**Supplemental Table S1.** Metabolites, enzymes, and hormones analyzed from newborn screening blood spots.

| | |
|---|---|
| Free carnitine umol/L (C0) | **Amino Acids (umol/L)** |
| **Acylcarnitines (umol/L)** | Arginine (ARG) |
| Acetylcarnitine (C2) | Argininosuccinate (ASA) |
| Propionylcarnitine (C3) | Citrulline (CIT) |
| Butyrylcarnitine+Isobutyrylcarnitine (C4) | Glycine (GLY) |
| Isovalerylcarnitine+Methylbutyrylcarnitine (C5) | Leucine (LEU) |
| Tiglylcarnitine (C5:1) | Methionine (MET) |
| Hexanoylcarnitine (C6) | Ornithine (ORN) |
| Methylglutarylcarnitine (C6-DC) | Phenylalanine (PHE) |
| Octanoylcarnitine (C8) | Succinylacetone (SUAC) |
| Decanoylcarnitine (C10) | Tyrosine (TYR) |
| Decenoylcarnitine (C10:1) | Valine (VAL) |
| Decadienoylcarnitine (C10:2) | **Enzymes and Hormones** |
| Tetradecanoylcarnitine (C14) | 17-Hydroxyprogesterone (17-OHP- ng/mL) |
| Tetradecenoylcarnitine (C14:1) | Biotinidase (U/dL) |
| 3-Hydroxytetradecanoylcarnitine (C14-OH) | Galactose-1-phosphate uridyl transferase (GALT- U/gHb) |
| Palmitoylcarnitine (C16) | Thyroid Stimulating Hormone (TSH- U/mL) |
| Palmitoleylcarnitine (C16:1) | |
| 3-Hydroxypalmitoylcarnitine (C16-OH) | |
| Stearoylcarnitine (C18) | |
| Oleoylcarnitine (C18:1) | |
| 3-Hydroxyoleoylcarnitine (C18:1-OH) | |
| Linoleoylcarnitine (C18:2) | |

**Supplemental Table S2.** Correlation between carnitine (acyl and free) values.

| | C0 | C2 | C3 | C4 | C5 | C5:1 | C6 | C6-DC | C8 | C10 | C10:1 | C10:2 | C14 | C14:1 | C14-OH | C16 | C16:1 | C16-OH | C18 | C18:1 | C18:1-OH | C18:2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **C0** | -- | 0.62 | 0.57 | 0.35 | 0.43 | 0.12 | 0.24 | 0.05 | 0.14 | 0.04 | 0.13 | 0.09 | 0.31 | -0.03 | -0.04 | 0.38 | 0.32 | 0.03 | 0.42 | 0.55 | 0.36 | 0.56 |
| **C2** | | -- | 0.58 | 0.44 | 0.30 | 0.16 | 0.47 | 0.28 | 0.37 | 0.33 | 0.14 | 0.03 | 0.62 | 0.39 | 0.30 | 0.72 | 0.65 | 0.39 | 0.59 | 0.66 | 0.49 | 0.25 |
| **C3** | | | -- | 0.47 | 0.43 | 0.21 | 0.32 | 0.11 | 0.13 | 0.06 | 0.05 | 0.05 | 0.39 | 0.16 | 0.05 | 0.45 | 0.42 | 0.14 | 0.36 | 0.44 | 0.29 | 0.32 |
| **C4** | | | | -- | 0.57 | 0.21 | 0.45 | 0.14 | 0.29 | 0.23 | 0.09 | 0.10 | 0.45 | 0.29 | 0.20 | 0.43 | 0.40 | 0.29 | 0.38 | 0.39 | 0.31 | 0.16 |
| **C5** | | | | | -- | 0.18 | 0.35 | 0.02 | 0.17 | 0.06 | 0.12 | 0.18 | 0.22 | <-0.01 | -0.01 | 0.18 | 0.07 | 0.04 | 0.26 | 0.28 | 0.15 | 0.37 |
| **C5:1** | | | | | | -- | 0.15 | 0.13 | 0.13 | 0.11 | 0.07 | 0.08 | 0.17 | 0.12 | 0.14 | 0.16 | 0.13 | 0.15 | 0.11 | 0.08 | 0.11 | 0.03 |
| **C6** | | | | | | | -- | 0.31 | 0.70 | 0.61 | 0.36 | 0.13 | 0.56 | 0.47 | 0.39 | 0.46 | 0.44 | 0.45 | 0.40 | 0.35 | 0.40 | 0.02 |
| **C6-DC** | | | | | | | | -- | 0.39 | 0.46 | 0.29 | 0.15 | 0.36 | 0.44 | 0.40 | 0.30 | 0.40 | 0.37 | 0.12 | 0.18 | 0.27 | -0.23 |
| **C8** | | | | | | | | | -- | 0.87 | 0.49 | 0.15 | 0.58 | 0.64 | 0.59 | 0.40 | 0.49 | 0.55 | 0.28 | 0.26 | 0.41 | -0.15 |
| **C10** | | | | | | | | | | -- | 0.45 | 0.11 | 0.62 | 0.77 | 0.70 | 0.41 | 0.55 | 0.63 | 0.26 | 0.23 | 0.42 | -0.29 |
| **C10:1** | | | | | | | | | | | -- | 0.33 | 0.19 | 0.24 | 0.22 | 0.09 | 0.10 | 0.16 | 0.05 | 0.08 | 0.14 | 0.12 |
| **C10:2** | | | | | | | | | | | | -- | 0.02 | 0.01 | 0.02 | -0.01 | -0.03 | 0.02 | -0.05 | <-0.01 | <-0.01 | 0.11 |
| **C14** | | | | | | | | | | | | | -- | 0.79 | 0.67 | 0.80 | 0.84 | 0.74 | 0.57 | 0.54 | 0.60 | -0.02 |
| **C14:1** | | | | | | | | | | | | | | -- | 0.82 | 0.54 | 0.76 | 0.79 | 0.31 | 0.30 | 0.50 | -0.37 |
| **C14-OH** | | | | | | | | | | | | | | | -- | 0.45 | 0.61 | 0.75 | 0.26 | 0.21 | 0.46 | -0.36 |
| **C16** | | | | | | | | | | | | | | | | -- | 0.82 | 0.60 | 0.74 | 0.66 | 0.57 | 0.06 |
| **C16:1** | | | | | | | | | | | | | | | | | -- | 0.69 | 0.49 | 0.57 | 0.59 | -0.12 |
| **C16-OH** | | | | | | | | | | | | | | | | | | -- | 0.36 | 0.28 | 0.52 | -0.32 |
| **C18** | | | | | | | | | | | | | | | | | | | -- | 0.84 | 0.64 | 0.34 |
| **C18:1** | | | | | | | | | | | | | | | | | | | | -- | 0.68 | 0.47 |
| **C18:1-OH** | | | | | | | | | | | | | | | | | | | | | -- | 0.12 |
| **C18:2** | | | | | | | | | | | | | | | | | | | | | | -- |

| **Cell Legend:** | **Spearman Correlation Coefficient** |
|---|---|
| **Correlation Color Code** | |
| r ≤-0.7 | Negative |
| ≥-0.7 r <-0.5 | Negative |
| ≥-0.5 r <-0.3 | Negative |
| ≥-0.3 r <0 | Negative |
| >0 r <0.3 | Positive |
| ≥0.3 r <0.5 | Positive |
| ≥0.5 r <0.7 | Positive |
| r ≥0.7 | Positive |

