

## Supplemental files for “Diagnostic accuracy of calculated serum osmolarity to predict dehydration in older people: adding value to pathology lab reports”

Lee Hooper, Asmaa Abdelhamid, Adam Ali, Diane K Bunn, Amy Jennings, Garry John, Susan Kerry, Gregor Lindner, Carmen A Pfortmueller, Fredrik Sjöstrand, Neil P Walsh, Susan J Fairweather-Tait, John Potter, Paul R Hunter, Lee Shepstone.

**Supplemental Table 1.** Osmolarity equations tested against directly measured osmolality used in this report.

| Equation                                   | Formula  | Reference |
|--|--|-----------|
| <b>Serum or plasma osmolality, mOsm/kg</b> | <b>Directly measured</b>   |           |
| Equation 1, mOsm/L                         | $1.75 \times \text{Na}^+ + \text{glucose} + 0.5 \times \text{urea} + 10.1$                     | (1)       |
| Equation 2, mOsm/L                         | $2.63 \times \text{Na}^+ - 65.4$   | (1)       |
| Equation 3, mOsm/L                         | $1.86 \times \text{Na}^+ + \text{glucose} + 0.5 \times \text{urea}$                            | (2)       |
| Equation 4, mOsm/L                         | $2 \times (\text{Na}^+ + \text{K}^+) + \text{glucose} + 0.5 \times \text{urea}$                | (3;4)     |
| Equation 5, mOsm/L                         | $2 \times \text{Na}^+$   | (5)       |
| Equation 6, mOsm/L                         | $2 \times \text{Na}^+ + \text{glucose} + 0.5 \times \text{urea}$                               | (6)       |
| Equation 7, mOsm/L                         | $2 \times \text{Na}^+ + 7$   | (7)       |
| Equation 8, mOsm/L                         | $2 \times \text{Na}^+ + 10$  | (8)       |
| Equation 9, mOsm/L                         | $2 \times \text{Na}^+ + \text{glucose}$  | (9;10)    |
| Equation 10, mOsm/L                        | $2.1 \times \text{Na}^+$   | (11)      |
| Equation 11, mOsm/L                        | $2 \times \text{Na}^+ + \text{glucose} + 0.93 \times 0.5 \times \text{urea}$                   | (12)      |
| Equation 12, mOsm/L                        | $(2 \times (\text{Na}^+ + \text{K}^+) + \text{glucose} + 0.5 \times \text{urea}) \times 0.985$ | (4)       |
| Equation 13, mOsm/L                        | $1.86 \times \text{Na}^+ + \text{glucose} + 0.5 \times \text{urea} + 5$                        | (13)      |
| Equation 14, mOsm/L                        | $2 \times \text{Na}^+ + 0.9 \times \text{glucose} + 0.93 \times \text{urea} \times 0.5$        | (14)      |
| Equation 15, mOsm/L                        | $2 \times \text{Na}^+ + 0.5 \times \text{urea}$  | (14)      |
| Equation 16, mOsm/L                        | $(1.86 \times \text{Na}^+ + \text{glucose} + 0.5 \times \text{urea})/0.93$                     | (15)      |
| Equation 17, mOsm/L                        | $1.9 \times (\text{Na}^+ + \text{K}^+) + \text{glucose} + 0.5 \times \text{urea}$              | (16)      |
| Equation 18, mOsm/L                        | $1.85 \times \text{Na}^+ + \text{glucose} + 0.5 \times \text{urea} + 8.55$                     | (17)      |
| Equation 19, mOsm/L                        | $1.86 \times \text{Na}^+ + \text{glucose} + 0.5 \times \text{urea} + 9$                        | (18)      |
| Equation 20, mOsm/L                        | $1.86 \times \text{Na}^+ + \text{glucose} + \text{urea} + 9$                                   | (18)      |
| Equation 21, mOsm/L                        | $2 \times (\text{Na}^+ + \text{K}^+) + \text{glucose} + 0.93 \times 0.5 \times \text{urea}$    | (19)      |

|                                |  |         |
|--------------------------------|--|---------|
| Equation 22, mOsm/L            | $1.89 \times \text{Na}^+ + 1.38 \times \text{K}^+ + 1.08 \times \text{glucose} + 1.03 \times \text{urea} + 7.47$ | (20)    |
| Equation 23, mOsm/L            | $1.86 \times (\text{Na}^+ + \text{K}^+) + \text{glucose} + \text{urea} + 10$                                     | (20)    |
| Equation 24, mOsm/L            | $2 \times \text{Na}^+ + 0.9 \times \text{glucose} + 0.93 \times 0.5 \times \text{urea} + 8$                      | (21)    |
| Equation 25, mOsm/L            | $1.86 \times \text{Na}^+ + 1.03 \times \text{glucose} + 1.28 \times 0.5 \times \text{urea}$                      | (22)    |
| Equation 25a, mOsm/L           | $(1.86 \times \text{Na}^+ + 1.03 \times \text{glucose} + 1.28 \times 0.5 \times \text{urea}) \times 0.985$       | (22)    |
| Equation 26, mOsm/L            | $1.36 \times \text{Na}^+ + 1.6 \times \text{glucose} + 0.45 \times \text{urea} + 91.75$                          | (23)    |
| Equation 27, mOsm/L            | $2 \times \text{Na}^+ + \text{glucose} + \text{urea} + 35.2$   | (24)    |
| Equation 27a, mOsm/L           | $(2 \times \text{Na}^+ + \text{glucose} + \text{urea} + 35.2) \times 0.985$                                      | (24)    |
| Equation 28, mOsm/L            | $1.897 \times \text{Na}^+ + \text{glucose} + \text{urea} \times 0.5 + 13.5$                                      | (25)    |
| Equation 29, mOsm/L            | $1.9 \times (\text{Na}^+ + \text{K}^+) + \text{glucose} + \text{urea} \times 0.5 + 5$                            | (25)    |
| Equation 30, mOsm/L            | $1.86 \times (\text{Na}^+ + \text{K}^+) + \text{glucose} + \text{urea}$  | (26)    |
| Equation 31, mOsm/L            | $2 \times \text{Na}^+ + 1.15 \times \text{glucose} + \text{urea}$  | (27)    |
| Equation 32, mOsm/L            | $1.86 \times (\text{Na}^+ + \text{K}^+) + 1.15 \times \text{glucose} + \text{urea} + 14$                         | (27)    |
| Equation 33, mOsm/L            | $1.09 \times 1.86 \times \text{Na}^+ + \text{glucose} + \text{urea}$   | (28)    |
| Equation 34, mOsm/L            | $2 \times (\text{Na}^+ + \text{K}^+) + \text{glucose} + \text{urea}$   | (29;30) |
| Equation 35 (tonicity), mOsm/L | $2 \times (\text{Na}^+ + \text{K}^+) + \text{glucose}$   | (10;31) |
| Equation 36, mOsm/L            | $1.86 \times \text{Na}^+ + \text{glucose} + \text{urea}$   | (32)    |
| Equation 37, mOsm/L            | $2 \times \text{Na}^+ + \text{urea} + \text{glucose}$  | (10;33) |

