Estimating the Prevalence of Rare Diseases: Long Chain Fatty Acid Oxidation Disorders as an Illustrative Example

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### SUPPLEMENTARY TABLES

**Table S1a** Literature-derived incidence inputs (Germany)

| Births       | 2005  | 2006  | 2007  | 2008  | 2009  | 2010  | 2011  | 2012  | 2013  | 2014  | 2015  | 2016  | Total   | Average |
|--------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|---------|---------|
|              | 687,963 | 672,724 | 684,862 | 682,514 | 665,126 | 677,947 | 662,685 | 673,544 | 682,069 | 714,927 | 737,575 | 792,131 | 8,334,067 | 694,506 |
| Screened     | 697,503 | 690,143 | 686,064 | 689,262 | 665,495 | 678,362 | 666,145 | 674,926 | 683,713 | 716,496 | 738,864 | 783,873 | 8,370,846 | 697,571 |

| Incidence, n (n/100,000) |
|---------------------------|
| VLCAD                     |
| (70)                      |
| (130)                     |
| (110)                     |
| (130)                     |
| (170)                     |
| (150)                     |
| (80)                      |
| (90)                      |
| (100)                     |
| LCHAD                     |
| (40)                      |
| (70)                      |
| (30)                      |
| (50)                      |
| (70)                      |
| (60)                      |
| (100)                     |
| (80)                      |
| (100)                     |
| TFP                       |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| CPT-1                     |
| (10)                      |
| (40)                      |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| (10)                      |
| CPT-2                     |
| (30)                      |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| (30)                      |
| CACT                      |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| (0)                       |
| All                       |
| (160)                     |
| (250)                     |
| (180)                     |
| (180)                     |
| (150)                     |
| (280)                     |
| (240)                     |
| (210)                     |
| (210)                     |
| (130)                     |
| (180)                     |
| (260)                     |
| (200)                     |

German Society for Newborn Screening (DGNS). National Screening Reports. Accessed 05 March 2019. Available from https://www.screening-dgns.de/reports.php

*CACT* carnitine-acylcarnitine translocase deficiency, *CPT-1* carnitine palmitoyltransferase 1, *CPT-2* carnitine palmitoyltransferase 2, *LC-FAOD* long-chain fatty acid oxidation disorders, *LCHAD* long-chain 3-hydroxy acyl-CoA dehydrogenase deficiency, *TFP* trifunctional protein, *VLCAD* very long–chain acyl-CoA dehydrogenase deficiency
| Variant | Screened, n | Screened positive, n | True positive, n | Incidence rate, n/100,000 | 95% confidence interval, n/100,000 |
|---------|-------------|---------------------|-----------------|--------------------------|----------------------------------|
| Bhattacharya K, et al. J Inherit Metab Dis. 2016;39(Suppl 1):S35–284 | Australia | VLCAD | N/A | 35 | 11 | |
| Merritt JL, 2nd, et al. Mol Genet Metab. 2014;111(4):484–92 | United States | VLCAD | 2,802,504 | 242 | 52 | 186 | 161-210 |
| Diekman E, et al. JIMD Rep. 2016;27:101–6 | Netherlands | VLCAD | 742,728 | 30 | 11 | 150 | 105-191 |
| Overall LC-FAOD rate, adjusted for all subtypes | | | | | | 250 | 178-322 |
| Martin JA, et al. Natl Vital Stat Rep. 2009;57(7) | United States | LC-FAOD | 3,333,129 | 186 | 45 | 135 | 115-154 |