**Supplemental Table S3.** Comparison of newborn screening metabolites between number of wheezing episodes in the past 12 months for the 1-year study visit.

| Metabolite | No Wheezing Episodes Median (IQR) | 1-3 Wheezing Episodes Median (IQR) | 4-12 Wheezing Episodes Median (IQR) | >12 Wheezing Episodes Median (IQR) | OR (95% CI) | p-value |
|---|---|---|---|---|---|---|
| **Sample Size**[‡] | **1,291 (73.3%)** | **353 (20.1%)** | **85 (4.8%)** | **32 (1.8%)** | | |
| Free carnitine (C0) | 18.00 (13.84-23.00) | 18.20 (14.19-22.81) | 19.02 (14.63-23.97) | 21.45 (15.31-25.40) | 1.22 (0.92-1.61) | 0.166 |
| Total carnitine (TC) | 47.01 (38.29-58.16) | 47.41 (39.69-58.07) | 47.29 (39.79-56.84) | 51.72 (37.41-58.47) | 1.09 (0.78-1.52) | 0.616 |
| **Acylcarnitines** | | | | | | |
| Short-chain (SC) | 0.49 (0.45-0.53) | 0.49 (0.46-0.53) | 0.48 (0.45-0.52) | 0.47 (0.45-0.51) | 0.69 (0.34-1.43) | 0.321 |
| C2 | 21.33 (16.95-27.00) | 21.25 (17.14-26.60) | 20.50 (16.86-26.00) | 20.79 (15.44-26.00) | 0.98 (0.74-1.29) | 0.858 |
| C3 | 1.41 (1.06-1.84) | 1.46 (1.17-1.91) | 1.41 (1.09-1.82) | 1.42 (1.13-1.83) | 1.32 (1.02-1.72) | 0.036* |
| C4 | 0.21 (0.17-0.26) | 0.21 (0.17-0.28) | 0.20 (0.16-0.25) | 0.21 (0.17-0.27) | 1.09 (0.82-1.45) | 0.551 |
| C5 | 0.08 (0.06-0.10) | 0.09 (0.07-0.11) | 0.08 (0.07-0.11) | 0.09 (0.07-0.12) | 1.42 (1.07-1.89) | 0.016* |
| C5:1 | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 1.42 (0.42-4.81) | 0.574 |
| Medium-chain (MC) | 0.005 (0.004-0.007) | 0.005 (0.004-0.007) | 0.005 (0.004-0.006) | 0.005 (0.004-0.006) | 1.03 (0.77-1.38) | 0.844 |
| C6 | 0.04 (0.04-0.06) | 0.05 (0.04-0.06) | 0.05 (0.04-0.05) | 0.05 (0.03-0.05) | 1.20 (0.89-1.62) | 0.244 |
| C6-DC | 0.10 (0.08-0.12) | 0.10 (0.08-0.13) | 0.10 (0.08-0.12) | 0.10 (0.08-0.12) | 1.40 (1.00-1.96) | 0.053 |
| C8 | 0.06 (0.05-0.07) | 0.06 (0.05-0.07) | 0.06 (0.05-0.08) | 0.06 (0.04-0.08) | 1.11 (0.84-1.47) | 0.476 |
| C10 | 0.08 (0.06-0.11) | 0.08 (0.06-0.11) | 0.08 (0.06-0.11) | 0.10 (0.06-0.11) | 0.96 (0.75-1.22) | 0.733 |
| C10:1 | 0.05 (0.04-0.06) | 0.05 (0.04-0.06) | 0.05 (0.04-0.06) | 0.05 (0.04-0.06) | 1.37 (0.94-2.00) | 0.100 |
| C10:2 | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 1.82 (0.97-3.42) | 0.061 |
| Long-chain (LC) | 0.12 (0.10-0.13) | 0.11 (0.10-0.13) | 0.11 (0.10-0.13) | 0.11 (0.09-0.12) | 0.76 (0.48-1.21) | 0.255 |
| C14 | 0.22 (0.17-0.27) | 0.22 (0.18-0.27) | 0.21 (0.17-0.26) | 0.21 (0.16-0.23) | 1.05 (0.78-1.42) | 0.736 |
| C14:1 | 0.13 (0.09-0.17) | 0.12 (0.09-0.17) | 0.12 (0.09-0.16) | 0.10 (0.07-0.14) | 0.91 (0.73-1.14) | 0.412 |
| C14-OH | 0.02 (0.01-0.02) | 0.01 (0.01-0.02) | 0.01 (0.01-0.02) | 0.01 (0.01-0.02) | 0.88 (0.69-1.12) | 0.301 |
| C16 | 2.83 (2.27-3.46) | 2.80 (2.23-3.42) | 2.68 (2.24-3.45) | 2.39 (2.03-2.94) | 0.89 (0.67-1.17) | 0.400 |
| C16:1 | 0.21 (0.16-0.27) | 0.21 (0.16-0.27) | 0.20 (0.15-0.26) | 0.18 (0.13-0.22) | 0.94 (0.75-1.18) | 0.586 |
| C16-OH | 0.02 (0.02-0.03) | 0.02 (0.02-0.03) | 0.02 (0.02-0.02) | 0.02 (0.01-0.02) | 0.88 (0.69-1.14) | 0.333 |
| C18 | 0.78 (0.62-0.96) | 0.76 (0.60-0.97) | 0.76 (0.63-0.87) | 0.73 (0.56-0.97) | 0.93 (0.68-1.27) | 0.649 |
| C18:1 | 1.15 (0.93-1.42) | 1.17 (0.92-1.42) | 1.15 (0.95-1.38) | 1.17 (0.86-1.43) | 1.08 (0.79-1.47) | 0.629 |
| C18:1-OH | 0.02 (0.01-0.02) | 0.02 (0.01-0.02) | 0.02 (0.01-0.02) | 0.02 (0.01-0.02) | 0.97 (0.74-1.28) | 0.836 |
| C18:2 | 0.15 (0.11-0.22) | 0.17 (0.12-0.24) | 0.16 (0.13-0.22) | 0.20 (0.12-0.27) | 1.38 (1.12-1.71) | 0.003* |
| Total hydroxy (total OH) | 0.05 (0.04-0.07) | 0.05 (0.04-0.07) | 0.05 (0.04-0.06) | 0.05 (0.04-0.06) | 0.91 (0.68-1.22) | 0.538 |
| **Amino Acids** | | | | | | |
| Arginine (ARG) | 8.0 (6.0-11.0) | 8.0 (5.0-11.0) | 9.0 (6.0-12.0) | 9.0 (6.0-15.0) | 1.01 (0.83-1.24) | 0.911 |
| Argininosuccinate (ASA) | 0.06 (0.05-0.08) | 0.07 (0.05-0.09) | 0.07 (0.05-0.09) | 0.06 (0.05-0.08) | 1.38 (1.06-1.79) | 0.017* |
| Citrulline (CIT) | 12.0 (10.0-15.0) | 12.0 (10.0-15.0) | 12.0 (10.0-15.0) | 12.0 (8.0-17.0) | 0.85 (0.59-1.24) | 0.405 |
| Glycine (GLY) | 382.0 (328.0-440.0) | 387.0 (337.0-449.0) | 381.0 (324.0-462.0) | 387.0 (299.0-486.0) | 1.33 (0.85-2.07) | 0.211 |
| Leucine (LEU) | 88.0 (76.0-103.0) | 91.0 (78.0-107.0) | 92.0 (76.0-106.0) | 91.0 (79.0-114.0) | 1.76 (1.14-2.73) | 0.011* |
| Methionine (MET) | 19.0 (16.0-22.0) | 19.0 (16.0-22.0) | 19.0 (17.0-22.0) | 19.0 (16.0-24.0) | 1.13 (0.73-1.74) | 0.595 |
| Ornithine (ORN) | 65.0 (55.0-81.0) | 67.0 (56.0-81.0) | 68.0 (55.0-86.0) | 74.5 (53.0-91.0) | 1.34 (0.93-1.92) | 0.118 |
| Phenylalanine (PHE) | 49.0 (44.0-55.0) | 50.0 (44.0-56.0) | 48.0 (42.0-56.0) | 47.0 (43.0-53.0) | 1.31 (0.64-1.99) | 0.668 |
| Succinylacetone (SUAC) | 0.39 (0.34-0.46) | 0.40 (0.35-0.47) | 0.41 (0.35-0.47) | 0.41 (0.33-0.48) | 1.39 (0.90-2.14) | 0.135 |
| Tyrosine (TYR) | 78.0 (62.0-98.0) | 79.0 (62.0-99.0) | 74.0 (55.0-100.0) | 74.0 (61.0-106.0) | 0.92 (0.69-1.22) | 0.561 |
| Valine (VAL) | 85.0 (72.0-100.5) | 87.0 (74.0-103.0) | 86.0 (69.0-104.0) | 91.5 (76.0-103.0) | 1.25 (0.82-1.89) | 0.301 |
| **Enzymes and Hormones** | | | | | | |
| 17-OHP | 6.0 (4.0-8.0) | 6.0 (4.0-8.0) | 6.0 (4.0-8.0) | 6.0 (3.0-7.0) | 0.98 (0.79-1.22) | 0.853 |
| Biotinidase | 128.0 (107.0-149.0) | 125.0 (107.0-148.0) | 133.0 (112.0-158.0) | 137.0 (112.0-157.0) | 1.06 (0.72-1.57) | 0.769 |
| GALT | 209.8 (154.0-271.8) | 199.9 (148.9-266.5) | 211.5 (150.2-260.5) | 177.3 (131.6-234.5) | 0.82 (0.64-1.05) | 0.122 |
| TSH | 8.0 (5.0-11.0) | 8.0 (5.0-12.0) | 9.0 (6.0-13.0) | 7.0 (5.0-10.0) | 1.09 (0.92-1.29) | 0.310 |