**Supplemental Table 2.** Correlation of directly measured serum osmolality (in mOsm/kg) with the biochemical parameters used in algorithms for the calculation of serum osmolality

|                         | <b>NU-AGE</b><br>(n=236) |                | <b>DRIE</b> (n=172) |                | <b>Fortes</b> (n=97) |                | <b>Sjöstrand</b><br>(n=36) |                | <b>Pfortmueller</b><br>(n=54) |                |
|-------------------------|--------------------------|----------------|---------------------|----------------|----------------------|----------------|----------------------------|----------------|-------------------------------|----------------|
|                         | <b>r</b>                 | <b>p-value</b> | <b>r</b>            | <b>p-value</b> | <b>r</b>             | <b>p-value</b> | <b>r</b>                   | <b>p-value</b> | <b>r</b>                      | <b>p-value</b> |
| Sodium, mmol/L          | 0.62                     | <0.001         | 0.74                | <0.001         | 0.76                 | <0.001         | 0.65                       | <0.001         | 0.20                          | 0.15           |
| Potassium, mmol/L       | 0.16                     | 0.02           | 0.15                | 0.05           | 0.20                 | 0.05           | -0.24                      | 0.16           | -0.02                         | 0.89           |
| Urea, mmol/L            | 0.16                     | 0.02           | 0.47                | <0.001         | 0.68                 | <0.001         | 0.54                       | <0.001         | 0.17                          | 0.21           |
| Creatinine, $\mu$ mol/L | 0.16                     | 0.02           | 0.32                | <0.001         | 0.51                 | <0.001         | 0.24                       | 0.15           | 0.21                          | 0.14           |
| Glucose, mmol/L         | 0.11                     | 0.10           | 0.36                | <0.001         | 0.08                 | 0.46           | 0.28                       | 0.10           | 0.16                          | 0.25           |

n= number of participants; r= Pearson's coefficient of correlation

**Supplemental Table 3.** Characterising by hydration status, across all five cohorts

|   | <b>Euhydrated</b><br>(n=296, 50%) | <b>Impending dehydration</b><br>(n=183, 31%) | <b>Current dehydration</b><br>(n=116, 19%) |
|---|-----------------------------------|--|--|
| Directly measured osmolality                  | 265 to <295 mOsm/kg               | 295 to 300 mOsm/kg                           | >300 mOsm/kg                               |
| Number with raised serum sodium (>145mmol/L)  | 0 (0%)                            | 3 (2%)                                       | 5 (4%)                                     |
| Number with raised serum potassium (>5mmol/L) | 15 (5%)                           | 8 (4%)                                       | 4 (3%)                                     |
| Number with raised serum urea (>7.1mmol/L)    | 66 (22%)                          | 55 (30%)                                     | 58 (50%)                                   |
| Number with raised serum glucose (>7.8mmol/L) | 41 (14%)                          | 20 (11%)                                     | 19 (16%)                                   |

### Supplemental Table 4: Comparison of directly measured serum osmolality (mOsm/kg) and calculated osmolality by each equation (mOsm/L)

For each of the five cohorts data show the mean directly measured serum osmolality (mOsm/kg), and mean calculated osmolality (mOsm/L) for each equation, p-value of the paired t-test comparing calculated osmolality vs directly measured osmolality, and difference between directly measured serum osmolality and calculated osmolality (mOsm, directly measured serum osmolality minus calculated osmolality).

| Characteristic               | NU-AGE (n=236) |            |     |            |      | DRIE (n=172) |            |      |            |      | Fortes (n=97) |             |      |            |      | Sjöstrand (n=36) |            |     |            |      | Pfortmueller (n=54) |            |      |            |      |      |
|------------------------------|----------------|------------|-----|------------|------|--------------|------------|------|------------|------|---------------|-------------|------|------------|------|------------------|------------|-----|------------|------|---------------------|------------|------|------------|------|------|
|                              | mean           | SD         | p   | Difference |      | mean         | SD         | p    | Difference |      | mean          | SD          | p    | Difference |      | mean             | SD         | p   | Difference |      | mean                | SD         | p    | Difference |      |      |
|                              |                |            |     | Mean       | SD   |              |            |      | Mean       | SD   |               |             |      | Mean       | SD   |                  |            |     | Mean       | SD   |                     |            |      |            |      |      |
| Directly measured osmolality | <b>296.0</b>   | <b>7.0</b> |     |            |      | <b>292.2</b> | <b>9.3</b> |      |            |      | <b>286.7</b>  | <b>14.4</b> |      |            |      | <b>299.7</b>     | <b>7.0</b> |     |            |      | <b>290.9</b>        | <b>8.6</b> |      |            |      |      |
| Equations, mOsm              | 1              | 264.2      | 4.0 | **         | 31.8 | 5.4          | 261.0      | 7.7  | **         | 30.9 | 4.3           | 260.7       | 10.4 | **         | 26.0 | 7.2              | 269.5      | 4.9 | **         | 30.3 | 4.6                 | 259.0      | 8.7  | **         | 31.8 | 10.2 |
|                              | 2              | 304.5      | 5.8 | **         | -8.6 | 5.7          | 296.2      | 10.0 | **         | -4.0 | 7.0           | 293.9       | 13.6 | **         | -7.2 | 9.6              | 309.6      | 6.1 | **         | -9.9 | 5.5                 | 291.3      | 11.5 | 0.80       | -0.5 | 12.9 |
|                              | 3              | 269.5      | 4.2 | **         | 26.5 | 5.4          | 266.0      | 8.0  | **         | 25.9 | 4.3           | 265.6       | 11.0 | **         | 21.1 | 7.2              | 275.0      | 5.2 | **         | 24.7 | 4.6                 | 263.9      | 9.1  | **         | 27.0 | 10.5 |
|                              | 4              | 297.8      | 4.6 | **         | -1.8 | 5.4          | 293.6      | 8.5  | **         | -1.7 | 4.1           | 293.5       | 11.7 | **         | -6.8 | 6.8              | 302.9      | 5.3 | *          | -3.2 | 4.7                 | 291.4      | 9.6  | 0.71       | -0.5 | 10.8 |
|                              | 5              | 281.3      | 4.4 | **         | 14.7 | 5.5          | 275.0      | 7.6  | **         | 17.1 | 6.3           | 273.2       | 10.3 | **         | 13.5 | 9.3              | 285.2      | 4.6 | **         | 14.6 | 5.3                 | 271.3      | 8.8  | **         | 19.6 | 11.0 |
|                              | 6              | 289.2      | 4.6 | **         | 6.8  | 5.4          | 285.2      | 8.5  | **         | 6.7  | 4.4           | 284.7       | 11.6 | *          | 2.0  | 7.1              | 295.0      | 5.5 | **         | 4.7  | 4.6                 | 282.8      | 9.7  | **         | 8.0  | 10.9 |
|                              | 7              | 288.3      | 4.4 | **         | 7.7  | 5.5          | 282.0      | 7.6  | **         | 10.1 | 6.3           | 280.2       | 10.3 | **         | 6.5  | 9.3              | 292.2      | 4.6 | **         | 7.6  | 5.3                 | 278.3      | 8.8  | **         | 12.6 | 11.0 |
|                              | 8              | 291.3      | 4.4 | *          | 4.7  | 5.5          | 285.0      | 7.6  | **         | 7.1  | 6.3           | 283.2       | 10.3 | *          | 3.5  | 9.3              | 295.2      | 4.6 | *          | 4.6  | 5.3                 | 281.3      | 8.8  | **         | 9.6  | 11.0 |
|                              | 9              | 286.5      | 4.4 | **         | 9.5  | 5.4          | 281.7      | 8.2  | **         | 10.2 | 5.0           | 280.3       | 10.3 | **         | 6.4  | 9.0              | 290.9      | 5.1 | **         | 8.8  | 5.3                 | 278.0      | 9.3  | **         | 12.9 | 10.9 |
|                              | 10             | 295.4      | 4.6 | 0.10       | 0.6  | 5.5          | 288.8      | 8.0  | **         | 3.3  | 6.4           | 286.9       | 10.8 | 0.86       | -0.2 | 9.3              | 299.4      | 4.9 | 0.74       | 0.3  | 5.3                 | 284.8      | 9.2  | *          | 6.0  | 11.3 |
|                              | 11             | 289.0      | 4.5 | **         | 6.9  | 5.4          | 285.0      | 8.5  | **         | 6.9  | 4.4           | 284.4       | 11.5 | *          | 2.3  | 7.2              | 294.7      | 5.4 | **         | 5.0  | 4.6                 | 282.5      | 9.6  | **         | 8.3  | 10.8 |
|                              | 12             | 293.3      | 4.6 | **         | 2.7  | 5.4          | 289.2      | 8.4  | **         | -2.6 | 4.1           | 289.1       | 11.6 | *          | -2.4 | 6.8              | 298.3      | 5.2 | 0.08       | 1.4  | 4.7                 | 287.0      | 9.5  | 0.01       | 3.8  | 10.7 |
|                              | 13             | 274.5      | 4.2 | **         | 21.5 | 5.4          | 271.0      | 8.0  | **         | 20.9 | 4.3           | 270.6       | 11.0 | **         | 16.1 | 7.2              | 280.0      | 5.2 | **         | 19.7 | 4.6                 | 268.9      | 9.1  | **         | 22.0 | 10.5 |
|                              | 14             | 288.5      | 4.5 | **         | 7.5  | 5.4          | 284.3      | 8.4  | **         | 7.6  | 4.5           | 283.7       | 11.5 | *          | 3.0  | 7.2              | 294.1      | 5.4 | **         | 5.6  | 4.6                 | 281.8      | 9.5  | **         | 9.0  | 10.8 |
|                              | 15             | 284.0      | 4.5 | **         | 12.0 | 5.5          | 278.5      | 7.8  | **         | 13.6 | 5.6           | 277.6       | 11.6 | **         | 9.1  | 7.5              | 289.3      | 5.0 | **         | 10.5 | 4.6                 | 274.6      | 8.8  | **         | 16.2 | 10.8 |
|                              | 16             | 289.8      | 4.6 | **         | 6.2  | 5.4          | 286.0      | 8.7  | **         | 5.9  | 4.3           | 285.6       | 11.8 | 0.13       | 1.1  | 7.0              | 295.7      | 5.6 | **         | 4.0  | 4.6                 | 283.7      | 9.8  | **         | 7.1  | 10.9 |

