**Supplemental Table S1**. Amino acids nutritional content of each oral supplement

| Amino acids (g/100ml) | Ensure® Plus Advance | Ensure® Plus High Protein |
|---|---|---|
| **Essential** | | |
| Histidine | 0.22 | 0.20 |
| Isoleucine | 0.45 | 0.37 |
| Leucine | 0.81 | 0.70 |
| Lysine | 0.68 | 0.57 |
| Methionine | 0.21 | 0.19 |
| Phenylalanine | 0.43 | 0.38 |
| Threonine | 0.41 | 0.33 |
| Tryptophan | 0.12 | 0.10 |
| Valine | 0.52 | 0.46 |
| Arginine | 0.35 | 0.32 |
| **Non-essential** | | |
| Alanine | 0.31 | 0.25 |
| Aspartic acid | 0.34 | 0.27 |
| Cystine | 0.07 | 0.04 |
| Glutamic acid | 0.95 | 0.84 |
| Glycine | 0.20 | 0.17 |
| Proline | 0.82 | 0.75 |
| Serine | 0.49 | 0.44 |
| Tyrosine | 0.42 | 0.39 |
| Asparagine | 0.40 | 0.34 |
| Glutamine | 0.90 | 0.79 |

**Supplemental Table S2.** Amino acid levels and analytical parameters at baseline

| Plasma amino acid concentration (µM) | HMB Group N=22 | HP Group N=21 | p |
|---|---|---|---|
| **phospho-Ser** | 2.50 [2.05;3.90] | 3.20 [2.18;4.31] | 0.474 |
| **Taurine** | 64.1 [53.4;81.3] | 72.7 [51.2;88.3] | 0.955 |
| **Asp** | 26.0 [21.4;35.5] | 30.3 [24.0;39.5] | 0.320 |
| **Thr** | 132 [102;172] | 133 [107;166] | 0.696 |
| **Ser** | 147 [129;171] | 161 [108;180] | 0.566 |
| **Asn** | 72.9 [59.2;80.1] | 74.6 [57.1;85.0] | 0.696 |
| **Glu** | 134 [118;184] | 182 [151;269] | 0.152 |
| **Gln** | 317 [224;390] | 308 [262;372] | 0.958 |
| **Aminoadipic acid** | 3.42 [2.92;4.33] | 4.08 [3.55;4.38] | 0.241 |
| **Gly** | 275 [258;295] | 277 [227;322] | 0.953 |
| **Ala** | 267 [216;340] | 331 [283;442] | 0.068 |
| **Citrulline** | 41.0 [30.1;50.2] | 42.5 [37.2;50.8] | 0.726 |
| **Aminobutyric acid** | 14.7 [9.50;19.3] | 15.4 [13.6;21.8] | 0.241 |
| **Val** | 144 [109;191] | 191 [160;253] | 0.051 |
| **Cystine** | 1.64 [0.59;2.77] | 1.54 [0.78;5.19] | 0.412 |
| **Met** | 30.8 [25.8;45.9] | 36.8 [27.8;42.6] | 0.389 |
| **Ile** | 53.3 [47.7;59.9] | 62.6 [49.6;71.9] | 0.163 |
| **Leu** | 92.4 [76.7;117] | 117 [95.5;137] | **0.047** |
| **Tyr** | 101 [73.1;129] | 104 [91.5;130] | 0.554 |
| **β-Ala** | 3.49 [1.57;4.50] | 2.60 [1.09;4.53] | 0.666 |
| **Phe** | 81.5 [72.8;94.2] | 102 [78.2;122] | 0.070 |
| **Ethanolamine** | 15.5 [11.7;22.9] | 20.1 [15.9;22.5] | 0.141 |
| **Ornithine** | 99.0 [71.3;110] | 89.2 [78.8;131] | 0.678 |
| **Lys** | 150 [113;170] | 180 [132;195] | 0.141 |
| **1-Methylhistidine** | 12.3 [8.41;25.3] | 11.7 [7.48;25.3] | 0.626 |
| **His** | 87.1 [74.9;92.7] | 90.3 [80.1;100] | 0.209 |
| **Trp** | 35.6 [30.8;45.6] | 51.3 [33.2;67.2] | **0.046** |
| **3-Methylhistidine** | 5.38 [4.17;8.66] | 6.51 [3.96;8.95] | 0.882 |
| **Arg** | 114 [103;150] | 133 [95.3;152] | 0.566 |
| **Hyp** | 17.0 [11.8;22.6] | 15.1 [9.42;23.2] | 0.687 |
| **Pro** | 228 [153;258] | 237 [170;278] | 0.414 |
| **BCAA** | 300 [244;361] | 370 [297;462] | 0.060 |
| **AAA** | 234 [188;265] | 270 [190;324] | 0.110 |
| **Fischer ratio** | 1.59 [1.32;2.43] | 1.80 [1.43;2.21] | 0.514 |
| **Gln/Glu ratio** | 2.16 [1.15;3.32] | 1.63 [1.10;2.79] | 0.267 |