IQR= Interquartile range (Q1 (25%)- Q3 (75%))

Odds ratios and p-values were estimated using separate ordinal logistic regression models.

[‡] n=1,761 (90.3% of baseline population) responded to questions pertaining to the wheezing outcome on the 1-year INSPIRE questionnaire.

*Marginally significant ($0.001 < \alpha < 0.05$); **Significant (Bonferroni correction<0.001)

NOTE: Median (IQR) were calculated using non-transformed variables. Ordinal logistic regression was performed using log-transformed variables.

**Supplemental Table S4.** Comparison of newborn screening metabolites between number of wheezing episodes in the past 12 months for the 2-year study visit.

| Metabolite | No Wheezing Episodes Median (IQR) | 1-3 Wheezing Episodes Median (IQR) | 4-12 Wheezing Episodes Median (IQR) | >12 Wheezing Episodes Median (IQR) | OR (95% CI) | p-value |
|---|---|---|---|---|---|---|
| **Sample Size**[‡] | **1,278 (76.4%)** | **293 (17.5%)** | **84 (5.0%)** | **18 (1.1%)** | | |
| Free carnitine (C0) | 18.11 (13.89-22.66) | 18.36 (14.28-24.32) | 18.08 (13.74-23.21) | 21.17 (16.90-29.16) | 1.28 (0.95-1.72) | 0.108 |
| Total carnitine (TC) | 46.97 (38.55-57.89) | 47.38 (39.81-58.46) | 50.14 (37.00-57.17) | 52.22 (43.17-66.33) | 1.17 (0.82-1.67) | 0.390 |
| **Acylcarnitines** | | | | | | |
| Short-chain (SC) | 0.49 (0.46-0.53) | 0.49 (0.46-0.52) | 0.49 (0.45-0.52) | 0.47 (0.41-0.53) | 0.59 (0.28-1.27) | 0.177 |
| C2 | 21.24 (17.0-26.86) | 21.25 (17.00-26.83) | 20.60 (16.86-27.45) | 22.73 (15.62-30.00) | 1.02 (0.76-1.38) | 0.890 |
| C3 | 1.42 (1.07-1.82) | 1.47 (1.11-1.94) | 1.37 (1.11-1.84) | 1.16 (0.76-2.03) | 1.12 (0.85-1.47) | 0.441 |
| C4 | 0.21 (0.17-0.26) | 0.20 (0.16-0.27) | 0.22 (0.16-0.29) | 0.20 (0.17-0.27) | 1.11 (0.82-1.50) | 0.508 |
| C5 | 0.08 (0.06-0.11) | 0.08 (0.07-0.11) | 0.08 (0.07-0.12) | 0.11 (0.08-0.15) | 1.45 (1.07-1.96) | 0.017* |
| C5:1 | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 0.68 (0.18-2.52) | 0.562 |
| Medium-chain (MC) | 0.005 (0.004-0.007) | 0.005 (0.004-0.007) | 0.006 (0.004-0.007) | 0.005 (0.004-0.006) | 1.00 (0.74-1.37) | 0.986 |
| C6 | 0.04 (0.04-0.05) | 0.04 (0.03-0.05) | 0.05 (0.04-0.06) | 0.05 (0.04-0.06) | 1.14 (0.83-1.57) | 0.428 |
| C6-DC | 0.10 (0.08-0.12) | 0.10 (0.08-0.12) | 0.10 (0.07-0.12) | 0.09 (0.07-0.12) | 0.97 (0.68-1.39) | 0.875 |
| C8 | 0.06 (0.05-0.07) | 0.06 (0.04-0.07) | 0.06 (0.05-0.08) | 0.06 (0.05-0.07) | 1.16 (0.86-1.57) | 0.323 |
| C10 | 0.08 (0.06-0.11) | 0.08 (0.06-0.11) | 0.08 (0.06-0.11) | 0.10 (0.06-0.10) | 0.97 (0.75-1.25) | 0.799 |
| C10:1 | 0.05 (0.04-0.06) | 0.05 (0.04-0.06) | 0.05 (0.04-0.07) | 0.06 (0.06-0.06) | 2.11 (1.41-3.17) | $3.18 \times 10^{-4}$** |
| C10:2 | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 2.64 (1.38-5.08) | 0.004* |
| Long-chain (LC) | 0.12 (0.10-0.13) | 0.11 (0.10-0.13) | 0.12 (0.10-0.13) | 0.11 (0.09-0.12) | 0.75 (0.46-1.23) | 0.259 |
| C14 | 0.22 (0.17-0.27) | 0.22 (0.17-0.27) | 0.21 (0.17-0.27) | 0.22 (0.15-0.23) | 1.00 (0.73-1.38) | 0.991 |
| C14:1 | 0.13 (0.09-0.17) | 0.12 (0.09-0.17) | 0.13 (0.09-0.17) | 0.11 (0.07-0.13) | 0.85 (0.67-1.08) | 0.190 |
| C14-OH | 0.02 (0.01-0.02) | 0.01 (0.01-0.02) | 0.01 (0.01-0.02) | 0.01 (0.01-0.02) | 0.68 (0.52-0.89) | 0.005* |
| C16 | 2.83 (2.29-3.45) | 2.86 (2.20-3.53) | 2.74 (2.20-3.48) | 2.46 (1.76-3.07) | 0.94 (0.70-1.26) | 0.656 |