|         |       |      |      |       |     |       |     |      |       |     |       |      |      |       |     |       |     |      |       |     |       |      |      |       |      |
|---------|-------|------|------|-------|-----|-------|-----|------|-------|-----|-------|------|------|-------|-----|-------|-----|------|-------|-----|-------|------|------|-------|------|
| 17      | 283.3 | 4.4  | **   | 12.7  | 5.4 | 279.5 | 8.2 | **   | 12.4  | 4.0 | 279.4 | 11.2 | **   | 7.3   | 6.8 | 288.2 | 5.1 | **   | 11.5  | 4.7 | 277.4 | 9.3  | **   | 13.4  | 10.6 |
| 18      | 276.7 | 4.2  | **   | 19.3  | 5.4 | 273.1 | 8.0 | **   | 18.7  | 4.3 | 272.8 | 10.9 | **   | 13.9  | 7.2 | 282.2 | 5.2 | **   | 17.5  | 4.6 | 271.0 | 9.1  | **   | 19.8  | 10.5 |
| 19      | 278.5 | 4.2  | **   | 17.5  | 5.4 | 275.0 | 8.0 | **   | 16.9  | 4.3 | 274.6 | 11.0 | **   | 12.1  | 7.2 | 284.0 | 5.2 | **   | 15.7  | 4.6 | 272.9 | 9.1  | **   | 18.0  | 10.5 |
| 20      | 281.3 | 4.4  | **   | 14.7  | 5.5 | 278.5 | 8.6 | **   | 13.4  | 4.0 | 279.0 | 12.9 | **   | 7.7   | 6.2 | 288.1 | 5.9 | **   | 11.6  | 4.3 | 277.7 | 10.5 | **   | 13.1  | 11.3 |
| 21      | 297.6 | 4.6  | **   | -1.6  | 5.4 | 293.4 | 8.5 | **   | -1.4  | 4.1 | 293.2 | 11.6 | **   | -6.5  | 6.9 | 302.6 | 5.3 | *    | -2.9  | 4.7 | 291.1 | 9.5  | 0.89 | -0.2  | 10.8 |
| 22      | 290.4 | 4.6  | **   | 5.6   | 5.4 | 287.6 | 8.8 | **   | 4.2   | 3.8 | 288.5 | 13.3 | *    | -1.8  | 6.1 | 297.0 | 5.9 | *    | 2.7   | 4.3 | 287.0 | 10.8 | 0.02 | 3.9   | 11.5 |
| 23      | 290.2 | 4.5  | **   | 5.8   | 5.4 | 287.3 | 8.6 | **   | 4.5   | 3.7 | 288.2 | 13.1 | 0.02 | -1.5  | 6.1 | 296.5 | 5.7 | *    | 3.3   | 4.3 | 286.7 | 10.6 | *    | 4.2   | 11.4 |
| 24      | 296.5 | 4.5  | 0.13 | -0.5  | 5.4 | 292.3 | 8.4 | 0.29 | -0.4  | 4.5 | 291.7 | 11.5 | **   | -5.0  | 7.2 | 302.1 | 5.4 | *    | -2.4  | 4.6 | 289.8 | 9.5  | 0.49 | 1.0   | 10.8 |
| 25      | 270.5 | 4.3  | **   | 25.5  | 5.4 | 267.2 | 8.2 | **   | 24.7  | 4.2 | 267.1 | 11.5 | **   | 19.6  | 6.8 | 276.4 | 5.4 | **   | 23.4  | 4.4 | 265.4 | 9.5  | **   | 25.4  | 10.6 |
| 25<br>a | 266.4 | 4.2  | **   | 29.6  | 5.4 | 263.1 | 8.1 | **   | 28.7  | 4.2 | 263.1 | 11.3 | **   | 23.6  | 6.8 | 272.2 | 5.3 | **   | 27.5  | 4.4 | 261.4 | 9.3  | **   | 29.4  | 10.5 |
| 26      | 293.8 | 3.2  | **   | 2.2   | 5.6 | 292.8 | 7.5 | 0.02 | -0.9  | 5.0 | 292.9 | 8.9  | **   | -6.2  | 8.3 | 298.5 | 4.5 | 0.15 | 1.2   | 4.8 | 291.3 | 8.5  | 0.72 | -0.5  | 10.0 |
| 27      | 327.1 | 4.7  | **   | -31.2 | 5.5 | 323.9 | 9.1 | **   | -32.0 | 4.1 | 324.4 | 13.5 | **   | -37.6 | 6.3 | 334.3 | 6.2 | **   | -34.7 | 4.8 | 322.9 | 10.9 | **   | -32.1 | 11.6 |
| 27<br>a | 322.2 | 4.7  | **   | -26.2 | 5.5 | 319.0 | 8.9 | **   | -27.1 | 4.0 | 319.5 | 13.3 | **   | -32.8 | 6.3 | 329.3 | 6.1 | **   | -34.6 | 4.3 | 318.1 | 10.8 | **   | -27.2 | 11.5 |
| 28      | 288.2 | 4.3  | **   | 7.7   | 5.4 | 284.5 | 8.2 | **   | 7.3   | 4.3 | 284.2 | 11.1 | *    | 2.5   | 7.1 | 293.8 | 5.3 | **   | 5.9   | 4.6 | 282.4 | 9.3  | **   | 8.5   | 10.6 |
| 29      | 288.3 | 4.4  | **   | 7.7   | 5.4 | 284.5 | 8.2 | **   | 7.4   | 4.0 | 284.4 | 11.2 | *    | 2.3   | 6.8 | 293.2 | 5.1 | **   | 6.5   | 4.7 | 282.4 | 9.3  | **   | 8.4   | 10.6 |
| 30      | 280.2 | 4.5  | **   | 15.8  | 5.4 | 277.3 | 8.6 | **   | 14.5  | 3.7 | 278.2 | 13.1 | **   | 8.5   | 6.1 | 286.5 | 5.7 | **   | 13.3  | 4.3 | 276.7 | 10.6 | **   | 14.2  | 11.4 |
| 31      | 292.7 | 4.7  | **   | 3.3   | 5.5 | 289.7 | 9.2 | **   | 2.1   | 4.0 | 290.2 | 13.6 | **   | -3.5  | 6.3 | 300.0 | 6.3 | 0.74 | -0.2  | 4.4 | 288.7 | 11.1 | 0.18 | 2.1   | 11.7 |
| 32      | 295.0 | 4.5  | *    | 1.0   | 5.4 | 292.3 | 8.8 | 0.12 | -0.4  | 3.7 | 293.2 | 13.1 | **   | -6.5  | 6.1 | 301.3 | 5.8 | 0.03 | -1.6  | 4.4 | 291.7 | 10.8 | 0.60 | -0.8  | 11.5 |
| 33      | 295.8 | 4.8  | 0.59 | 0.2   | 5.5 | 292.5 | 9.1 | 0.07 | -0.5  | 4.1 | 292.9 | 13.7 | **   | -6.2  | 6.3 | 303.0 | 6.2 | *    | -3.3  | 4.3 | 291.4 | 11.0 | 0.72 | -0.6  | 11.7 |
| 34      | 300.5 | 4.8  | **   | -4.5  | 5.4 | 297.1 | 9.0 | **   | 5.2   | 3.7 | 297.9 | 13.7 | **   | -11.2 | 6.1 | 307.0 | 6.0 | **   | -7.3  | 4.4 | 296.3 | 11.1 | *    | -5.4  | 11.7 |
| 35      | 295.1 | 4.5  | *    | 0.9   | 5.4 | 290.1 | 8.2 | **   | 1.7   | 4.8 | 289.1 | 10.3 | *    | -2.4  | 8.5 | 298.8 | 4.9 | 0.30 | 0.9   | 5.4 | 286.5 | 9.0  | *    | 4.3   | 10.8 |
| 36      | 272.3 | 23.7 | **   | 23.7  | 5.5 | 269.5 | 8.6 | **   | 7.4   | 4.3 | 270.0 | 12.9 | **   | 16.7  | 6.2 | 279.1 | 5.9 | **   | 20.6  | 4.3 | 268.7 | 10.5 | **   | 22.1  | 11.3 |