*LC-FAOD* long-chain fatty acid oxidation disorders, N/A not applicable, *VLCAD* very long-chain acyl-CoA dehydrogenase deficiency
| Disorder | Reference | Newborn screening diagnosis | Symptomatic diagnosis |
|----------|-----------|-----------------------------|----------------------|
| VLCAD    | Spiekerkoetter U, et al. J Inherit Metab Dis. 2009;32(4):488–97 | 20 0 | 0.0 | 10 2 | 20.0 |
|         | Obaid A, et al. JIMD Rep. 2018;40:47–53 | 37 23 | 62.0 | – – | – |
|         | Baruteau J, et al. J Inherit Metab Dis. 2012;36(5):795–803 | – – | – | 33 20 | 61.0 |
|         | Evans M, et al. Mol Genet Metab. 2016;118:282–7 | 22 0 | 0.0 | – – | – |
|         | Klose DA, et al. Pediatrics. 2002;110(6):1204–11 | – – | – | 2 0 | 0.0 |
|         | Zheng J, et al. Europe PMC. 2017;46(3):248–55 | 3 0 | 0.0 | – – | – |
|         | Andresen BS, et al. Am J Hum Genet. 1999;64:479–94 | – – | – | – – | 75.0 |
|         | Wilson C, et al. NZMJ. 2012;125(1346):42–50 | 1 0 | 0.0 | 1 0 | 0.0 |
| LCHAD    | Spiekerkoetter U, et al. J Inherit Metab Dis. 2009;32(4):488–97 | 7 0 | 0.0 | 13 3 | 23.0 |
|         | Sykut-Cegielska J, et al. J Inherit Metab Dis. 2011;34:185–95 | 15 1 | 6.6 | 44 20 | 45.5 |
|         | Baruteau J, et al. J Inherit Metab Dis. 2012;36(5):795–803 | – – | – | 41 26 | 63.4 |
|         | den Boer MEJ, et al. Pediatrics. 2002;109(1):99–104 | – – | – | 50 19 | 38.0 |
|         | Immonen T, et al. Acta Paediatrica. 2016;105:549–54 | – – | – | 16 6 | 37.5 |
|         | Klose DA, et al. Pediatrics. 2002;110(6):1204–11 | – – | – | 3 2 | 66.7 |
| Tyni T, et al. | J Pediatrics. 1997;130(1):67–76 | – | – | – | 13 | 12 | 92.3 |
| Tyni T, et al. | Pediatri Pathol Lab Med. 1997;17(3):427–47 | – | – | – | 16 | 15 | 93.8 |
| Vockley J, et al. | Mol Genet Metab. 2016;17(3):427–47 | – | – | – | 187 | – | ≥50.0 |
| Spiekerkoetter U, et al. | J Hum Genet. 2017;62:809–14 | 3 | 2 | 66.7 | 4 | 3 | 75.0 |
| Sperk A, et al. | Mol Genet Metab. 2010;119(3):223–31 | 6 | 1 | 16.7 | – | – | – |
| den Boer MEJ, et al. | J Pediatr. 2003;142:684–9 | – | – | – | 21 | 16 | 76.0 |
| Bo R, et al. | J Hum Genet. 2017;62:809–14 | 14 | 6 | 43.0 | – | – | – |
| Vockley J, et al. | Mol Genet Metab. 2016;119(3):223–31 | – | – | – | 4 | 1 | 25.0 |
| Jalan A, et al. | J Inborn Errors Metab Screen. 2017;5:1–413 | – | – | – | 8 | 2 | 25.0 |
| Zheng J, et al. | Europe PMC. 2017;46(3):248–55 | 2 | 0 | 0 | – | – | – |
| CACT | Baruteau J, et al. J Inherit Metab Dis. 2012;36(5):795–803 | – | – | – | 15 | 10 | 66.7 |
| Klose DA, et al. | Pediatrics. 2002;110(6):1204–11 | – | – | – | 1 | 1 | 100.0 |
| Zheng J, et al. | Europe PMC. 2017;46(3):248–55 | 2 | 2 | 100 | – | – | – |
| Spiekerkoetter U, et al. | J J Inherit Metab Dis. 2009;32(4):488–97 | 3 | 2 | 67.0 | 2 | 0 | 0.0 |
| Wilson C, et al. | NZMJ. 2012;125(1348):42–50 | – | – | – | 3 | 1 | 33.3 |
| Vitoria I, et al. | JIMD Reports. 2015;20:11–20 | – | – | – | 43 | 28 | 65.0 |