| C16:1 | 0.21 (0.16-0.27) | 0.21 (0.15-0.27) | 0.19 (0.14-0.27) | 0.17 (0.10-0.23) | 0.86 (0.68-1.08) | 0.183 |
| C16-OH | 0.02 (0.02-0.03) | 0.02 (0.02-0.03) | 0.02 (0.02-0.03) | 0.02 (0.01-0.02) | 0.86 (0.66-1.13) | 0.283 |
| C18 | 0.77 (0.62-0.95) | 0.76 (0.60-0.97) | 0.76 (0.59-0.94) | 0.86 (0.68-1.03) | 0.98 (0.71-1.36) | 0.909 |
| C18:1 | 1.15 (0.92-1.42) | 1.17 (0.96-1.46) | 1.13 (0.84-1.37) | 1.30 (1.16-1.78) | 1.13 (0.81-1.57) | 0.461 |
| C18:1-OH | 0.02 (0.01-0.02) | 0.02 (0.01-0.02) | 0.02 (0.01-0.02) | 0.02 (0.02-0.02) | 0.96 (0.71-1.28) | 0.757 |
| C18:2 | 0.15 (0.11-0.21) | 0.17 (0.12-0.23) | 0.17 (0.11-0.24) | 0.26 (0.18-0.40) | 1.47 (1.17-1.84) | 0.001** |
| Total hydroxy (total OH) | 0.05 (0.04-0.07) | 0.05 (0.04-0.07) | 0.05 (0.04-0.07) | 0.05 (0.04-0.06) | 0.84 (0.62-1.15) | 0.277 |
| **Amino Acids** | | | | | | |
| Arginine (ARG) | 8.0 (5.0-11.0) | 8.0 (6.0-11.0) | 9.0 (6.0-12.0) | 13.0 (7.0-18.0) | 1.36 (1.09-1.69) | 0.006* |
| Argininosuccinate (ASA) | 0.06 (0.05-0.08) | 0.07 (0.05-0.09) | 0.07 (0.05-0.08) | 0.06 (0.04-0.07) | 1.04 (0.79-1.38) | 0.772 |
| Citrulline (CIT) | 12.0 (10.0-15.0) | 12.0 (10.0-14.0) | 12.0 (10.0-15.0) | 12.5 (11.0-15.0) | 0.73 (0.49-1.08) | 0.118 |
| Glycine (GLY) | 384.0 (330.0-440.0) | 382.5 (327.0-459.0) | 380.0 (329.0-452.0) | 381.0 (299.0-473.0) | 1.26 (0.78-2.02) | 0.344 |
| Leucine (LEU) | 89.0 (76.0-104.0) | 91.0 (78.0-106.0) | 91.0 (79.0-106.0) | 113.5 (89.0-135.0) | 1.52 (0.96-2.41) | 0.078 |
| Methionine (MET) | 19.0 (16.0-22.0) | 19.0 (16.0-22.0) | 20.0 (17.0-23.0) | 20.5 (18.0-25.0) | 1.29 (0.81-2.06) | 0.276 |
| Ornithine (ORN) | 66.0 (55.0-82.0) | 68.0 (56.0-80.0) | 66.0 (55.0-85.0) | 78.5 (73.0-107.0) | 1.22 (0.83-1.79) | 0.325 |
| Phenylalanine (PHE) | 49.0 (44.0-55.0) | 48.0 (43.0-54.0) | 48.0 (44.0-56.0) | 51.5 (49.0-57.0) | 0.90 (0.49-1.64) | 0.719 |
| Succinylacetone (SUAC) | 0.39 (0.34-0.45) | 0.39 (0.34-0.46) | 0.40 (0.35-0.45) | 0.35 (0.28-0.44) | 0.95 (0.59-1.52) | 0.829 |
| Tyrosine (TYR) | 78.0 (62.0-98.0) | 78.0 (59.0-100.0) | 76.0 (62.0-98.0) | 101.5 (75.0-111.0) | 0.93 (0.69-1.26) | 0.628 |
| Valine (VAL) | 85.0 (73.0-101.0) | 86.0 (72.0-103.0) | 89.0 (71.0-100.0) | 103.0 (94.0-123.0) | 1.12 (0.72-1.75) | 0.611 |
| **Enzymes and Hormones** | | | | | | |
| 17-OHP | 6.0 (4.0-8.0) | 6.0 (4.0-8.0) | 6.0 (4.0-8.0) | 6.0 (4.0-7.0) | 1.02 (0.81-1.29) | 0.872 |
| Biotinidase | 128.0 (107.0-149.3) | 127.0 (110.0-149.0) | 120.0 (106.0-154.0) | 135.0 (105.0-174.0) | 1.18 (0.77-1.81) | 0.449 |
| GALT | 209.6 (153.7-269.1) | 200.2 (146.6-263.5) | 194.7 (142.9-260.0) | 209.2 (138.5-277.0) | 0.78 (0.60-1.01) | 0.063 |
| TSH | 8.0 (5.0-11.0) | 8.0 (5.0-12.0) | 8.0 (6.0-11.0) | 6.5 (2.0-10.0) | 1.05 (0.88-1.25) | 0.601 |

IQR= Interquartile range (Q1 (25%)- Q3 (75%))

Odds ratios and p-values were estimated using separate ordinal logistic regression models.

[‡] n=1,673 (85.8% of baseline population) responded to questions pertaining to the wheezing outcome on the 2-year INSPIRE questionnaire.

*Marginally significant ($0.001 < \alpha < 0.10$); **Significant (Bonferroni correction<0.001)

NOTE: Median (IQR) were calculated using non-transformed variables. Ordinal logistic regression was performed using log-transformed variables.

**Supplemental Table S5.** Comparison of newborn screening metabolites between number of wheezing episodes in the past 12 months for the 3-year study visit.