|  |    |       |     |    |     |     |       |     |    |     |     |       |      |   |      |     |       |     |      |     |     |       |      |      |     |      |
|--|----|-------|-----|----|-----|-----|-------|-----|----|-----|-----|-------|------|---|------|-----|-------|-----|------|-----|-----|-------|------|------|-----|------|
|  | 37 | 291.9 | 4.7 | ** | 4.0 | 5.5 | 288.7 | 9.1 | ** | 3.2 | 4.1 | 289.2 | 13.5 | * | -2.4 | 6.3 | 299.1 | 6.2 | 0.40 | 0.6 | 4.3 | 287.7 | 10.9 | 0.05 | 3.1 | 11.6 |
|--|----|-------|-----|----|-----|-----|-------|-----|----|-----|-----|-------|------|---|------|-----|-------|-----|------|-----|-----|-------|------|------|-----|------|

SD= standard deviation

p-value refers to the p-value of the paired t-test, comparing the results of the equation vs directly measured osmolality, \*\*<0.0001, \*<0.01

**Supplemental Table 5:** Correlation analysis of the association of difference ( $\Delta$ , measured serum osmolality minus osmolarity) with osmolality, biochemical parameters, age, and measures of nutritional, cognitive and functional status. Pearson's coefficients of correlation (r) are shown for each of the five potential equations in each cohort.

