Ref.                          | 1.65 (1.51 to 1.81) | 1.53 (1.00 to 2.32) | 1.51 (1.36 to 1.68) | 1.51 (1.36 to 1.68) | 1.51 (1.36 to 1.68) | 1.51 (1.36 to 1.68) |
| adjusted RR (95% CI)  | Ref.                          | 1.10 (0.96 to 1.23) | 1.13 (0.71 to 1.79) | 1.26 (1.12 to 1.40) | 1.26 (1.12 to 1.40) | 1.26 (1.12 to 1.40) | 1.26 (1.12 to 1.40) |
| RR (95% CI) after PSM | Ref.                          | 1.23 (1.07 to 1.41) | 1.24 (0.65 to 2.38) | Ref. | N/A | Ref. | 1.27 (1.08 to 1.49) |
| **1-year readmission** | mean (SD)                  | 697008 (30.0) | 280 (37.0) | 311 (44.1) | 16 (42.1) | 17 (43.6) | 226 (35.1) | 267 (41.1) |
| unadjusted RR (95% CI) | Ref.                          | 1.47 (1.35 to 1.60) | 1.45 (1.02 to 2.07) | 1.37 (1.25 to 1.50) | 1.37 (1.25 to 1.50) | 1.37 (1.25 to 1.50) | 1.37 (1.25 to 1.50) |
| adjusted RR (95% CI)  | Ref.                          | 1.06 (0.86 to 1.17) | 1.18 (0.80 to 1.75) | 1.19 (1.08 to 1.31) | 1.19 (1.08 to 1.31) | 1.19 (1.08 to 1.31) | 1.19 (1.08 to 1.31) |
| RR (95% CI) after PSM | Ref.                          | 1.19 (1.05 to 1.35) | 1.04 (0.62 to 1.73) | Ref. | Ref. | Ref. | 1.17 (1.02 to 1.35) |

**Abbreviations:** AD, disorders of peptide, amine and amino acid metabolism; CD, disorders of carbohydrate metabolism; CI, confidence interval; FD, disorders of fatty acid and ketone body metabolism mellitus; ICU, Intensive Care Unit; IMD, Inherited Metabolic Disorder; PS, Propensity Score; PSM, Propensity Score Matching; PY, person-years; Ref., Reference; RR, Risk Ratio.
| In-hospital mortality | Overall controls (n=4'909'425) | AD | FD | CD |
|----------------------|---------------------------------|----|----|----|
|                      | PSM controls (n=1'276) | IM cases (n=1'276) | PSM controls (n=55) | IM cases (n=55) | PSM controls (n=1'271) | IM cases (n=1'271) |
| events, n (%)        | 168'793 (3.4) | 102 (8.0) | 157 (12.3) | 4 (7.3) | 2 (3.6) | 56 (4.4) | 38 (3.0) |
| unadjusted RR (95% CI) | Ref. | 3.58 (3.09 to 4.14) | 1.06 (0.27 to 4.12) | 0.87 (0.64 to 1.19) |
| adjusted RR (95% CI) | Ref. | 2.19 (1.88 to 2.55) | 1.01 (0.26 to 3.90) | 0.74 (0.54 to 1.00) |
| RR (95% CI) after PSM | Ref. | 1.54 (1.21 to 1.95) | Ref. | 0.50 (0.10 to 2.62) | 0.68 (0.45 to 1.02) |

| Length of hospital stay (d) | mean (SD) | 11.9 (13.5) | 16.4 (24.7) | 10.1 (10.4) | 8.9 (9.1) | 8.8 (9.7) | 11.1 (13.7) |
|-----------------------------|-----------|-------------|-------------|-------------|-----------|-----------|-------------|
| unadjusted Cl. (95% CI)     | Ref. | 8.91 (8.34 to 9.49) | 1.42 (-1.37 to 4.22) | 3.60 (3.02 to 4.18) |
| adjusted Cl. (95% CI)       | Ref. | 4.87 (4.34 to 5.40) | -0.62 (-3.20 to 1.96) | 1.91 (1.37 to 2.44) |
| Cl. (95% CI) after PSM      | Ref. | 4.48 (2.93 to 6.03) | Ref. | -1.20 (-4.92 to 2.51) | 2.33 (1.40 to 3.25) |

| ICU admission | events, n (%) | 673'744 (13.7) | 333 (26.1) | 499 (39.1) | 16 (29.1) | 9 (16.4) | 219 (17.2) | 277 (21.8) |
|----------------|--------------|---------------|------------|-------------|-----------|-----------|----------|----------|
| unadjusted RR (95% CI) | Ref. | 2.85 (2.66 to 3.05) | 1.19 (0.86 to 1.77) | 1.59 (1.43 to 1.76) |
| adjusted RR (95% CI) | Ref. | 1.79 (1.65 to 1.95) | 0.82 (0.44 to 1.51) | 1.22 (1.10 to 1.36) |
| RR (95% CI) after PSM | Ref. | 1.50 (1.34 to 1.68) | Ref. | 0.56 (0.27 to 1.16) | 1.26 (1.08 to 1.48) |

