Supplement 2. Characteristics, tuberculosis screening results, and outcomes of 300 severely malnourished hospitalized Malawian children evaluated for pulmonary tuberculosis by Xpert/culture and NIH clinical case definitions

|                                      |                      |              | NIH clinical case definitions |             |                         |              |             |              |                           |              |
|--------------------------------------|----------------------|--------------|-------------------------------|-------------|-------------------------|--------------|-------------|--------------|---------------------------|--------------|
|                                      | Total<br>N = 300 (%) |              | Confirmed TB<br>N = 2 (%)     |             | Probable TB Possible TB |              |             |              | Unlikely TB<br>N = 81 (%) |              |
|                                      |                      |              |                               |             | N = 20 (%)              |              | N = 197 (%) |              |                           |              |
| Baseline Demographics                |                      |              |                               |             |                         |              |             |              |                           |              |
| <u>Gender</u>                        | 4.46                 | (40.7)       |                               | (50.0)      | 42                      | (60.0)       | 00          | (50.2)       | 2.4                       | (42.0)       |
| Male                                 | 146                  | (48.7)       | 1                             | (50.0)      | 12                      | (60.0)       | 99          | (50.3)       | 34                        | (42.0)       |
| Female                               | 154                  | (51.3)       | 1                             | (50.0)      | 8                       | (40.0)       | 98          | (49.7)       | 47                        | (58.0)       |
| Age in months, median                | 18.5                 | (12.1-25.6)  | 15.5                          | (11.2-19.9) | 15.6                    | (11.0-24.9)  | 18.0        | (12.2-24.2)  | 20.2                      | (13.5-28.2)  |
| (IQR)                                |                      |              |                               |             |                         |              |             |              |                           |              |
| HIV status <sup>1</sup>              |                      |              |                               |             |                         |              |             |              |                           |              |
| Infected <sup>2</sup>                | 52/295               | (17.6)       | 0                             | (0.0)       | 5                       | (25.0)       | 39/192      | (20.3)       | 8                         | (9.9)        |
| Exposed <sup>3</sup>                 | 35/295               | (11.9)       | 1                             | (50.0)      | 5                       | (25.0)       | 25/192      | (13.0)       | 4                         | (4.9)        |
| Unexposed                            | 208/295              | (70.5)       | 1                             | (50.0)      | 10                      | (50.0)       | 128/192     | (66.7)       | 69                        | (85.2)       |
| Severe malnutrition                  |                      |              |                               |             |                         |              |             |              |                           |              |
| <u>criteria</u>                      |                      |              |                               |             |                         |              |             |              |                           |              |
| WFH z-score $\leq$ -3SD <sup>4</sup> | 61/127               | (48.0)       | 1/1                           | (100.0)     | 7/13                    | (53.8)       | 42/84       | (50.0)       | 12/29                     | (41.4)       |
| WFH z-score, median (IQR)            | -2.9                 | (-3.8, -2.2) | -2.2                          | N/A         | -3.2                    | (-3.7, -2.8) | -3.0        | (-3.7, -2.3) | -2.6                      | (-3.9, -1.8) |
| MUAC <u>&lt;</u> 115 mm              | 193                  | (64.3)       | 2                             | (100.0)     | 14                      | (70.0)       | 131         | (66.5)       | 46                        | (56.8)       |
| Edema                                | 173                  | (57.7)       | 1                             | (50.0)      | 7                       | (35.0)       | 113         | (57.4)       | 52                        | (64.2)       |
| TB Screening                         |                      |              |                               |             |                         |              |             |              |                           |              |
| Clinical signs/symptoms              |                      |              |                               |             |                         |              |             |              |                           |              |
| suggestive of TB                     |                      |              |                               |             |                         |              |             |              |                           |              |
| Severe malnutrition <sup>5</sup>     | 300                  | (100.0)      | 2                             | (100.0)     | 20                      | (100.0)      | 197         | (100.0)      | 81                        | (100.0)      |
| Cough ≥ 2 weeks <sup>6</sup>         | 36                   | (12.0)       | 2                             | (100.0)     | 5                       | (25.0)       | 26          | (13.2)       | 3                         | (3.7)        |
| Lethargy/                            | 269/299              | (90.0)       | 2                             | (100.0)     | 17                      | (85.0)       | 177/196     | (90.3)       | 73                        | (90.1)       |
| Reduced playfulness <sup>1</sup>     | ,                    | , ,          |                               |             |                         | , ,          | •           |              |                           |              |
| Fever > 1 week                       | 78                   | (26.0)       | 2                             | (100.0)     | 7                       | (35.0)       | 51          | (25.9)       | 18                        | (22.2)       |
| TB exposure                          |                      |              |                               |             |                         |              |             |              |                           |              |
| Contact <sup>1</sup>                 | 48/297               | (16.2)       | 1                             | (50.0)      | 8                       | (40.0)       | 37/195      | (19.0)       | 2/80                      | (2.5)        |
| $TST \ge 5 \text{ mm}^1$             | 40/287               | (13.9)       | 1                             | (50.0)      | 10/19                   | (52.6)       | 29/189      | (15.3)       | 0/77                      | (0.0)        |
| CXR consistent with TB <sup>1</sup>  | 48/299               | (16.1)       | 2                             | (100.0)     | 20                      | (100.0)      | 26/196      | (13.3)       | 0                         | (0.0)        |
| Outcomes                             |                      |              |                               |             |                         |              |             |              |                           |              |
| Microbiologic                        |                      |              |                               |             |                         |              |             |              |                           |              |
| confirmation                         |                      |              |                               |             |                         |              |             |              |                           |              |
| Smear positive                       | 1                    | (0.3)        | 1                             | (50.0)      | 0                       | (0.0)        | 0           | (0.0)        | 0                         | (0.0)        |
| Culture positive                     | 2                    | (0.7)        | 2                             | (100.0)     | 0                       | (0.0)        | 0           | (0.0)        | 0                         | (0.0)        |
| Xpert positive                       | 3                    | (1.0)        | 2                             | (100.0)     | 0                       | (0.0)        | 1           | (0.5)        | 0                         | (0.0)        |
| Prescribed anti-TB therapy           | 132                  | (44.0)       | 2                             | (100.0)     | 16                      | (80.0)       | 97          | (49.2)       | 17                        | (21.0)       |
| Returned for follow-up               | 134/271              | (49.4)       | 0                             | (0.0)       | 14/19                   | (73.7)       | 85/176      | (48.3)       | 35/74                     | (47.3)       |
| Response to anti-TB                  | 44/58                | (75.9)       | 0                             | (0.0)       | 11/13                   | (84.6)       | 33/44       | (75.0)       | 0/0                       | (0.0)        |
| therapy at follow-up <sup>7,8</sup>  |                      | (73.5)       | 0                             | (0.0)       | 11/13                   | (04.0)       | 33/ 44      | (75.0)       | 0,0                       | (0.0)        |
| <u>Death</u> <sup>9</sup>            | 29                   | (9.7)        | 0                             | (0.0)       | 1                       | (5.0)        | 21          | (10.7)       | 7                         | (8.6)        |
|                                      |                      |              |                               |             |                         |              |             |              |                           |              |