| Equation  | NU-AGE        |               |               |               |               | DRIE            |                  |                  |                  |                  | Fortes |        |        |       |       | Sjöstrand |       |       |       |       | Pfortmueller |        |        |        |        |
|---|---------------|---------------|---------------|---------------|---------------|-----------------|------------------|------------------|------------------|------------------|--------|--------|--------|-------|-------|-----------|-------|-------|-------|-------|--------------|--------|--------|--------|--------|
|   | 10            | 24            | 26            | 32            | 33            | 10              | 24               | 26               | 32               | 33               | 10     | 24     | 26     | 32    | 33    | 10        | 24    | 25    | 32    | 33    | 10           | 24     | 26     | 32     | 33     |
| <b>Osmolality,</b><br><i>mOsm/kg</i>            | 0.75*         | 0.76*         | 0.89*         | 0.76*         | 0.73*         | 0.54*           | 0.47*            | 0.63*            | 0.39*            | 0.31*            | 0.66*  | 0.61*  | 0.82*  | 0.41* | 0.33  | 0.72*     | 0.64* | 0.77* | 0.56* | 0.47  | 0.60*        | 0.54*  | 0.59*  | 0.46*  | 0.44*  |
| <b>Sodium,</b><br><i>mmol/L</i>                 | -0.06         | -0.03         | 0.23*         | 0.01          | -0.06         | -0.17*          | -0.14            | -0.40*           | -0.02            | -0.21*           | 0.02   | 0.01   | 0.44*  | 0.00  | -0.16 | -0.07     | -0.11 | 0.16  | -0.05 | -0.18 | -0.66*       | -0.63* | -0.37* | -0.49* | -0.59* |
| <b>Potassium,</b><br><i>mmol/L</i>              | 0.16*         | 0.14*         | 0.15*         | 0.03          | 0.12          | 0.38*           | 0.46*            | 0.33*            | 0.28*            | 0.46*            | 0.40*  | 0.37*  | 0.30*  | 0.04  | 0.23  | -0.05     | -0.02 | -0.10 | -0.18 | 0.02  | 0.21         | 0.10   | 0.02   | -0.16  | 0.00   |
| <b>Urea,</b><br><i>mmol/L</i>                   | 0.08          | -0.01         | 0.03          | -0.13*        | -0.13         | 0.57*           | 0.42*            | 0.34*            | 0.06             | 0.09             | 0.69*  | 0.50*  | 0.57*  | 0.02  | 0.05  | 0.60*     | 0.37* | 0.37* | 0.06  | 0.04  | 0.12         | -0.10  | -0.05  | -0.41* | -0.37* |
| <b>Creatinine,</b><br><i>μmol/L</i>             | 0.11          | 0.05          | 0.06          | -0.03         | -0.01         | 0.40*           | 0.31*            | 0.26*            | 0.07             | 0.09             | 0.60*  | 0.45*  | 0.47*  | 0.03  | 0.08  | 0.27      | 0.11  | 0.09  | -0.03 | -0.05 | 0.26         | 0.14   | 0.16   | -0.09  | -0.07  |
| <b>Glucose,</b><br><i>mmol/L</i>                | 0.16*         | 0.06          | -0.03         | 0.03          | 0.05          | 0.62*           | 0.19*            | -0.31*           | -0.09            | 0.06             | 0.28*  | 0.01   | -0.26* | -0.13 | -0.06 | 0.16      | -0.10 | -0.12 | -0.21 | -0.21 | 0.19         | -0.10  | -0.40* | -0.15  | -0.08  |
| <b>eGFR</b><br><i>mL/min/1.73 m<sup>2</sup></i> | -0.07         | -0.02         | -0.05         | 0.05          | 0.05          | -0.38*          | -0.28*           | -0.23*           | -0.06            | -0.08            | -0.54* | -0.40* | -0.41* | -0.02 | -0.06 | -0.39*    | -0.24 | -0.21 | -0.08 | -0.06 | -0.31*       | -0.16  | -0.18  | 0.08   | 0.04   |
| <b>Age,</b><br><i>years</i>                     | 0.05          | 0.05          | 0.06          | 0.04          | 0.04          | 0.01            | 0.03             | -0.11            | -0.09            | -0.06            | 0.16   | 0.13   | 0.05   | 0.02  | 0.07  | 0.15      | 0.16  | 0.15  | 0.12  | 0.15  | -0.11        | -0.09  | -0.05  | -0.03  | -0.07  |
| <b>BMI,</b><br><i>kg/m<sup>2</sup></i>          | 0.17*         | 0.14*         | 0.15*         | 0.12          | 0.13          | 0.11            | 0.06             | 0.01             | 0.04             | 0.05             | ND     | ND     | ND     | ND    | ND    | 0.20      | 0.18  | 0.16  | 0.16  | 0.14  | ND           | ND     | ND     | ND     | ND     |
| <b>Hb,</b> g/dL                                 | -0.01         | -0.03         | -0.02         | -0.04         | -0.04         | -0.16*          | -0.05            | 0.08             | 0.12             | 0.05             | -0.06  | 0.05   | 0.06   | 0.25* | 0.20  | ND        | ND    | ND    | ND    | ND    | ND           | ND     | ND     | ND     | ND     |
| <b>Cognitive status</b>                         | MMS E<br>0.06 | MMS E<br>0.06 | MMS E<br>0.04 | MMS E<br>0.06 | MMS E<br>0.06 | MMS E -<br>0.12 | MMS E -<br>0.16* | MMS E -<br>0.22* | MMS E -<br>0.21* | MMS E -<br>0.16* | ND     | ND     | ND     | ND    | ND    | ND        | ND    | ND    | ND    | ND    | ND           | ND     | ND     | ND     | ND     |
| <b>Functional status</b>                        | IADL<br>-0.09 | IADL<br>-0.07 | IADL<br>-0.05 | IADL<br>-0.02 | IADL<br>-0.05 | BI -<br>0.01    | BI<br>0.03       | BI<br>0.08       | BI<br>0.09       | BI<br>0.05       | ND     | ND     | ND     | ND    | ND    | ND        | ND    | ND    | ND    | ND    | ND           | ND     | ND     | ND     | ND     |

BMI: body mass index; eGFR: estimated glomerular filtration rate; Hb: haemoglobin; MMSE=Mini Mental State Examination; BI Barthel Index; ND no data.  
\*p<0.05; \*\* p<0.001.

**Supplemental Table 6.** ROC plots, areas under the curve, with standard errors and 95% confidence intervals. Diagnostic accuracy of each formula compared to serum or plasma osmolality (current dehydration defined as >300mOsm/kg).

| equation  | <b>NU-AGE</b><br>(n=236) |                 | <b>DRIE</b><br>(n=172) |                 | <b>Fortes</b><br>(n=97) |                 | <b>Sjöstrand</b><br>(n=36) |                 | <b>Pfortmueller</b><br>(n=54) |                 |
|-----------|--------------------------|-----------------|------------------------|-----------------|-------------------------|-----------------|----------------------------|-----------------|-------------------------------|-----------------|
|           | <b>AUC (SE*)</b>         | <b>95%CI</b>    | <b>AUC (SE)</b>        | <b>95%CI</b>    | <b>AUC (SE)</b>         | <b>95%CI</b>    | <b>AUC (SE)</b>            | <b>95%CI</b>    | <b>AUC (SE)</b>               | <b>95%CI</b>    |
| <b>10</b> | 0.685<br>(0.040)         | 0.606,<br>0.764 | 0.731<br>(0.048)       | 0.637,<br>0.826 | 0.773<br>(0.078)        | 0.620,<br>0.925 | 0.788<br>(0.075)           | 0.641,<br>0.935 | 0.569 (0.131)                 | 0.313,<br>0.825 |
| <b>24</b> | 0.686<br>(0.041)         | 0.606,<br>0.766 | 0.901<br>(0.027)       | 0.848,<br>0.954 | 0.965<br>(0.019)        | 0.927,<br>1.000 | 0.873<br>(0.060)           | 0.757,<br>0.990 | 0.684 (0.100)                 | 0.489,<br>0.880 |
| <b>26</b> | 0.681<br>(0.040)         | 0.602,<br>0.760 | 0.904<br>(0.025)       | 0.856,<br>0.952 | 0.968<br>(0.017)        | 0.934,<br>1.000 | 0.877<br>(0.058)           | 0.763,<br>0.990 | 0.681 (0.113)                 | 0.460,<br>0.901 |
| <b>32</b> | 0.679<br>(0.042)         | 0.597,<br>0.761 | 0.936<br>(0.019)       | 0.898,<br>0.973 | 0.968<br>(0.017)        | 0.934,<br>1.000 | 0.903<br>(0.052)           | 0.802,<br>1.000 | 0.731 (0.100)                 | 0.535,<br>0.927 |
| <b>33</b> | 0.681<br>(0.042)         | 0.599,<br>0.762 | 0.925<br>(0.021)       | 0.884,<br>0.966 | 0.992<br>(0.009)        | 0.975,<br>1.000 | 0.897<br>(0.056)           | 0.788,<br>1.000 | 0.743 (0.096)                 | 0.555,<br>0.931 |

AUC: area under the curve in the ROC plot.