HMB: ß-Hydroxy-ß-methylbutyrate, HP: High Protein, BCAA: branched chain amino acids, AAA: aromatic amino acids.

**Supplemental Table S3**. Amino acid levels (median) during follow-up

| | HMB Group | | | HP Group | | |
|---|---|---|---|---|---|---|
| | **Baseline** | **6 weeks** | **12 weeks** | **Baseline** | **6 weeks** | **12 weeks** |
| **Phospho-Ser** | 2.50 [2.05;3.90] | 3.30 [2.60;4.28] | 3.26 [1.92;3.64] | 3.20 [2.18;4.31] | 3.52 [2.40;4.16] | 3.23 [2.36;4.86] |
| **Taurine** | 64.1 [53.4;81.3] | 57.1 [52.4;77.2] | 79.0 [55.8;88.7] | 72.7 [51.2;88.3] | 75.0 [66.1;113] | 85.0 [65.2;95.6] |
| **Asp** | 26.0 [21.4;35.5] | 37.1 [19.8;44.5] | 32.0 [24.8;39.1] | 30.3 [24.0;39.5] | 40.2 [27.4;44.3] | 35.8 [28.6;41.8] |
| **Thr** | 132 [102;172] | 120 [106;182] | 144 [122;163] | 133 [107;166] | 156 [132;163] | 171 [136;193] |
| **Ser** | 147 [129;171] | 152 [138;185] | 166 [146;174] | 161 [108;180] | 165 [150;185] | 171 [140;182] |
| **Asn** | 72.9 [59.2;80.1] | 66.7 [60.5;88.9] | 70.2 [67.7;84.9] | 74.6 [57.1;85.0] | 77.2 [71.4;91.1] | 82.0 [67.7;91.2] |
| **Glu** | 134 [118;184] | 223 [170;302] | 180 [142;235] | 182 [151;269] | 190 [118;252] | 212 [178;249] |
| **Gln** | 317 [224;390] | 284 [227;348] | 322 [215;344] | 308 [262;372] | 315 [264;400] | 332 [275;381] |
| **Aminoadipic acid** | 3.42 [2.92;4.33] | 3.56 [2.20;3.84] | 4.60 [3.34;5.75] | 4.08 [3.55;4.38] | 3.90 [1.84;4.63] | 4.44 [2.73;5.05] |
| **Gly** | 275 [258;295] | 280 [263;334] | 300 [263;330] | 277 [227;322] | 292 [259;308] | 289 [270;316] |
| **Ala** | 267 [216;340] | 371 [268;464] | 360 [332;427] | 331 [283;442] | 392 [332;476] | 391 [302;428] |
| **Citrulline** | 41.0 [30.1;50.2] | 43.5 [32.7;49.1] | 44.0 [38.0;51.4] | 42.5 [37.2;50.8] | 49.7 [45.1;60.2] | 50.7 [44.7;61.6] |
| **Aminobutyric acid** | 14.7 [9.50;19.3] | 16.0 [11.8;21.1] | 16.3 [12.4;19.7] | 15.4 [13.6;21.8] | 14.1 [10.9;23.5] | 14.8 [12.0;19.0] |
| **Val** | 144 [109;191] | 199 [180;245] | 194 [161;210] | 191 [160;253] | 220 [173;244] | 215 [167;237] |