| Metabolite | No Wheezing Episodes Median (IQR) | 1-3 Wheezing Episodes Median (IQR) | 4-12 Wheezing Episodes Median (IQR) | >12 Wheezing Episodes Median (IQR) | OR (95% CI) | p-value |
|---|---|---|---|---|---|---|
| **Sample Size**[‡] | **1,063 (79.3%)** | **211 (15.8%)** | **55 (4.1%)** | **11 (0.8%)** | | |
| Free carnitine (C0) | 18.11 (14.07-23.30) | 18.63 (14.18-22.56) | 19.73 (14.46-26.95) | 16.03 (11.71-20.93) | 1.12 (0.79-1.59) | 0.525 |
| Total carnitine (TC) | 47.31 (38.85-58.08) | 48.71 (39.11-57.18) | 53.05 (39.36-66.42) | 45.18 (36.33-55.88) | 1.06 (0.70-1.62) | 0.772 |
| **Acylcarnitines** | | | | | | |
| Short-chain (SC) | 0.49 (0.45-0.53) | 0.49 (0.45-0.53) | 0.50 (0.45-0.53) | 0.51 (0.48-0.54) | 0.75 (0.31-1.80) | 0.519 |
| C2 | 21.50 (17.00-27.10) | 21.42 (16.87-26.64) | 23.75 (16.50-30.45) | 23.09 (16.44-25.13) | 0.99 (0.70-1.40) | 0.943 |
| C3 | 1.43 (1.09-1.85) | 1.38 (1.10-1.83) | 1.48 (0.99-2.11) | 1.62 (1.14-2.01) | 0.93 (0.68-1.28) | 0.669 |
| C4 | 0.21 (0.17-0.26) | 0.20 (0.16-0.26) | 0.21 (0.16-0.25) | 0.26 (0.18-0.28) | 0.86 (0.60-1.23) | 0.412 |
| C5 | 0.08 (0.07-0.11) | 0.09 (0.07-0.11) | 0.09 (0.07-0.12) | 0.08 (0.07-0.13) | 1.42 (1.00-2.01) | 0.053 |
| C5:1 | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 1.36 (0.30-6.28) | 0.693 |
| Medium-chain (MC) | 0.005 (0.004-0.007) | 0.005 (0.004-0.007) | 0.005 (0.004-0.007) | 0.007 (0.005-0.008) | 1.48 (1.03-2.14) | 0.035* |
| C6 | 0.04 (0.04-0.06) | 0.04 (0.03-0.05) | 0.05 (0.04-0.07) | 0.05 (0.03-0.05) | 1.20 (0.82-1.74) | 0.347 |
| C6-DC | 0.10 (0.08-0.12) | 0.10 (0.08-0.12) | 0.10 (0.08-0.14) | 0.11 (0.10-0.15) | 1.32 (0.87-2.01) | 0.199 |
| C8 | 0.06 (0.05-0.07) | 0.06 (0.05-0.08) | 0.07 (0.05-0.08) | 0.06 (0.05-0.08) | 1.46 (1.03-2.09) | 0.036* |
| C10 | 0.08 (0.06-0.11) | 0.09 (0.06-0.12) | 0.10 (0.07-0.12) | 0.09 (0.09-0.12) | 1.39 (1.02-1.89) | 0.037* |
| C10:1 | 0.05 (0.04-0.06) | 0.05 (0.04-0.06) | 0.05 (0.04-0.07) | 0.06 (0.05-0.07) | 2.56 (1.59-4.11) | $1.04 \times 10^{-4}$** |
| C10:2 | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 0.01 (0.01-0.01) | 2.56 (1.27-5.14) | 0.008* |
| Long-chain (LC) | 0.12 (0.10-0.13) | 0.12 (0.10-0.13) | 0.11 (0.09-0.13) | 0.12 (0.11-0.12) | 0.81 (0.46-1.43) | 0.472 |
| C14 | 0.22 (0.17-0.27) | 0.22 (0.18-0.27) | 0.24 (0.18-0.32) | 0.21 (0.20-0.31) | 1.06 (0.73-1.54) | 0.777 |
| C14:1 | 0.13 (0.09-0.17) | 0.13 (0.09-0.18) | 0.16 (0.10-0.19) | 0.17 (0.13-0.28) | 1.15 (0.87-1.53) | 0.329 |
| C14-OH | 0.02 (0.01-0.02) | 0.01 (0.01-0.02) | 0.02 (0.01-0.02) | 0.03 (0.01-0.03) | 1.11 (0.81-1.50) | 0.525 |
| C16 | 2.85 (2.29-3.51) | 2.89 (2.29-3.50) | 3.00 (2.28-3.74) | 2.74 (2.53-3.22) | 0.92 (0.65-1.29) | 0.621 |
| C16:1 | 0.22 (0.16-0.27) | 0.21 (0.16-0.27) | 0.23 (0.16-0.28) | 0.25 (0.19-0.31) | 0.93 (0.71-1.22) | 0.588 |
| C16-OH | 0.02 (0.02-0.03) | 0.02 (0.02-0.03) | 0.02 (0.02-0.03) | 0.03 (0.02-0.04) | 1.15 (0.84-1.60) | 0.385 |
| C18 | 0.77 (0.61-0.96) | 0.78 (0.60-0.96) | 0.76 (0.60-1.06) | 0.68 (0.51-0.81) | 0.98 (0.67-1.43) | 0.901 |
| C18:1 | 1.16 (0.93-1.42) | 1.16 (0.93-1.39) | 1.26 (0.92-1.51) | 0.97 (0.86-1.20) | 0.95 (0.65-1.39) | 0.786 |
| C18:1-OH | 0.02 (0.01-0.02) | 0.02 (0.01-0.02) | 0.02 (0.01-0.02) | 0.02 (0.02-0.02) | 0.95 (0.67-1.33) | 0.754 |
| C18:2 | 0.15 (0.11-0.21) | 0.16 (0.12-0.21) | 0.15 (0.11-0.25) | 0.13 (0.11-0.16) | 1.06 (0.80-1.40) | 0.685 |
| Total hydroxy (total OH) | 0.06 (0.04-0.07) | 0.05 (0.04-0.07) | 0.06 (0.05-0.07) | 0.08 (0.05-0.09) | 1.10 (0.76-1.60) | 0.603 |
| **Amino Acids** | | | | | | |
| Arginine (ARG) | 8.0 (5.0-11.0) | 8.5 (6.0-12.0) | 8.0 (5.0-12.0) | 12.0 (8.0-17.0) | 1.24 (0.97-1.60) | 0.090 |
| Argininosuccinate (ASA) | 0.07 (0.05-0.08) | 0.06 (0.05-0.09) | 0.07 (0.05-0.09) | 0.08 (0.05-0.10) | 1.21 (0.87-1.69) | 0.257 |
| Citrulline (CIT) | 12.0 (10.0-15.0) | 11.5 (10.0-14.5) | 13.0 (11.0-16.0) | 12.5 (11.0-17.0) | 1.13 (0.71-1.81) | 0.601 |
| Glycine (GLY) | 380.0 (325.0-440.0) | 380.5 (321.5-445.5) | 423.0 (366.0-494.0) | 388.5 (355.0-447.0) | 1.57 (0.90-2.76) | 0.114 |
| Leucine (LEU) | 89.0 (76.0-104.0) | 93.0 (76.5-106.0) | 97.0 (79.0-119.0) | 87.0 (77.0-98.0) | 1.69 (0.99-2.90) | 0.055 |
| Methionine (MET) | 19.0 (16.0-22.0) | 20.0 (17.0-23.0) | 19.0 (17.0-22.0) | 20.0 (18.0-29.0) | 2.11 (1.22-3.66) | 0.007* |
| Ornithine (ORN) | 66.0 (55.0-82.0) | 67.0 (56.0-81.0) | 75.0 (60.0-88.5) | 57.0 (54.0-79.0) | 1.35 (0.86-2.13) | 0.190 |
| Phenylalanine (PHE) | 48.0 (43.0-55.0) | 48.5 (42.0-56.0) | 50.0 (46.0-58.0) | 46.5 (45.0-59.0) | 1.37 (0.67-2.81) | 0.390 |
| Succinylacetone (SUAC) | 0.39 (0.34-0.46) | 0.40 (0.34-0.46) | 0.39 (0.36-0.46) | 0.38 (0.32-0.42) | 1.10 (0.64-1.89) | 0.731 |
| Tyrosine (TYR) | 78.0 (62.0-98.0) | 75.5 (61.5-98.0) | 87.0 (68.0-109.0) | 82.5 (74.0-94.0) | 1.07 (0.74-1.53) | 0.728 |
| Valine (VAL) | 86.0 (73.0-101.0) | 86.0 (71.0-104.3) | 92.0 (75.0-112.0) | 84.0 (72.0-92.0) | 1.20 (0.71-2.03) | 0.491 |
| **Enzymes and Hormones** | | | | | | |
| 17-OHP | 6.0 (4.0-8.0) | 6.0 (4.0-8.0) | 6.0 (4.0-7.0) | 6.0 (5.0-7.0) | 0.97 (0.73-1.27) | 0.796 |
| Biotinidase | 127.0 (107.0-148.0) | 126.0 (109.5-149.5) | 124.0 (108.0-144.0) | 140.0 (116.0-184.0) | 1.14 (0.68-1.91) | 0.615 |
| GALT | 209.2 (152.6-269.8) | 204.7 (147.3-256.6) | 193.8 (153.5-268.1) | 234.5 (211.6-286.5) | 0.97 (0.71-1.33) | 0.867 |
| TSH | 8.0 (5.0-11.0) | 8.0 (5.0-11.5) | 8.0 (6.0-11.0) | 8.0 (6.0-14.0) | 1.04 (0.84-1.28) | 0.715 |

IQR= Interquartile range (Q1 (25%)- Q3 (75%))

Odds ratios and p-values were estimated using separate ordinal logistic regression models.