SE: standard error

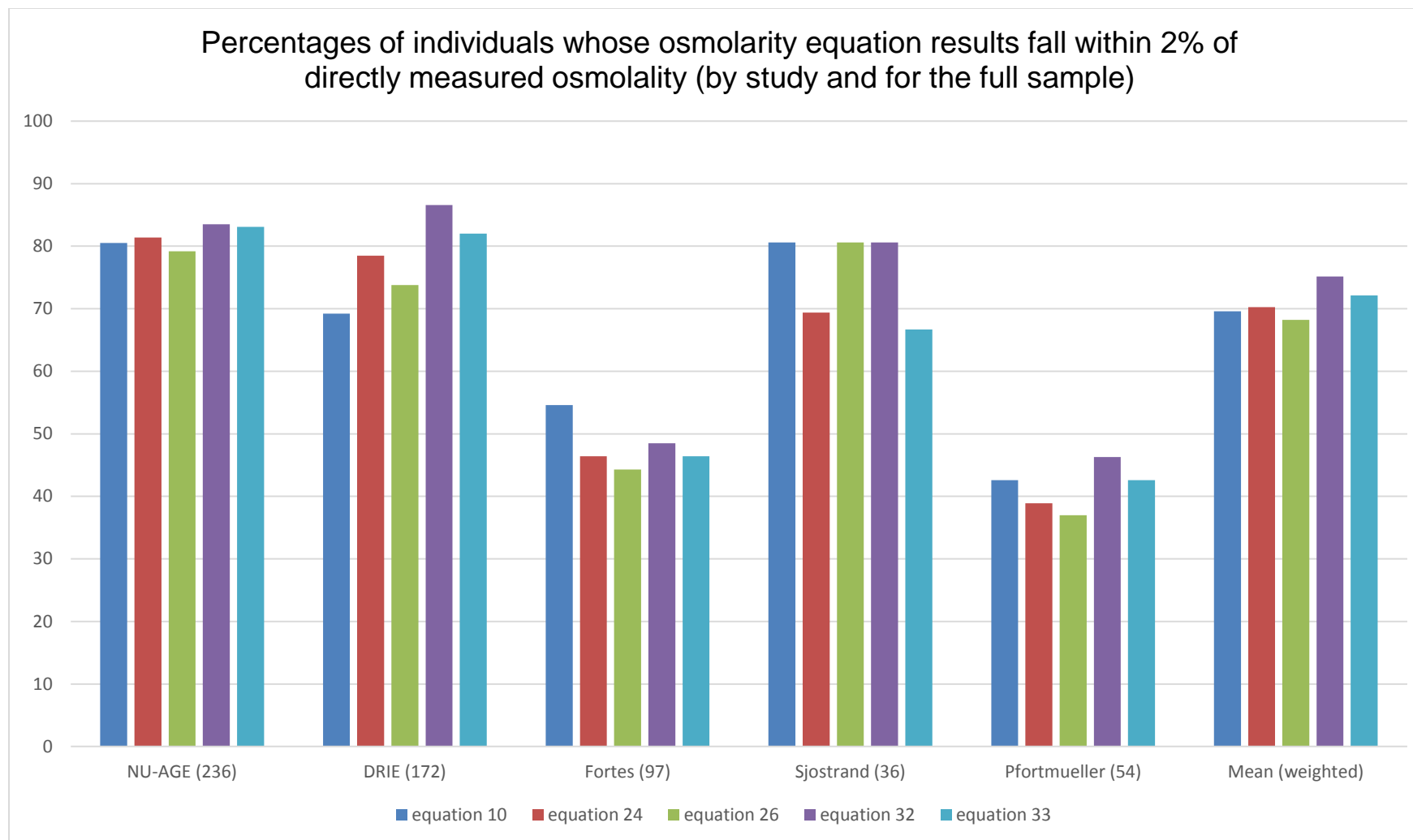
95%CI: 95% confidence interval



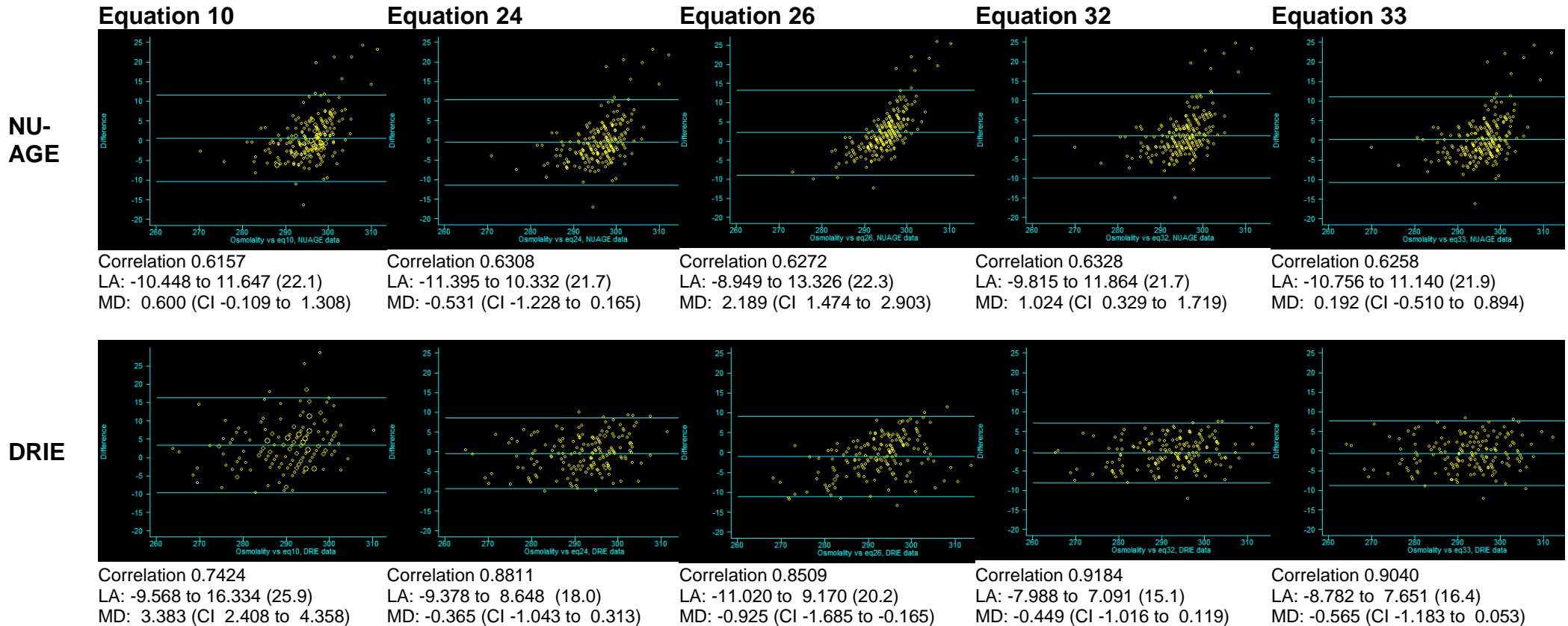
**Supplemental Table 7.** Sensitivity and specificity cut-offs for the combined datasets for current dehydration (measured serum or plasma osmolality >300mOsm/kg).