CACT carnitine-acylcarnitine translocase deficiency, CPT-1 carnitine palmitoyltransferase 1, CPT-2 carnitine palmitoyltransferase 2, LC-FAOD long-chain fatty acid oxidation disorders, LCHAD long-chain 3-hydroxy acyl-CoA dehydrogenase deficiency, TFP trifunctional protein, VLCAD very long–chain acyl-CoA dehydrogenase deficiency
Table S3 Prevalence outputs worldwide, by regions and selected countries

| Prevalence, n (%) | 2021  | 2030  | 2040  | Dx rate, % | Pediatric | Adult | Total | Dx rate, % | Pediatric | Adult | Total | Dx rate, % |
|------------------|-------|-------|-------|------------|-----------|-------|-------|------------|-----------|-------|-------|------------|
|                  | Pediatric | Adult | Total | Dx rate, % | Pediatric | Adult | Total | Dx rate, % | Pediatric | Adult | Total | Dx rate, % |
| North America    |       |       |       |            |           |       |       |            |           |       |       |            |
| United States    | 1355  | 1515  | 2871  | 72         | 1407      | 1743  | 3150  | 79         | 1452      | 1973  | 3425  | 85         |
| (47)             | (53)  | (100) |       | (45)       | (55)      | (100) |       | (42)       | (58)      | (100) |       |            |
| Canada           | 125   | 149   | 274   | 71         | 130       | 167   | 297   | 78         | 133       | 188   | 320   | 84         |
| (46)             | (54)  | (100) |       | (44)       | (56)      | (100) |       | (41)       | (59)      | (100) |       |            |
| Canada - Low variant | 116   | 149   | 264   | 70         | 103       | 167   | 269   | 76         | 92        | 180   | 272   | 81         |
| (44)             | (56)  | (100) |       | (38)       | (62)      | (100) |       | (34)       | (66)      | (100) |       |            |
| Mexico           | 575   | 746   | 1321  | 41         | 552       | 817   | 1369  | 46         | 532       | 866   | 1399  | 51         |
| (44)             | (56)  | (100) |       | (40)       | (60)      | (100) |       | (38)       | (62)      | (100) |       |            |
| Latin America    |       |       |       |            |           |       |       |            |           |       |       |            |
| Argentina        | 185   | 214   | 399   | 41         | 186       | 238   | 424   | 46         | 190       | 259   | 449   | 52         |
| (46)             | (54)  | (100) |       | (44)       | (56)      | (100) |       | (42)       | (58)      | (100) |       |            |
| Brazil           | 744   | 1160  | 1904  | 41         | 691       | 1222  | 1913  | 45         | 656       | 1240  | 1897  | 50         |
| (39)             | (61)  | (100) |       | (36)       | (64)      | (100) |       | (35)       | (65)      | (100) |       |            |
| Chile            | 60    | 92    | 152   | 41         | 58        | 96    | 154   | 45         | 57        | 97    | 155   | 51         |
| (39)             | (61)  | (100) |       | (38)       | (62)      | (100) |       | (37)       | (63)      | (100) |       |            |
| Colombia         | 188   | 278   | 466   | 41         | 174       | 296   | 470   | 45         | 166       | 303   | 469   | 50         |
| (40)             | (60)  | (100) |       | (37)       | (63)      | (100) |       | (35)       | (65)      | (100) |       |            |
| Europe 4 + UK    |       |       |       |            |           |       |       |            |           |       |       |            |
| France           | 208   | 280   | 488   | 57         | 212       | 299   | 511   | 64         | 219       | 318   | 538   | 70         |
| (43)             | (57)  | (100) |       | (42)       | (58)      | (100) |       | (41)       | (59)      | (100) |       |            |
| Country          | 2021   | 2030   | 2040   |
|------------------|--------|--------|--------|
|                  | Pediatric | Adult | Total | Dx rate (%) | Pediatric | Adult | Total | Dx rate (%) | Pediatric | Adult | Total | Dx rate (%) |
| Germany          | 191    | 329    | 519    | 55       | 201    | 329    | 530    | 62       | 199    | 333    | 532    | 68       |
|                  | (37)   | (63)   | (100)  |          | (38)   | (62)   | (100)  |          | (37)   | (63)   | (100)  |          |
| Italy            | 139    | 252    | 391    | 54       | 133    | 251    | 385    | 60       | 135    | 246    | 381    | 67       |
|                  | (35)   | (65)   | (100)  |          | (35)   | (65)   | (100)  |          | (35)   | (65)   | (100)  |          |
| Spain            | 116    | 185    | 301    | 55       | 106    | 193    | 299    | 61       | 103    | 194    | 297    | 67       |