Abbreviations: NIH= National Institutes of Health, TB=tuberculosis, IQR=interquartile range, WFH= weight-for-height, SD= standard deviations, MUAC=mid-upper arm circumference, mm = millimeters, TST=tuberculin skin test, CXR=chest radiograph.

<sup>&</sup>lt;sup>1</sup> N <300 due to missing data.

<sup>&</sup>lt;sup>2</sup> HIV infected includes both confirmed HIV infection (50/300) and presumed severe HIV disease (2/300).

<sup>&</sup>lt;sup>3</sup> Includes 6 children who were HIV-exposed but final status pending due to definitive HIV test result pending or were still breast-feeding

<sup>&</sup>lt;sup>4</sup> Denominator excludes children with edema, per World Health Organization (WHO) guidelines.

<sup>&</sup>lt;sup>5</sup> WHO severe acute malnutrition criteria for children aged 6-60 months: WFH z-score <-3 SD, MUAC <115mm, or bilateral pedal edema

<sup>&</sup>lt;sup>6</sup> Without response to antibiotics

<sup>&</sup>lt;sup>7</sup> Denominator includes only those patients that were started on anti-tuberculosis therapy AND returned for follow-up.

<sup>&</sup>lt;sup>8</sup> Resolution of presenting clinical signs/symptoms suggestive of tuberculosis (cough, lethargy/reduced playfulness, fever) and improvement in weight-for-height, edema, or MUAC.

<sup>&</sup>lt;sup>9</sup> 1 death occurred prior to 6-week follow-up, all others occurred during hospitalization.