|      | Best specificity at sensitivity of $\geq 75\%$ | Cut-point    | Correctly classified | LR+  | LR-  |
|------|--|--------------|----------------------|------|------|
| Eq10 | 58%  | $\geq 294.0$ | 62%                  | 1.82 | 0.41 |
| Eq24 | 69%  | $\geq 297.3$ | 70%                  | 2.40 | 0.36 |
| Eq26 | 68%  | $\geq 295.0$ | 69%                  | 2.32 | 0.37 |
| Eq32 | 71%  | $\geq 296.7$ | 72%                  | 2.57 | 0.35 |
| Eq33 | 73%  | $\geq 297.6$ | 73%                  | 2.74 | 0.34 |
|      | Best specificity at sensitivity of $\geq 80\%$ |              |                      |      |      |
| Eq32 | 67%  | $\geq 296.1$ | 69%                  | 2.42 | 0.30 |
| Eq33 | 67%  | $\geq 296.8$ | 70%                  | 2.45 | 0.30 |
|      | Best specificity at sensitivity of $\geq 85\%$ |              |                      |      |      |
| Eq32 | 56%  | $\geq 294.7$ | 62%                  | 1.95 | 0.26 |
| Eq33 | 60%  | $\geq 295.8$ | 65%                  | 2.15 | 0.24 |
|      | Best specificity at sensitivity of $\geq 90\%$ |              |                      |      |      |
| Eq32 | 48%  | $\geq 293.6$ | 56%                  | 1.75 | 0.20 |
| Eq33 | 50%  | $\geq 294.1$ | 58%                  | 1.80 | 0.19 |

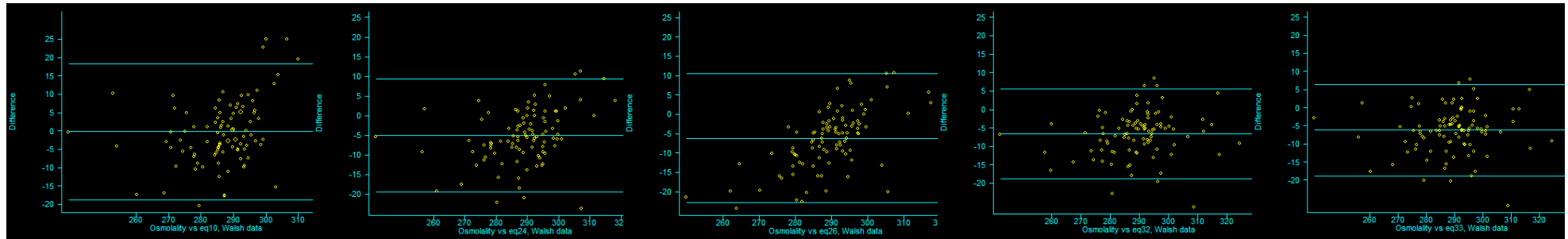
**Supplemental Figure 1.** Percentages of individuals whose osmolarity equation results fall within 2% of measured osmolality, by cohort and for the full (weighted) sample.



**Supplemental Figure 2.** Bland Altman plots, comparing measured serum osmolality (mOsm/kg) with five equations for osmolality (all in mOsm/L). Each plot compares (measured osmolality + osmolality using that equation)/2 on the x-axis with measured osmolality – osmolality using that equation on the y-axis.

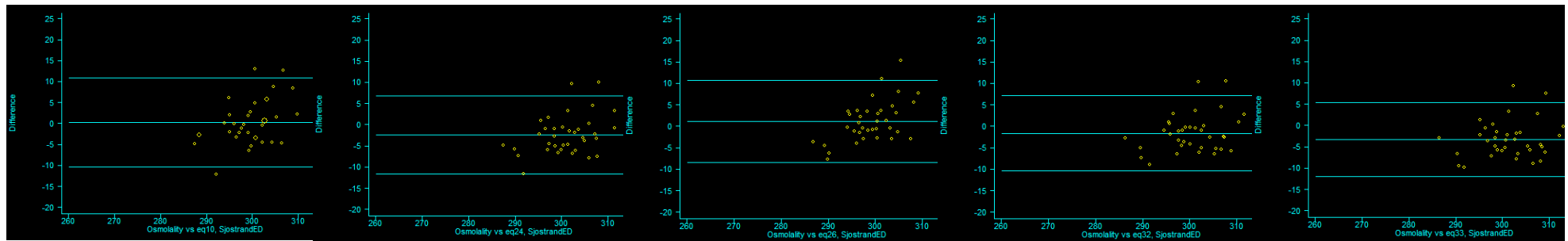


**Forte  
S**



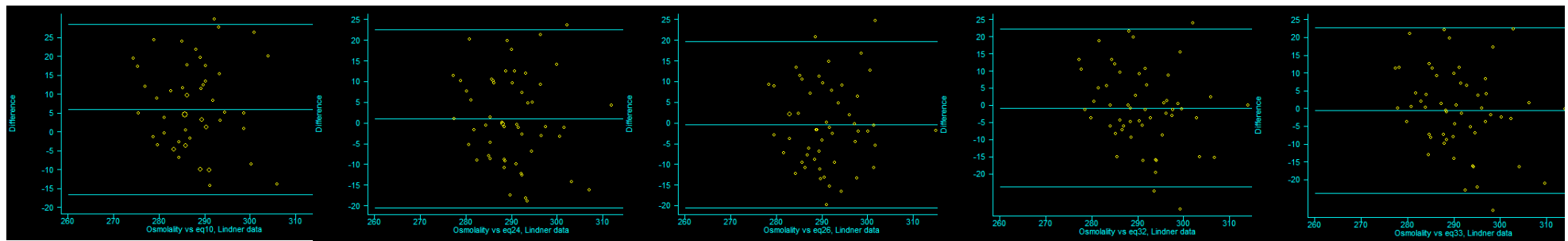
|   |   |  |   |   |
|---|---|--|---|---|
| Correlation 0.7644<br>LA: -18.731 to 18.388 (37.1)<br>MD: -0.171 (CI -2.041 to 1.699) | Correlation 0.8679<br>LA: -19.452 to 9.411 (28.9)<br>MD: -5.021 (CI -6.475 to -3.566) | Correlation 0.8479<br>LA: -22.835 to 10.445 (33.3)<br>MD: -6.195 (CI -7.872 to -4.518) | Correlation 0.9056<br>LA: -18.745 to 5.679 (24.4)<br>MD: -6.533 (CI -7.764 to -5.302) | Correlation 0.9007<br>LA: -18.773 to 6.393 (25.2)<br>MD: -6.190 (CI -7.458 to -4.922) |
|---|---|--|---|---|