| Length of ICU stay (d) | mean (SD) | 5.5 (11.2) | 7.5 (12.7) | 2.5 (3.6) | 4.5 (5.3) | 2.6 (4.2) | 3.1 (6.5) |
|------------------------|-----------|------------|------------|-----------|-----------|-----------|----------|
| unadjusted Cl. (95% CI) | Ref. | 6.67 (6.10 to 7.23) | 2.73 (-1.44 to 6.90) | 1.23 (0.46 to 2.00) |
| adjusted Cl. (95% CI) | Ref. | 4.22 (3.70 to 4.73) | 0.71 (-3.10 to 4.52) | 0.51 (0.20 to 1.22) |
| Cl. (95% CI) after PSM | Ref. | 2.42 (0.33 to 4.52) | Ref. | 2.45 (-1.97 to 6.86) | 0.47 (-0.86 to 1.81) |

| Mechanical ventilation | events, n (%) | 153'876 (3.1) | 125 (9.8) | 273 (21.4) | 6 (10.9) | 2 (3.6) | 55 (4.3) | 79 (6.2) |
|------------------------|--------------|-------------|-------------|-------------|-----------|-----------|----------|----------|
| unadjusted RR (95% CI) | Ref. | 6.83 (6.14 to 7.58) | 1.16 (0.30 to 4.52) | 1.98 (1.60 to 2.46) |
| adjusted RR (95% CI) | Ref. | 2.70 (2.39 to 3.06) | 0.46 (0.11 to 1.92) | 1.27 (1.03 to 1.56) |
| RR (95% CI) after PSM | Ref. | 2.18 (1.79 to 2.66) | Ref. | 0.33 (0.07 to 1.58) | 1.44 (1.03 to 2.01) |

| 30-day readmission | events, n (%) | 416'762 (8.8) | 138 (11.8) | 144 (12.9) | 7 (13.7) | 4 (7.6) | 120 (9.9) | 126 (10.2) |
|--------------------|--------------|-------------|------------|-------------|-----------|-----------|----------|----------|
| unadjusted RR (95% CI) | Ref. | 1.46 (1.26 to 1.70) | 0.86 (0.33 to 2.20) | 1.16 (0.99 to 1.37) |
| adjusted RR (95% CI) | Ref. | 1.09 (0.93 to 1.28) | 0.85 (0.34 to 2.15) | 1.05 (0.89 to 1.24) |
| RR (95% CI) after PSM | Ref. | 1.09 (0.88 to 1.36) | Ref. | 0.55 (0.17 to 1.77) | 1.03 (0.82 to 1.31) |

| 1-year readmission | events, n (%) | 1'495'093 (31.5) | 407 (34.7) | 426 (38.1) | 20 (39.2) | 24 (45.3) | 401 (33.0) | 446 (36.2) |
|-------------------|--------------|-------------|------------|-------------|-----------|-----------|----------|----------|
| unadjusted RR (95% CI) | Ref. | 1.21 (1.12 to 1.30) | 1.44 (1.07 to 1.93) | 1.15 (1.07 to 1.24) |
| adjusted RR (95% CI) | Ref. | 1.01 (0.93 to 1.09) | 1.43 (1.07 to 1.91) | 1.09 (1.01 to 1.17) |
| RR (95% CI) after PSM | Ref. | 1.10 (0.99 to 1.22) | Ref. | 1.15 (0.73 to 1.81) | 1.10 (0.98 to 1.22) |

| 2-year readmission | events, n (%) | 1'827'425 (38.6) | 471 (40.1) | 471 (42.1) | 21 (41.2) | 26 (49.1) | 485 (39.9) | 512 (41.5) |
|-------------------|--------------|-------------|------------|-------------|-----------|-----------|----------|----------|
| unadjusted RR (95% CI) | Ref. | 1.09 (1.02 to 1.17) | 1.27 (0.97 to 1.67) | 1.08 (1.01 to 1.15) |
| adjusted RR (95% CI) | Ref. | 0.95 (0.88 to 1.02) | 1.29 (0.99 to 1.68) | 1.05 (0.98 to 1.12) |
| RR (95% CI) after PSM | Ref. | 1.05 (0.95 to 1.16) | Ref. | 1.19 (0.78 to 1.83) | 1.04 (0.95 to 1.14) |

Abbreviations: AD, disorders of peptide, amine and amino acid metabolism; CD, disorders of carbohydrate metabolism; Cl., Regression Coefficient; CI, confidence interval; FD, disorders of fatty acid and ketone body metabolism mellitus; ICU, Intensive Care Unit; IMD, Inherited Metabolic Disorder; PS, Propensity Score; PSM, Propensity Score Matching; PY, person-years; Ref., Reference; RR, Risk Ratio.
| Table S4A – Hospitalization causes for patients with IMD per IMDs group and overall controls |