|                  | (38)   | (62)   | (100)  |          | (35)   | (65)   | (100)  |          | (35)   | (65)   | (100)  |          |
| United Kingdom   | 212    | 273    | 485    | 57       | 221    | 294    | 515    | 64       | 222    | 320    | 542    | 70       |
|                  | (44)   | (56)   | (100)  |          | (43)   | (57)   | (100)  |          | (41)   | (59)   | (100)  |          |
| **Eastern Europe**|        |        |        |          |        |        |        |          |        |        |        |          |
| Czechia          | 29     | 51     | 80     | 54       | 28     | 50     | 78     | 61       | 27     | 50     | 76     | 67       |
|                  | (36)   | (64)   | (100)  |          | (36)   | (64)   | (100)  |          | (35)   | (65)   | (100)  |          |
| Hungary          | 24     | 52     | 77     | 53       | 24     | 49     | 72     | 59       | 22     | 46     | 69     | 66       |
|                  | (32)   | (68)   | (100)  |          | (32)   | (68)   | (100)  |          | (33)   | (67)   | (100)  |          |
| Poland           | 99     | 209    | 308    | 54       | 89     | 202    | 290    | 59       | 79     | 192    | 271    | 65       |
|                  | (32)   | (68)   | (100)  |          | (31)   | (69)   | (100)  |          | (29)   | (71)   | (100)  |          |
| Russia           | 460    | 748    | 1208   | 55       | 454    | 744    | 1198   | 61       | 417    | 761    | 1178   | 68       |
|                  | (38)   | (62)   | (100)  |          | (38)   | (62)   | (100)  |          | (35)   | (65)   | (100)  |          |
| Turkey           | 351    | 480    | 831    | 57       | 346    | 520    | 866    | 63       | 332    | 556    | 888    | 69       |
|                  | (42)   | (58)   | (100)  |          | (40)   | (60)   | (100)  |          | (37)   | (63)   | (100)  |          |
| Ukraine          | 124    | 249    | 373    | 54       | 118    | 239    | 357    | 60       | 107    | 231    | 338    | 66       |
|                  | (33)   | (67)   | (100)  |          | (33)   | (67)   | (100)  |          | (32)   | (68)   | (100)  |          |
| **Northern Europe**|        |        |        |          |        |        |        |          |        |        |        |          |
| Denmark          | 17     | 24     | 41     | 56       | 18     | 25     | 43     | 63       | 19     | 27     | 46     | 70       |
|                  | (41)   | (59)   | (100)  |          | (41)   | (59)   | (100)  |          | (42)   | (58)   | (100)  |          |
| Country       | Pediatric 2021 | Adult 2021 | Total 2021 | Dx rate, % 2021 | Pediatric 2030 | Adult 2030 | Total 2030 | Dx rate, % 2030 | Pediatric 2040 | Adult 2040 | Total 2040 | Dx rate, % 2040 |
|--------------|----------------|------------|------------|----------------|----------------|------------|------------|----------------|----------------|------------|------------|----------------|
| Finland      | 16             | 25         | 41         | 55             | 17             | 25         | 42         | 62             | 17             | 26         | 43         | 69             |
|              | (39)           | (61)       | (100)      |                | (40)           | (60)       | (100)      |                | (39)           | (61)       | (100)      |                |
| Ireland      | 18             | 22         | 40         | 58             | 17             | 24         | 42         | 64             | 18             | 26         | 44         | 70             |
|              | (45)           | (55)       | (100)      |                | (42)           | (58)       | (100)      |                | (40)           | (60)       | (100)      |                |
| Norway       | 17             | 21         | 38         | 57             | 18             | 23         | 41         | 64             | 20             | 25         | 44         | 71             |
|              | (44)           | (56)       | (100)      |                | (45)           | (55)       | (100)      |                | (44)           | (56)       | (100)      |                |
| Sweden       | 31             | 38         | 69         | 58             | 34             | 41         | 74         | 65             | 35             | 45         | 80         | 71             |
|              | (45)           | (55)       | (100)      |                | (45)           | (55)       | (100)      |                | (44)           | (56)       | (100)      |                |
| Southern Europe |              |            |            |                |                |            |            |                |                |            |            |                |