| **Cystine** | 1.64 [0.59;2.77] | 2.30 [0.99;4.53] | 1.25 [0.84;3.68] | 1.54 [0.78;5.19] | 1.03 [0.00;2.24] | 0.65 [0.00;2.97] |
| **Met** | 30.8 [25.8;45.9] | 32.5 [24.6;50.2] | 36.5 [27.4;48.6] | 36.8 [27.8;42.6] | 41.5 [36.3;49.3] | 35.5 [33.2;46.0] |
| **Ile** | 53.3 [47.7;59.9] | 63.1 [56.7;72.8] | 61.9 [52.8;70.9] | 62.6 [49.6;71.9] | 57.9 [50.2;66.2] | 56.3 [49.3;75.5] |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Leu** | 92.4 [76.7;117] | 120 [105;132] | 117 [105;130] | 117 [95.5;137] | 116 [102;134] | 118 [93.9;140] |
| **Tyr** | 101 [73.1;129] | 119 [74.0;150] | 118 [80.5;137] | 104 [91.5;130] | 131 [110;158] | 106 [98.3;119] |
| **ß-Ala** | 3.49 [1.57;4.50] | 3.85 [2.89;6.44] | 4.29 [1.23;7.28] | 2.60 [1.09;4.53] | 3.65 [0.36;5.50] | 5.06 [0.00;6.49] |
| **Phe** | 81.5 [72.8;94.2] | 118 [81.4;128] | 111 [96.6;118] | 102 [78.2;122] | 115 [86.7;129] | 102 [92.6;119] |
| **Ethanolamine** | 15.5 [11.7;22.9] | 15.1 [13.1;19.6] | 15.8 [13.9;19.6] | 20.1 [15.9;22.5] | 19.2 [16.8;30.6] | 20.9 [16.3;24.5] |
| **Ornithine** | 99.0 [71.3;110] | 113 [86.0;144] | 105 [95.3;115] | 89.2 [78.8;131] | 98.7 [84.6;125] | 108 [95.2;121] |
| **Lys** | 150 [113;170] | 171 [144;195] | 173 [133;208] | 180 [132;195] | 181 [153;201] | 179 [143;214] |
| **1.Methylhistidine** | 12.3 [8.41;25.3] | 9.38 [6.14;24.6] | 11.8 [7.34;17.5] | 11.7 [7.48;25.3] | 15.0 [10.1;20.5] | 16.9 [8.55;20.8] |
| **His** | 87.1 [74.9;92.7] | 82.2 [71.4;96.0] | 83.7 [76.3;94.3] | 90.3 [80.1;100] | 89.0 [83.5;99.0] | 87.5 [77.8;101] |
| **Trp** | 35.6 [30.8;45.6] | 47.7 [39.4;59.6] | 48.2 [34.2;61.8] | 51.3 [33.2;67.2] | 59.1 [44.6;62.2] | 56.7 [40.8;64.8] |
| **3-Methylhistidine** | 5.38 [4.17;8.66] | 8.57 [6.75;11.4] | 8.80 [5.41;12.3] | 6.51 [3.96;8.95] | 7.15 [3.67;9.27] | 6.61 [5.28;9.71] |
| **Arg** | 114 [103;150] | 134 [109;153] | 133 [116;155] | 133 [95.3;152] | 130 [111;152] | 129 [116;147] |
| **Hyp** | 17.1 [11.8;22.6] | 18.3 [15.1;24.7] | 17.4 [13.9;27.1] | 15.1 [9.42;23.2] | 15.8 [9.40;20.7] | 16.7 [11.0;24.5] |
| **Pro** | 228 [153;258] | 241 [182;269] | 219 [198;242] | 237 [170;278] | 235 [217;309] | 214 [170;289] |