[‡] n=1,340 (68.7% of baseline population) responded to questions pertaining to the wheezing outcome on the 3-year INSPIRE questionnaire.

*Marginally significant ($0.001 < \alpha < 0.05$); **Significant (Bonferroni correction<0.001)

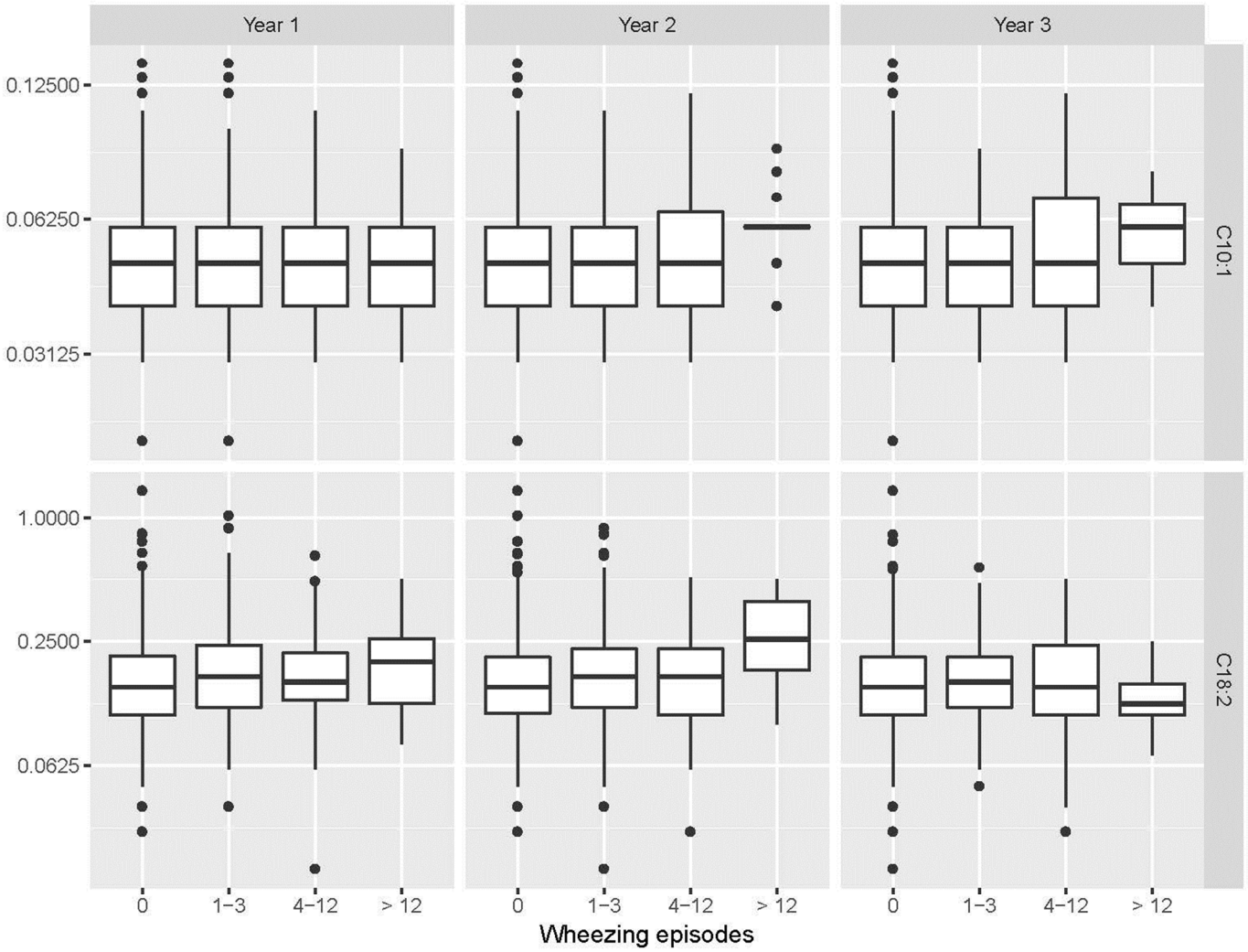
NOTE: Median (IQR) were calculated using non-transformed variables. Ordinal logistic regression was performed using log-transformed variables.

**Supplemental Table S6.** Odds ratios for the association of newborn screening metabolites with the number of wheezing episodes in the past 12 months for the 1-year, 2-year, and 3-year study visits.