| Portugal     | 24             | 55         | 79         | 53             | 21             | 53         | 74         | 58             | 20             | 49         | 70         | 64             |
|              | (31)           | (69)       | (100)      |                | (28)           | (72)       | (100)      |                | (29)           | (71)       | (100)      |                |
| Western Europe |              |            |            |                |                |            |            |                |                |            |            |                |
| Austria      | 22             | 34         | 56         | 56             | 23             | 35         | 58         | 62             | 23             | 37         | 60         | 69             |
|              | (39)           | (61)       | (100)      |                | (40)           | (60)       | (100)      |                | (38)           | (62)       | (100)      |                |
| Belgium      | 34             | 46         | 80         | 57             | 36             | 49         | 84         | 64             | 36             | 52         | 88         | 70             |
|              | (43)           | (57)       | (100)      |                | (42)           | (58)       | (100)      |                | (41)           | (59)       | (100)      |                |
| Netherlands  | 50             | 73         | 123        | 56             | 51             | 76         | 127        | 63             | 51             | 79         | 131        | 69             |
|              | (40)           | (60)       | (100)      |                | (40)           | (60)       | (100)      |                | (39)           | (61)       | (100)      |                |
| Switzerland  | 22             | 30         | 52         | 57             | 24             | 31         | 56         | 64             | 25             | 34         | 59         | 70             |
|              | (43)           | (57)       | (100)      |                | (44)           | (56)       | (100)      |                | (42)           | (58)       | (100)      |                |
| Asia Pacific |                |            |            |                |                |            |            |                |                |            |            |                |
| China        | 1395           | 2392       | 3787       | 69             | 1281           | 2468       | 3749       | 75             | 1137           | 2529       | 3666       | 81             |
|              | (37)           | (63)       | (100)      |                | (34)           | (66)       | (100)      |                | (31)           | (69)       | (100)      |                |
| Prevalence, \( n \) (%) | 2021 | 2020 | 2040 |
|-------------------------|------|------|------|
|                         | Pediatric | Adult | Total | Dx rate, | Pediatric | Adult | Total | Dx rate, | Pediatric | Adult | Total | Dx rate, |
|                         | %     |       |       | %        | %     |       |       | %        | %     |       |       | %        |
| Japan                   | 90    | 167   | 256   | 68       | 84    | 165   | 249   | 75       | 79    | 164   | 243   | 82       |
| (35)                    | (65)  |       | (100) | (34)     | (66)  | (100) |       | (32)     | (68)  | (100) |       |          |
| South Korea             | 39    | 77    | 116   | 68       | 38    | 79    | 117   | 74       | 37    | 79    | 116   | 80       |
| (33)                    | (67)  |       | (100) | (33)     | (67)  | (100) |       | (32)     | (68)  | (100) |       |          |
| Thailand                | 64    | 112   | 176   | 70       | 57    | 120   | 176   | 75       | 52    | 122   | 174   | 81       |
| (36)                    | (64)  |       | (100) | (32)     | (68)  | (100) |       | (30)     | (70)  | (100) |       |          |
| Vietnam                 | 129   | 159   | 288   | 75       | 127   | 183   | 309   | 81       | 115   | 206   | 321   | 85       |
| (45)                    | (55)  |       | (100) | (41)     | (59)  | (100) |       | (36)     | (64)  | (100) |       |          |
| Australia & New Zealand | 81    | 84    | 166   | 59       | 88    | 96    | 185   | 66       | 93    | 112   | 204   | 72       |
| Australia               | 17    | 20    | 37    | 58       | 17    | 22    | 39    | 65       | 18    | 24    | 42    | 71       |
| New Zealand             |       |       |       |          |       |       |       |          |       |       |       |          |
| Global                  | 32772 | 34599 | 67371 | 63       | 33702 | 40368 | 74070 | 68       | 34442 | 46188 | 80630 | 72       |