|-------------------------------------------------|----------------|----------------|----------------|----------------|
|                                                 | AD (n=3'638)   | CD (n=3'153)   | FD (n=502)     | Overall Control (n=10'086'18) |
| **Infectious & Parasitic, n (%)**               |                |                |                |                             |
| Infectious & Parasitic                          |                |                |                |                             |
| Intestinal Infectious                           | 266 (7.3)      | 195 (6.2)      | 143 (28.5)     | 301'799 (3.0)               |
| Bacterial Disease                               | 115 (43.2)     | 99 (50.8)      | 116 (81.1)     | 108'676 (36.0)              |
| Viral Infections incl. Hepatitis & HIV          | 106 (39.8)     | 59 (30.3)      | 13 (9.1)       | 127'535 (42.3)              |
| Mycoses, Protozoal and others                   | 23 (8.6)       | 23 (11.8)      | 12 (8.4)       | 31'092 (10.3)               |
| Other Infectious & Parasitic                    | 15 (5.6)       | 10 (5.1)       | 1 (0.7)        | 18'876 (6.3)                |
| Neoplasms, n (%)                                | 301'799 (799)  | 3 (0.7)        | 15'620 (5.2)   |                             |
| Malignant Neoplasms                             | 223 (7.1)      | 10 (100.0)     | 799 (3.0)      | 3776'385 (78.2)             |
| In situ and Benign Neoplasms                    | 241 (10.3)     | 45 (20.2)      | 216'312 (21.8) |
| Blood & Immune System, n (%)                    |                |                |                |                             |
| Anaemias                                        | 272 (89.7)     | 178 (79.8)     | 10 (100.0)     | 3776'385 (78.2)             |
| Other Diseases of Blood                         | 25 (10.3)      | 45 (20.2)      | 0 (0.0)        | 216'312 (21.8)              |
| Immune System                                   | 206 (71.0)     | 123 (61.3)     | 31 (30.4)      |                             |
| Endocrine & Metabolic, n (%)                    |                |                |                |                             |
| Disorders of Thyroid Gland                      | 23 (59)        | 26 (55)        | n.a.           | 29'821 (56.0)               |
| Diabetes Mellitus                               | 20 (18.2)      | 27 (11.7)      | 2 (8.7)        | 55'818 (31.2)               |
| Hypoglycemia                                    | 7 (6.4)        | 25 (10.8)      | 5 (21.7)       | 1'223 (0.7)                 |
| Other Endocrine Glands                          | 7 (6.4)        | 8 (3.5)        | 6 (26.1)       | 10'725 (6.0)                |
| Nutrition                                       | 16 (14.5)      | 60 (26.0)      | 3 (13.0)       | 50'263 (28.1)               |
| Metabolic Disorders                             | 56 (50.9)      | 106 (45.9)     | 7 (30.4)       | 36'273 (20.2)               |
| Mental & Behavioural, n (%)                     |                |                |                |                             |
| Other Nervous System                            | 3 (8)          | 4 (9)          | n.a.           | 3'054 (5.7)                 |
| Nervous System, n (%)                           | 241 (10.3)     | 45 (20.2)      | 0 (0.0)        | 216'312 (21.8)              |