| | Year 1 (n=1,761) | | Year 2 (n=1,673) | | Year 3 (n=1,340) | |
|---|---|---|---|---|---|---|
| **Metabolite** | **OR (95% CI)** | **p-value** | **OR (95% CI)** | **p-value** | **OR (95% CI)** | **p-value** |
| Free carnitine (C0) | 1.22 (0.92-1.61) | 0.166 | 1.28 (0.95-1.72) | 0.108 | 1.12 (0.79-1.59) | 0.525 |
| Total carnitine (TC) | 1.09 (0.78-1.52) | 0.616 | 1.17 (0.82-1.67) | 0.390 | 1.06 (0.70-1.62) | 0.772 |
| **Acylcarnitines** | | | | | | |
| Short-chain (SC) | 0.69 (0.34-1.43) | 0.321 | 0.59 (0.28-1.27) | 0.177 | 0.75 (0.31-1.80) | 0.519 |
| C2 | 0.98 (0.74-1.29) | 0.858 | 1.02 (0.76-1.38) | 0.890 | 0.99 (0.70-1.40) | 0.943 |
| C3 | 1.32 (1.02-1.72) | 0.036* | 1.12 (0.85-1.47) | 0.441 | 0.93 (0.68-1.28) | 0.669 |
| C4 | 1.09 (0.82-1.45) | 0.551 | 1.11 (0.82-1.50) | 0.508 | 0.86 (0.60-1.23) | 0.412 |
| C5 | 1.42 (1.07-1.89) | 0.016* | 1.45 (1.07-1.96) | 0.017* | 1.42 (1.00-2.01) | 0.053 |
| C5:1 | 1.42 (0.42-4.81) | 0.574 | 0.68 (0.18-2.52) | 0.562 | 1.36 (0.30-6.28) | 0.693 |
| Medium-chain (MC) | 1.03 (0.77-1.38) | 0.844 | 1.00 (0.74-1.37) | 0.986 | 1.48 (1.03-2.14) | 0.035* |
| C6 | 1.20 (0.89-1.62) | 0.244 | 1.14 (0.83-1.57) | 0.428 | 1.20 (0.82-1.74) | 0.347 |
| C6-DC | 1.40 (1.00-1.96) | 0.053 | 0.97 (0.68-1.39) | 0.875 | 1.32 (0.87-2.01) | 0.199 |
| C8 | 1.11 (0.84-1.47) | 0.476 | 1.16 (0.86-1.57) | 0.323 | 1.46 (1.03-2.09) | 0.036* |
| C10 | 0.96 (0.75-1.22) | 0.733 | 0.97 (0.75-1.25) | 0.799 | 1.39 (1.02-1.89) | 0.037* |
| C10:1 | 1.37 (0.94-2.00) | 0.100 | 2.11 (1.41-3.17) | $3.18 \times 10^{-4}$** | 2.56 (1.59-4.11) | $1.04 \times 10^{-4}$** |
| C10:2 | 1.82 (0.97-3.42) | 0.061 | 2.64 (1.38-5.08) | 0.004* | 2.56 (1.27-5.14) | 0.008* |
| Long-chain (LC) | 0.76 (0.48-1.21) | 0.255 | 0.75 (0.46-1.23) | 0.259 | 0.81 (0.46-1.43) | 0.472 |
| C14 | 1.05 (0.78-1.42) | 0.736 | 1.00 (0.73-1.38) | 0.991 | 1.06 (0.73-1.54) | 0.777 |
| C14:1 | 0.91 (0.73-1.14) | 0.412 | 0.85 (0.67-1.08) | 0.190 | 1.15 (0.87-1.53) | 0.329 |
| C14-OH | 0.88 (0.69-1.12) | 0.301 | 0.68 (0.52-0.89) | 0.005* | 1.11 (0.81-1.50) | 0.525 |
| C16 | 0.89 (0.67-1.17) | 0.400 | 0.94 (0.70-1.26) | 0.656 | 0.92 (0.65-1.29) | 0.621 |
| C16:1 | 0.94 (0.75-1.18) | 0.586 | 0.86 (0.68-1.08) | 0.183 | 0.93 (0.71-1.22) | 0.588 |
| C16-OH | 0.88 (0.69-1.14) | 0.333 | 0.86 (0.66-1.13) | 0.283 | 1.15 (0.84-1.60) | 0.385 |
| C18 | 0.93 (0.68-1.27) | 0.649 | 0.98 (0.71-1.36) | 0.909 | 0.98 (0.67-1.43) | 0.901 |
| C18:1 | 1.08 (0.79-1.47) | 0.629 | 1.13 (0.81-1.57) | 0.461 | 0.95 (0.65-1.39) | 0.786 |
| C18:1-OH | 0.97 (0.74-1.28) | 0.836 | 0.96 (0.71-1.28) | 0.757 | 0.95 (0.67-1.33) | 0.754 |
| C18:2 | 1.38 (1.12-1.71) | 0.003* | 1.47 (1.17-1.84) | 0.001** | 1.06 (0.80-1.40) | 0.685 |
| Total hydroxy (total OH) | 0.91 (0.68-1.22) | 0.538 | 0.84 (0.62-1.15) | 0.277 | 1.10 (0.76-1.60) | 0.603 |
| **Amino Acids** | | | | | | |
| Arginine (ARG) | 1.01 (0.83-1.24) | 0.911 | 1.36 (1.09-1.69) | 0.006* | 1.24 (0.97-1.60) | 0.090 |
| Argininosuccinate (ASA) | 1.38 (1.06-1.79) | 0.017* | 1.04 (0.79-1.38) | 0.772 | 1.21 (0.87-1.69) | 0.257 |
| Citrulline (CIT) | 0.85 (0.59-1.24) | 0.405 | 0.73 (0.49-1.08) | 0.118 | 1.13 (0.71-1.81) | 0.601 |
| Glycine (GLY) | 1.33 (0.85-2.07) | 0.211 | 1.26 (0.78-2.02) | 0.344 | 1.57 (0.90-2.76) | 0.114 |
| Leucine (LEU) | 1.76 (1.14-2.73) | 0.011* | 1.52 (0.96-2.41) | 0.078 | 1.69 (0.99-2.90) | 0.055 |
| Methionine (MET) | 1.13 (0.73-1.74) | 0.595 | 1.29 (0.81-2.06) | 0.276 | 2.11 (1.22-3.66) | 0.007* |
| Ornithine (ORN) | 1.34 (0.93-1.92) | 0.118 | 1.22 (0.83-1.79) | 0.325 | 1.35 (0.86-2.13) | 0.190 |
| Phenylalanine (PHE) | 1.31 (0.64-1.99) | 0.668 | 0.90 (0.49-1.64) | 0.719 | 1.37 (0.67-2.81) | 0.390 |
| Succinylacetone (SUAC) | 1.39 (0.90-2.14) | 0.135 | 0.95 (0.59-1.52) | 0.829 | 1.10 (0.64-1.89) | 0.731 |
| Tyrosine (TYR) | 0.92 (0.69-1.22) | 0.561 | 0.93 (0.69-1.26) | 0.628 | 1.07 (0.74-1.53) | 0.728 |
| Valine (VAL) | 1.25 (0.82-1.89) | 0.301 | 1.12 (0.72-1.75) | 0.611 | 1.20 (0.71-2.03) | 0.491 |
| **Enzymes and Hormones** | | | | | | |
| 17-OHP | 0.98 (0.79-1.22) | 0.853 | 1.02 (0.81-1.29) | 0.872 | 0.97 (0.73-1.27) | 0.796 |
| Biotinidase | 1.06 (0.72-1.57) | 0.769 | 1.18 (0.77-1.81) | 0.449 | 1.14 (0.68-1.91) | 0.615 |
| GALT | 0.82 (0.64-1.05) | 0.122 | 0.78 (0.60-1.01) | 0.063 | 0.97 (0.71-1.33) | 0.867 |
| TSH | 1.09 (0.92-1.29) | 0.310 | 1.05 (0.88-1.25) | 0.601 | 1.04 (0.84-1.28) | 0.715 |

Odds ratios and p-values were estimated using separate ordinal logistic regression models.
*Marginally significant ($0.001 < \alpha < 0.05$); **Significant (Bonferroni correction<0.001)

**Supplemental Figure S1.** Distribution of C10:1 and C18:2 at years 1, 2, and 3.




Rectangles represent IQRs for C10:1 and C18:2 within each study year. The horizontal line within the rectangle is the median value. Vertical lines indicate 1.5xIQR and dots indicate outliers (i.e., individuals with metabolite levels ≥3xIQR above the third quartile or ≤3xIQR below the first quartile).