Some totals may not equal pediatric + adult owing to rounding

*Dx* diagnosis, *RoW* rest of the world
### SUPPLEMENTARY APPENDIX – MORTALITY SCENARIO ANALYSES

#### Base case (US)

|                       | 2021          | 2025          | 2030          | 2040          |
|-----------------------|---------------|---------------|---------------|---------------|
| **LC-FAOD Prevalent Patients** |               |               |               |               |
| Dx                    | %             | %             | %             | %             |
| 2021                  | 2,871         | 2,998         | 1,150         | 3,425         |
| 2025                  | 2,871         | 2,998         | 1,150         | 3,425         |
| 2030                  | 2,871         | 2,998         | 1,150         | 3,425         |
| 2040                  | 2,871         | 2,998         | 1,150         | 3,425         |
| **LC-FAOD Dx Patients** | 2,057         | 2,254         | 2,489         | 2,791         |
| % Asymptomatic        | 72%           | 75%           | 79%           | 82%           |
| % Moderate            | 281 (21% of Total Ped Dx) | 292 (21% of Total Ped Dx) | 297 (21% of Total Ped Dx) | 307 (21% of Total Ped Dx) |
| % Severe              | 505 (38% of Total Ped Dx) | 518 (38% of Total Ped Dx) | 528 (38% of Total Ped Dx) | 544 (38% of Total Ped Dx) |
| **LC-FAOD Dx Ped**    | 1,329 (65% of Dx) | 1,371 (61% of Dx) | 1,397 (56% of Dx) | 1,441 (49% of Dx) |
| % Asymptomatic        | 122 (9% of Total Ped) | 128 (9% of Total Ped) | 131 (9% of Total Ped) | 135 (9% of Total Ped) |
| % Mild                | 281 (21% of Total Ped Dx) | 292 (21% of Total Ped Dx) | 297 (21% of Total Ped Dx) | 307 (21% of Total Ped Dx) |
| % Moderate            | 421 (32% of Total Ped Dx) | 433 (32% of Total Ped Dx) | 441 (32% of Total Ped Dx) | 455 (32% of Total Ped Dx) |
| % Severe              | 505 (38% of Total Ped Dx) | 518 (38% of Total Ped Dx) | 528 (38% of Total Ped Dx) | 544 (38% of Total Ped Dx) |
| **LC-FAOD Dx Adults** | 728 (35% of Dx) | 884 (39% of Dx) | 1,092 (44% of Dx) | 1,472 (51% of Dx) |
| % Asymptomatic        | 71 (10% of Total Adult) | 92 (10% of Total Adult) | 122 (11% of Total Adult) | 181 (12% of Total Adult) |
| % Mild                | 247 (34% of Total Adult Dx) | 288 (33% of Total Adult Dx) | 347 (32% of Total Adult Dx) | 465 (32% of Total Adult Dx) |
| % Moderate            | 298 (41% of Total Adult Dx) | 347 (39% of Total Adult Dx) | 413 (38% of Total Adult Dx) | 535 (36% of Total Adult Dx) |
| % Severe              | 112 (15% of Total Adult Dx) | 157 (18% of Total Adult Dx) | 209 (19% of Total Adult Dx) | 291 (20% of Total Adult Dx) |
| **LC-FAOD Dx Total (Ped + Adults)** | 2,057 (100% of Dx) | 2,254 (100% of Dx) | 2,489 (100% of Dx) | 2,913 (100% of Dx) |
| % Asymptomatic        | 194 (9% of Total Ped+Adult Dx) | 220 (10% of Total Ped+Adult Dx) | 253 (10% of Total Ped+Adult Dx) | 316 (11% of Total Ped+Adult Dx) |
| % Mild                | 527 (26% of Total Ped+Adult Dx) | 579 (26% of Total Ped+Adult Dx) | 645 (26% of Total Ped+Adult Dx) | 772 (27% of Total Ped+Adult Dx) |
| % Moderate            | 719 (35% of Total Ped+Adult Dx) | 780 (35% of Total Ped+Adult Dx) | 854 (34% of Total Ped+Adult Dx) | 990 (34% of Total Ped+Adult Dx) |
| % Severe              | 618 (30% of Total Ped+Adult Dx) | 675 (30% of Total Ped+Adult Dx) | 738 (30% of Total Ped+Adult Dx) | 834 (29% of Total Ped+Adult Dx) |