| Inflammatory Diseases                           | 279 (7.7)      | 98 (3.1)       | 24 (4.8)       | 252'854 (2.5)               |
| Degenerative and Demyelinating                  | 9 (3.2)        | 2 (2.0)        | 0 (0.0)        | 7'322 (2.9)                 |
| Episodic and Paroxysmal Disorders               | 22 (7.9)       | 14 (14.3)      | 1 (4.2)        | 45'017 (17.8)               |
| Other Nervous System                            | 169 (60.6)     | 51 (52.0)      | 12 (50.0)      | 131'104 (51.8)              |
| Other Nervous System                            | 79 (28.3)      | 31 (31.6)      | 11 (45.8)      | 69'411 (27.5)               |
| Eye & Ear, n (%)                                |                |                |                |                             |
| Circulatory System, n (%)                       | 338 (10.6)     | 382 (12.1)     | 12 (2.4)       | 1'166'094 (11.5)            |
| Heart Disease incl. Hypertensive                | 176 (45.7)     | 282 (73.8)     | 10 (83.3)      | 775'768 (66.5)              |
| Cerebrovascular and Arteries                    | 191 (49.6)     | 82 (21.5)      | 0 (0.0)        | 286'087 (24.5)              |
| Veins and Lymphatic Vessels                     | 18 (4.7)       | 18 (4.7)       | 2 (16.7)       | 104'239 (8.9)               |
| Respiratory System, n (%)                       |                |                |                |                             |
| Respiratory Infections                          | 147 (70.3)     | 140 (54.3)     | 91 (82.0)      | 324'808 (47.6)              |
| Disorder                                      | AD (n=3'638) | CD (n=3'153) | FD (n=502) | Overall Control (n=10'108'618) |
|-----------------------------------------------|--------------|--------------|------------|---------------------------------|
| Chronic Lower Respiratory Diseases            | 18 (8.6)     | 52 (20.2)    | 0 (0.0)    | 101'722 (14.9)                  |
| Other Respiratory System                      | 44 (21.1)    | 66 (25.6)    | 20 (18.0)  | 256'397 (37.5)                  |
| **Digestive System, n (%)**                   | **557 (15.3)**| **379 (12.0)**| **27 (5.4)**| **1'016'861 (10.1)**           |
| Appendix                                      | 7 (1.3)      | 16 (4.2)     | 6 (22.2)   | 106'292 (10.5)                  |
| Hernia                                        | 19 (3.4)     | 35 (9.2)     | 0 (0.0)    | 231'318 (22.7)                  |
| Intestines                                    | 69 (12.4)    | 154 (40.6)   | 5 (18.5)   | 302'644 (29.8)                  |
| Liver                                         | 339 (60.9)   | 21 (5.5)     | 1 (3.7)    | 35'019 (3.4)                    |
| Gallbladder, Biliary Tract and Pancreas       | 42 (7.5)     | 70 (18.5)    | 4 (14.8)   | 202'982 (20.0)                  |
| Other Digestive System                        | 81 (14.5)    | 83 (21.9)    | 11 (40.7)  | 138'606 (13.6)                  |
| **Skin & Subcutaneous Tissue, n (%)**         | **19 (0.5)** | **60 (1.9)** | **2 (0.4)**| **134'067 (1.3)**               |
| **Musculoskeletal System, n (%)**             | **141 (3.9)**| **214 (6.8)**| **25 (5.0)**| **1'400'826 (13.9)**            |
| Arthropathies                                 | 83 (58.9)    | 98 (45.8)    | 7 (28.0)   | 753'325 (53.8)                  |