**Sjös-  
trand**



|  |   |   |   |   |
|--|---|---|---|---|
| Correlation 0.6480<br>LA: -10.365 to 10.959 (21.3)<br>MD: 0.297 (CI -1.507 to 2.101) | Correlation 0.7513<br>LA: -11.650 to 6.795 (18.4)<br>MD: -2.428 (CI -3.988 to -0.868) | Correlation 0.7302<br>LA: -8.432 to 10.799 (19.2)<br>MD: 1.183 (CI -0.443 to 2.810) | Correlation 0.7801<br>LA: -10.375 to 7.169 (17.5)<br>MD: -1.603 (CI -3.087 to -0.119) | Correlation 0.7910<br>LA: -11.942 to 5.380 (17.3)<br>MD: -3.281 (CI -4.746 to -1.815) |
|--|---|---|---|---|

**Pfort-  
mueller**



|  |  |  |  |  |
|--|--|--|--|--|
| Correlation 0.1989<br>LA: -16.540 to 28.599 (45.1) | Correlation 0.2947<br>LA: -20.558 to 22.595 (43.2) | Correlation 0.3124<br>LA: -20.591 to 19.617 (40.2) | Correlation 0.3136<br>LA: -23.806 to 22.151 (46.0) | Correlation 0.3137<br>LA: -23.932 to 22.795 (46.7) |
|--|--|--|--|--|

MD: 6.030 (CI 2.949 to 9.110)    MD: 1.019 (CI -1.926 to 3.963)    MD: -0.487 (CI -3.231 to 2.257)    MD: -0.828 (CI -3.964 to 2.308)    MD: -0.569 (CI -3.757 to 2.620)

Eq: osmolarity equation

LA: limits of agreement (followed by the size of the gap in brackets)

MD: mean difference

## References

- (1) Edelman IS, Leibman J, O'Meara MP, Birkenfeld LW. Interrelations between serum sodium concentration, serum osmolality, and total exchangeable sodium, total exchangeable potassium, and total body water. *J Clin Invest* 1958;37:1236-56.
- (2) Holmes JH. Measurement of osmolality in serum, urine and other biologic fluids by the freezing point determination. Chicago, IL: American Society of Clinical Pathologists; 1962.
- (3) Jackson WP, Forman R. Hyperosmolar nonketotic diabetic coma. *Diabetes* 1966;15:714-22.
- (4) Gerich JE, Martin MM, Recant L. Clinical and metabolic characteristics of hyperosmolar nonketotic coma. *Diabetes* 1971;20:228-38.
- (5) Winters RW. Disorders of electrolyte and acid-base metabolisms. In: Barnett HL, editor. *Pediatrics*. 14th ed. New York: Appleton-Century-Crofts; 1968. p. 336-68.
- (6) Mahon WA, Holland J, Urowitz MB. Hyperosmolar, non-ketotic diabetic coma. *Can Med Assoc J* 1968;99:1090-2.
- (7) Jetter WW. Clinical osmometry. *Pa Med* 1969;72:75-9.
- (8) Ross EJ, Christie SB. Hyponatremia. *Medicine (Baltimore)* 1969;48:441-73.
- (9) Stevenson RE, Bowyer FP. Hyperglycemia with hyperosmolal dehydration in nondiabetic infants. *J Pediat* 1970;77:818-23.
- (10) Joint British Diabetes Societies. The management of the hyperosmolar hyperglycaemic state (HHS) in adults with diabetes . <http://www.diabetes.org.uk/Documents/Position%20statements/JBDS-IP-HHS-Adults.pdf> 2012JBDS 06
- (11) Hoffman WS. *The biochemistry of clinical medicine*. 4th ed. Chicago, IL: Imprint Unknown; 1970.
- (12) Sadler JH. Personal communication to Fazekas. 1970.
- (13) Boyd DR, Baker RJ. Osmometry: a new bedside laboratory aid for the management of surgical patients. *Surg Clin North Am* 1971;51:241-50.
- (14) Weisberg HF. Osmolality. *Clinical Chemistry Check Sample*. CC-71 ed. Chicago, IL: American Society of Clinical Pathologists; 1971.
- (15) Glasser L, Sternglanz PD, Combie J, Robinson A. A serum osmolality and its applicability to drug overdose. *Am J Clin Pathol* 1973;60:695-9.
- (16) Wilson RF. *Fluids, electrolytes, and metabolism*. Springfield, IL: Charles C Thomas; 1973.
- (17) Dorwart WV. Serum osmolality-methods of calculation from chemistry values and use of these values as a prognostic indicator. *Clin Chem* 1973;19(abstract 020):643.

- (18) Dorwart WV, Chalmers L. Comparison of methods for calculating serum osmolality from chemical concentrations, and the prognostic value of such calculations. *Clin Chem* 1975;21:190-4.
- (19) Jenkins PG, Larmore C. Letter: hyperglycemia-induced hyponatremia. *New Engl J Med* 1974;290:573.
- (20) Bhagat CI, Garcia-Webb C, Fletcher E, Beilby JP. Calculated vs measured plasma osmolalities revisited. *Clin Chem* 1984;30:1703-5.
- (21) Snyder H, Williams D, Zink B, Reilly K. Accuracy of blood ethanol determination using serum osmolality. *J Emerg Med* 1992;10:129-33.
- (22) Hoffman RS, Smilkstein MJ, Howland MA, Goldfrank LR. Osmol gaps revisited: normal values and limitations. *J Toxicol Clin Toxicol* 1993;31:81-93.
- (23) Wojtysiak B, Duma D, Solski J. The new equation for calculated osmolality. *Ann Univ Mariae Curie Sklodowska* 1999;7:59-64.
- (24) Koga Y, Purssell RA, Lynd LD. The irrationality of the present use of the osmole gap: applicable physical chemistry principles and recommendations to improve the validity of current practices. *Toxicol Rev* 2004;23:203-11.
- (25) Rasouli M, Kalantari KR. Comparison of methods for calculating serum osmolality: multivariate linear regression analysis. *Clin Chem Lab Med* 2005;43:635-40.
- (26) Varley H, Gowenlock AH, Bell M. *Practical clinical biochemistry*. 5th ed. London: Heinemann; 1980.
- (27) Khajuria A, Krahn J. Osmolality revisited-deriving and validating the best formula for calculated osmolality. *Clin Biochem* 2005;38:514-9.
- (28) Bianchi V, Bidone P, Arfini C. Siero ed urine: osmolalita calcolata o osmolalita misurata? *RIMeL/IJLaM* 2009;5:206-11.
- (29) Wikipedia the free encyclopedia. Plasma osmolality. [http://en.wikipedia.org/wiki/Plasma\\_osmolality](http://en.wikipedia.org/wiki/Plasma_osmolality) 2014 [cited 2015 Feb 19];
- (30) Longmore M, Wilkinson IB, Davidson EH, Foulkes A, Mafi AR. *Clinical Chemistry. Oxford Handbook of Clinical Medicine*. 8th ed. Oxford: Oxford University Press; 2010. p. 682.
- (31) Stookey JD, Purser JL, Pieper CF, Cohen HJ. Plasma hypertonicity: Another marker of frailty? *J Am Geriatr Soc* 2004;52(8):1313-20.
- (32) Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey. <http://www.cdc.gov/nchs/nhanes.htm> 2015 [cited 2015 Feb 19];
- (33) MDcalc. Serum Osmolality/Osmolarity. <http://www.mdcalc.com/serum-osmolality-osmolarity/#about-equation> 2015 [cited 2015 Mar 24];