*Dx diagnosis, Ped pediatric*
|                     | 2021         | 2025         | 2030         | 2040         |
|---------------------|--------------|--------------|--------------|--------------|
| **LC-FAOD Prevalent Patients** |             |              |              |              |
| % Dx                | 71%          | 75%          | 78%          | 81%          |
| **LC-FAOD Dx Patients** | 2,599 (63% of Dx) | 2,821 (63% of Dx) | 3,090 (63% of Dx) | 3,445 (63% of Dx) |
| % Asymptomatic      | 122 (41% of Total Dx) | 128 (41% of Total Dx) | 131 (42% of Total Dx) | 135 (43% of Total Dx) |
| % Mild              | 282 (20% of Total Dx) | 293 (20% of Total Dx) | 298 (20% of Total Dx) | 309 (20% of Total Dx) |
| % Moderate          | 444 (23% of Total Dx) | 456 (23% of Total Dx) | 464 (23% of Total Dx) | 480 (23% of Total Dx) |
| % Severe            | 594 (41% of Total Dx) | 607 (41% of Total Dx) | 618 (41% of Total Dx) | 638 (41% of Total Dx) |
| **LC-FAOD Dx Adults** | 1,157 (45% of Dx) | 1,337 (47% of Dx) | 1,578 (51% of Dx) | 2,030 (57% of Dx) |
| % Asymptomatic      | 73 (6% of Total Adult Dx) | 93 (7% of Total Adult Dx) | 123 (8% of Total Adult Dx) | 182 (9% of Total Adult Dx) |
| % Mild              | 276 (24% of Total Adult Dx) | 316 (24% of Total Adult Dx) | 373 (24% of Total Adult Dx) | 488 (24% of Total Adult Dx) |
| % Moderate          | 499 (43% of Total Adult Dx) | 550 (41% of Total Adult Dx) | 619 (39% of Total Adult Dx) | 750 (37% of Total Adult Dx) |
| % Severe            | 310 (27% of Total Adult Dx) | 378 (28% of Total Adult Dx) | 462 (29% of Total Adult Dx) | 609 (30% of Total Adult Dx) |
| **LC-FAOD Dx Total (Ped + Adults)** | 2,599 (100% of Dx) | 2,821 (100% of Dx) | 3,090 (100% of Dx) | 3,591 (100% of Dx) |
| % Asymptomatic      | 195 (8% of Total Ped+Adult Dx) | 222 (8% of Total Ped+Adult Dx) | 254 (8% of Total Ped+Adult Dx) | 317 (9% of Total Ped+Adult Dx) |
| % Mild              | 558 (21% of Total Ped+Adult Dx) | 609 (22% of Total Ped+Adult Dx) | 672 (22% of Total Ped+Adult Dx) | 797 (22% of Total Ped+Adult Dx) |
| % Moderate          | 943 (36% of Total Ped+Adult Dx) | 1,006 (36% of Total Ped+Adult Dx) | 1,084 (35% of Total Ped+Adult Dx) | 1,230 (34% of Total Ped+Adult Dx) |
| % Severe            | 903 (35% of Total Ped+Adult Dx) | 985 (35% of Total Ped+Adult Dx) | 1,080 (35% of Total Ped+Adult Dx) | 1,247 (35% of Total Ped+Adult Dx) |