**Supplemental Table S7.** Summary of effect estimates for comparison of newborn screening metabolites between children with no wheezing episodes and those with >4 wheezing episodes in the past 12 months for the 1-, 2-, and 3-year study visits.

| | Year 1 (n=1,761) | | Year2 (n=1,673) | | Year 3 (n=1,340) | |
|---|---|---|---|---|---|---|
| **Metabolite** | **OR (95% CI)** | **p-value** | **OR (95% CI)** | **p-value** | **OR (95% CI)** | **p-value** |
| Free carnitine (C0) | 1.51 (0.91-2.51) | 0.109 | 1.61 (0.94-2.74) | 0.082 | 1.54 (0.80-2.97) | 0.196 |
| Total carnitine (TC) | 1.12 (0.61-2.06) | 0.720 | 1.34 (0.70-2.56) | 0.373 | 1.77 (0.80-3.94) | 0.161 |
| **Acylcarnitines** | | | | | | |
| Short-chain (SC) | 0.38 (0.12-1.23) | 0.106 | 0.35 (0.10-1.20) | 0.096 | 1.06 (0.19-5.92) | 0.944 |
| C2 | 0.91 (0.55-1.51) | 0.701 | 1.06 (0.61-1.82) | 0.841 | 1.57 (0.79-3.13) | 0.203 |
| C3 | 1.06 (0.66-1.70) | 0.820 | 0.86 (0.52-1.41) | 0.543 | 1.08 (0.58-1.99) | 0.818 |
| C4 | 0.96 (0.57-1.62) | 0.883 | 1.30 (0.75-2.23) | 0..350 | 0.96 (0.49-1.90) | 0.905 |
| C5 | 1.29 (0.77-2.17) | 0.337 | 2.23 (1.31-3.81) | 0.003* | 2.05 (1.06-3.96) | 0.032* |
| C5:1 | 2.28 (0.30-17.30) | 0.424 | 0.34 (0.03-3.46) | 0.361 | 3.22 (0.22-46.76) | 0.391 |
| Medium-chain (MC) | 1.01 (0.59-1.71) | 0.985 | 1.22 (0.70-2.12) | 0.487 | 1.71 (0.86-3.40) | 0.124 |
| C6 | 1.00 (0.58-1.72) | 1.000 | 1.75 (0.99-3.10) | 0.053 | 2.58 (1.27-5.24) | 0.009* |
| C6-DC | 1.17 (0.63-2.18) | 0.614 | 0.82 (0.43-1.55) | 0.539 | 1.79 (0.81-3.97) | 0.153 |
| C8 | 1.16 (0.70-1.91) | 0.577 | 1.67 (0.99-2.84) | 0.057 | 2.55 (1.32-4.93) | 0.005* |
| C10 | 1.05 (0.67-1.63) | 0.843 | 1.18 (0.74-1.88) | 0.479 | 2.27 (1.27-4.05) | 0.006* |
| C10:1 | 1.32 (0.67-2.61) | 0.420 | 4.30 (2.08-8.90) | $8.30 \times 10^{-5}$** | 3.55 (1.49-8.48) | 0.004* |
| C10:2 | 1.08 (0.30-3.85) | 0.911 | 2.92 (0.95-8.96) | 0.062 | 2.78 (0.81-9.53) | 0.104 |
| Long-chain (LC) | 0.48 (0.22-1.06) | 0.069 | 0.51 (0.22-1.20) | 0.123 | 0.68 (0.24-1.92) | 0.470 |
| C14 | 0.87 (0.50-1.49) | 0.610 | 0.96 (0.54-1.70) | 0.883 | 2.01 (0.94-4.27) | 0.071 |
| C14:1 | 0.72 (0.48-1.09) | 0.118 | 0.81 (0.53-1.25) | 0.344 | 1.78 (1.02-3.11) | 0.041* |
| C14-OH | 0.68 (0.43-1.08) | 0.099 | 0.74 (0.46-1.20) | 0.228 | 2.02 (1.13-3.62) | 0.018* |
| C16 | 0.76 (0.47-1.22) | 0.254 | 0.83 (0.50-1.38) | 0.464 | 1.26 (0.63-2.53) | 0.519 |
| C16:1 | 0.79 (0.54-1.15) | 0.216 | 0.73 (0.50-1.07) | 0.104 | 1.23 (0.69-2.17) | 0.484 |
| C16-OH | 0.73 (0.46-1.15) | 0.179 | 0.72 (0.45-1.16) | 0.181 | 1.91 (1.00-3.63) | 0.049* |
| C18 | 0.81 (0.46-1.42) | 0.460 | 1.05 (0.58-1.89) | 0.872 | 1.08 (0.52-2.24) | 0.833 |
| C18:1 | 0.89 (0.51-1.54) | 0.673 | 1.134 (0.63-2.05) | 0.675 | 1.12 (0.54-2.33) | 0.767 |
| C18:1-OH | 0.85 (0.52-1.38) | 0.503 | 1.15 (0.68-1.95) | 0.603 | 1.25 (0.64-2.42) | 0.519 |
| C18:2 | 1.40 (0.95-2.07) | 0.089 | 1.67 (1.11-2.52) | 0.014* | 0.99 (0.59-1.65) | 0.958 |
| Total hydroxy (total OH) | 0.73 (0.43-1.22) | 0.225 | 0.86 (0.50-1.50) | 0.598 | 2.21 (1.05-4.64) | 0.036* |
| **Amino Acids** | | | | | | |
| Arginine (ARG) | 1.36 (0.94-1.98) | 0.108 | 1.65 (1.12-2.43) | 0.012* | 1.58 (0.98-2.54) | 0.060 |
| Argininosuccinate (ASA) | 1.37 (0.85-2.21) | 0.196 | 1.08 (0.66-1.79) | 0.754 | 1.59 (0.84-3.03) | 0.156 |
| Citrulline (CIT) | 1.00 (0.50-1.97) | 0.988 | 1.09 (0.54-2.23) | 0.811 | 2.34 (0.97-5.64) | 0.058 |
| Glycine (GLY) | 1.24 (0.56-2.75) | 0.605 | 1.40 (0.59-3.33) | 0.447 | 5.21 (1.72-15.79) | 0.004* |
| Leucine (LEU) | 1.86 (0.85-4.09) | 0.124 | 2.95 (1.32-6.57) | 0.008* | 2.61 (0.96-7.10) | 0.061 |
| Methionine (MET) | 1.47 (0.67-3.23) | 0.344 | 3.03 (1.31-6.98) | 0.009* | 3.12 (1.13-8.62) | 0.028* |
| Ornithine (ORN) | 1.69 (0.88-3.23) | 0.113 | 1.63 (0.83-3.21) | 0.154 | 2.01 (0.87-4.65) | 0.102 |
| Phenylalanine (PHE) | 0.70 (0.25-1.99) | 0.507 | 1.99 (0.66-6.03) | 0.225 | 3.23 (0.80-13.02) | 0.099 |
| Succinylacetone (SUAC) | 1.49 (0.67-3.30) | 0.329 | 1.01 (0.44-2.36) | 0.974 | 1.09 (0.39-3.03) | 0.873 |
| Tyrosine (TYR) | 0.81 (0.48-1.36) | 0.420 | 1.14 (0.66-1.97) | 0.640 | 1.91 (0.95-3.83) | 0.068 |
| Valine (VAL) | 1.14 (0.54-2.43) | 0.726 | 1.84 (0.84-4.04) | 0.130 | 2.09 (0.79-5.54) | 0.137 |
| **Enzymes and Hormones** | | | | | | |
| 17-OHP | 0.90 (0.60-1.34) | 0.600 | 0.99 (0.65-1.50) | 0.964 | 0.85 (0.51-1.43) | 0.551 |
| Biotinidase | 1.48 (0.71-3.07) | 0.298 | 0.88 (0.42-1.86) | 0.741 | 1.27 (0.48-3.39) | 0.631 |
| GALT | 0.85 (0.54-1.33) | 0.466 | 0.72 (0.45-1.17) | 0.184 | 1.07 (0.59-1.93) | 0.820 |
| TSH | 1.26 (0.91-1.73) | 0.161 | 1.09 (0.78-1.51) | 0.620 | 1.13 (0.75-1.68) | 0.567 |

Odds ratios and p-values were estimated using univariate logistic regression models.

*Marginally significant ($0.001 < \alpha < 0.05$); **Significant (Bonferroni correction<0.001)