| Systemic Connective Tissue Disorders          | 4 (2.8)      | 10 (4.7)     | 0 (0.0)    | 15'196 (1.1)                    |
| Other Musculoskeletal                         | 54 (38.3)    | 106 (49.5)   | 18 (72.0)  | 632'305 (45.1)                  |
| **Genitourinary System, n (%)**               | **366 (10.1)**| **285 (9.0)**| **22 (4.4)**| **694'231 (6.9)**               |
| Urinary Tract Diseases                        | 344 (94.0)   | 236 (82.8)   | 20 (90.9)  | 372'293 (53.6)                  |
| Disorders of Genital Organs                   | 22 (6.0)     | 49 (17.2)    | 2 (9.1)    | 321'938 (46.4)                  |
| **Injuries, n (%)**                           | **235 (6.5)**| **235 (7.5)**| **26 (5.2)**| **1'422'224 (14.1)**            |
| **Other, n (%)**                              | **560 (15.4)**| **410 (13.0)**| **60 (12.0)**| **1'418'525 (14.0)**            |

**Abbreviations:** AD, disorders of peptide, amine and amino acid metabolism; CD, disorders of carbohydrate metabolism; FD, disorders of fatty acid and ketone body metabolism mellitus; IMD, Inherited Metabolic Disorder
|                        | Age 0-9 years | Age 10-19 years | Age 20-39 years | Age 40-59 years | Age 60-90 years |
|------------------------|--------------|-----------------|-----------------|-----------------|-----------------|
| **Infectious & Parasitic, n (%)** |              |                 |                 |                 |                 |
| Intestinal Infectious  | 254 (18.4)   | 30'697 (8.4)    | 57 (8.1)        | 14'382 (3.8)    | 70 (6.2)        |
| Bacterial Disease      | 214 (84.3)   | 25'464 (65.8)   | 43 (75.4)       | 6'903 (48.0)    | 33 (47.1)       |
| Viral Infections incl. Hepatitis & HIV | 27 (10.6) | 7'413 (19.2)    | 7 (12.3)        | 3'595 (25.0)    | 11 (15.7)       |
| Mycoses, Protozoal and others | 4 (1.6)  | 1'109 (2.9)     | 2 (3.5)         | 658 (46.8)      | 5 (7.1)         |
| Other Infectious & Parasitic | 2 (0.8) | 2'244 (5.8)     | 0 (0.0)         | 1'635 (11.4)    | 3 (4.3)         |
| **Neoplasms, n (%)**   |              |                 |                 |                 |                 |
| Malignant Neoplasms    | 25 (1.8)     | 13'842 (3.0)    | 32 (4.5)        | 13'654 (3.6)    | 30 (2.7)        |
| In situ and Benign Neoplasms | 23 (92.0) | 11'128 (80.4)   | 28 (87.5)       | 9'075 (66.5)    | 17 (56.7)       |
| Blood & Immune System, n (%) |          |                 |                 |                 |                 |
| Anaemias               | 15 (1.1)     | 4'113 (0.9)     | 8 (1.1)         | 2'342 (0.6)     | 24 (2.1)        |
| Other Diseases of Blood| 6 (40.0)     | 2'323 (56.5)    | 0 (0.0)         | 951 (40.6)      | 10 (41.7)       |
| Immune System          | 2 (13.3)     | 145 (3.5)       | 1 (12.5)        | 61 (26.0)       | 3 (12.5)        |
| **Endocrine & Metabolic, n (%)** |              |                 |                 |                 |                 |
| Disorders of Thyroid Gland | 66 (4.8) | 4'273 (0.9)     | 91 (12.9)       | 6'612 (1.7)     | 74 (6.6)        |
| Diabetes Mellitus      | 0 (0.0)      | 44 (1.0)        | 0 (0.0)         | 254 (3.8)       | 2 (2.7)         |
| Hypoglycemia           | 23 (34.8)    | 304 (71.1)      | 7 (7.7)         | 50 (0.8)        | 5 (6.8)         |