*Dx* diagnosis, *Ped* pediatric
### High mortality 200% (US)

|                      | 2021           | 2025           | 2030           | 2040           |
|----------------------|----------------|----------------|----------------|----------------|
| LC-FAOD Prevalent Patients |                |                |                |                |
| % Dx                 | 73%            | 77%            | 81%            | 83%            |
| LC-FAOD Dx Patients  | 1,581          | 1,743          | 1,932          | 2,169          |
| % Asymptomatic       | 122 (11% of Total Ped Dx) | 128 (11% of Total Ped Dx) | 131 (11% of Total Ped Dx) | 135 (11% of Total Ped Dx) |
| % Mild               | 278 (24% of Total Ped Dx) | 289 (24% of Total Ped Dx) | 295 (24% of Total Ped Dx) | 305 (24% of Total Ped Dx) |
| % Moderate           | 380 (33% of Total Ped Dx) | 391 (33% of Total Ped Dx) | 399 (33% of Total Ped Dx) | 411 (33% of Total Ped Dx) |
| % Severe             | 377 (33% of Total Ped Dx) | 388 (32% of Total Ped Dx) | 396 (32% of Total Ped Dx) | 405 (32% of Total Ped Dx) |
| LC-FAOD Dx Adults    |                |                |                |                |
| % Asymptomatic       | 69 (16% of Total Adult Dx) | 90 (16% of Total Adult Dx) | 120 (17% of Total Adult Dx) | 179 (18% of Total Adult Dx) |
| % Mild               | 200 (47% of Total Adult Dx) | 243 (44% of Total Adult Dx) | 304 (43% of Total Adult Dx) | 426 (42% of Total Adult Dx) |
| % Moderate           | 133 (31% of Total Adult Dx) | 172 (32% of Total Adult Dx) | 224 (31% of Total Adult Dx) | 313 (31% of Total Adult Dx) |
| % Severe             | 23 (5% of Total Adult Dx) | 43 (8% of Total Adult Dx) | 64 (9% of Total Adult Dx) | 89 (9% of Total Adult Dx) |
| LC-FAOD Dx Total (Ped + Adults) | 1,581 (100% of Dx) | 1,743 (100% of Dx) | 1,932 (100% of Dx) | 2,263 (100% of Dx) |
| % Asymptomatic       | 191 (12% of Total Ped+Adult Dx) | 218 (13% of Total Ped+Adult Dx) | 251 (13% of Total Ped+Adult Dx) | 315 (14% of Total Ped+Adult Dx) |
| % Mild               | 478 (30% of Total Ped+Adult Dx) | 532 (31% of Total Ped+Adult Dx) | 599 (31% of Total Ped+Adult Dx) | 730 (32% of Total Ped+Adult Dx) |
| % Moderate           | 512 (32% of Total Ped+Adult Dx) | 563 (32% of Total Ped+Adult Dx) | 623 (32% of Total Ped+Adult Dx) | 724 (32% of Total Ped+Adult Dx) |
| % Severe             | 399 (25% of Total Ped+Adult Dx) | 430 (25% of Total Ped+Adult Dx) | 459 (24% of Total Ped+Adult Dx) | 494 (22% of Total Ped+Adult Dx) |

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