| Other Endocrine Glands | 4 (6.1)      | 251 (59.9)      | 3 (3.3)         | 211 (3.2)       | 5 (6.8)         |
| Nutrition              | 7 (10.6)     | 274 (64.6)      | 5 (5.5)         | 840 (12.7)      | 18 (24.3)       |
| Metabolic Disorders    | 31 (47.0)    | 1'549 (36.3)    | 68 (74.7)       | 1754 (26.5)     | 35 (47.3)       |
| **Mental & Behavioural, n (%)** |              |                 |                 |                 |                 |
| Nervous System         | 67 (4.9)     | 10'920 (2.4)    | 44 (6.2)        | 10'851 (2.9)    | 44 (3.9)        |
| Inflammatory Diseases  | 0 (0.0)      | 701 (6.4)       | 1 (2.3)         | 446 (4.1)       | 3 (6.8)         |
| Degenerative and Demyelinating | 6 (9.0)    | 511 (4.7)       | 3 (6.8)         | 652 (6.0)       | 3 (6.8)         |
| Episodic and Paroxysmal Disorders | 42 (62.7) | 8'421 (77.1)    | 32 (72.7)       | 7'622 (70.2)    | 24 (54.5)       |
| Other Nervous System   | 19 (28.4)    | 1'287 (11.8)    | 8 (18.2)        | 2'131 (19.6)    | 14 (31.8)       |
| Eye & Ear, n (%) | Circulatory System, n (%) | Heart Disease incl. Hypertensive | Cerebrovascular and Arteries | Veins and Lymphatic Vessels | Disorders of Genital Organs | Urinary Tract Diseases | Other Respiratory System | Overall controls (n=2'602) | IMD (n=1'479) | Overall controls (n=2'341'845) | IMD (n=1'128) | Overall controls (n=2'015'176) | IMD (n=707) | Overall controls (n=379'511) | IMD (n=3'77) | Overall controls (n=426'261) |
|-----------------|--------------------------|-----------------------------|----------------------------|----------------------------|--------------------------|------------------------|----------------------|-------------------------|-----------------|--------------------------|-----------------|--------------------------|---------------|---------------------------|---------------|--------------------------|
| Other, n (%)    | Injuries, n (%)          | Skin & Subcutaneous Tissue, n (%) | Digestive System, n (%)   | Circulatory System, n (%) | Eye & Ear, n (%)         | Digestive System, n (%) | Respiratory System, n (%) | Overall controls (n=1'128) | IMD (n=1'377) | Overall controls (n=379'511) | IMD (n=3'77) | Overall controls (n=426'261) |
| 11 (0.8)        | 346 (25.1)               | 11 (0.8)                    | 77 (5.6)                  | 346 (25.1)                 | 11 (0.8)                 | 53 (3.8)               | 251 (18.2)          | 57 (4.1)                 | 3 (5.3)        | 11 (0.8)                 | 9 (0.6)         | 346 (25.1)                | 4 (0.6)        | 346 (25.1)                |
| 6'706 (1.4)     | 101'899 (22.0)           | 3'728 (1.0)                 | 21'333 (0.5)              | 4'029 (2.1)                | 20'911 (0.8)             | 10'333 (4.8)          | 36'277 (9.6)        | 41'255 (10.9)           | 25 (1.2)       | 611'793 (9.4)            | 30 (0.8)        | 611'793 (9.4)            | 27 (1.0)       | 611'793 (9.4)            |
| 4 (0.6)         | 143 (20.2)               | 3'728 (1.0)                 | 21'333 (0.5)              | 4'029 (2.1)                | 20'911 (0.8)             | 10'333 (4.8)          | 36'277 (9.6)        | 41'255 (10.9)           | 25 (1.2)       | 611'793 (9.4)            | 30 (0.8)        | 611'793 (9.4)            | 27 (1.0)       | 611'793 (9.4)            |