**Supplementary Material**

Tribble AC, Gerber JS, Bilker WB, Lautenbach E. **Impact of Rapid Diagnostics with Antimicrobial Stewardship Support for Children with Positive Blood Cultures: A Quasi-Experimental Study with Time Trend Analysis.**

**Supplementary Table 1.** Number (%) of Subjects Included in Time-To-Therapy Subgroups

**Supplementary Table 2.** Demographic and Clinical Characteristics of Time-to-Therapy Subgroups

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**Supplementary Table 1.** Number (%) of Subjects Included in Time-To-Therapy Subgroups

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Gram-positive | | Gram-negative | |
| Pre-BC-GP | Post-BC-GP | Pre-BC-GP | Post-BC-GP |
| Time to optimal therapy (primary cohort) | 191 | 168 | 73 | 89 |
| Time to effective therapy | 32 (17) | 27 (16) | 11 (15) | 16 (18) |
| Time to definitive therapy | 108 (57) | 89 (53) | 49 (67) | 51 (57) |
| Time to stopping vancomycin | 130 (68) | 108 (64) | 47 (64) | 55 (62) |

BC-GP: VERIGENE® Gram-Positive Blood Culture Test.

Patients were included in time-to-therapy subgroups if 1) the corresponding endpoint was reached after culture positivity or 2) they were censored due to death or transfer after culture positivity but prior to reaching the endpoint. Times to effective and definitive therapy were not determined for contaminants, as no therapy was indicated.

**Supplementary Table 2.** Demographic and Clinical Characteristics of Time-to-Therapy Subgroups

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Characteristic** | **TOT-GP** | **TET-GP** | **TDT-GP** | **TSV-GP** | **TOT-GN** | **TET-GN** | **TDT-GN** | **TSV-GN** |
| **Post-intervention period** (*n* [%]) | 168 (47) | 27 (46) | 89 (45) | 108 (45) | 89 (55) | 16 (59) | 51 (51) | 55 (54) |
| **Gram-positive isolates** | 359 (69) | 59 (67) | 197 (66) | 238 (70) |  |  |  |  |
| **Age** (years; median [IQR]) | 3.3 (0.4, 10.2) | 7.2 (2.0, 12.1)\* | 3.3 (0.5, 10.2) | 2.5 (0.3, 9.4) | 2.3 (0.2, 10.0) | 2.7 (1.1, 6.9) | 1.6 (0.2, 9.0) | 1.7 (0.2, 9.8) |
| **Male sex** | 205 (57) | 37 (63) | 115 (58) | 130 (55) | 80 (49) | 17 (63) | 56 (56) | 46 (45) |
| **Race** |  |  |  |  |  |  |  |  |
| White | 173 (48) | 29 (49) | 94 (48) | 115 (48) | 64 (40) | 7 (26) | 39 (39) | 40 (39) |
| Black | 90 (25) | 10 (17) | 49 (25) | 66 (28) | 49 (30) | 10 (37) | 28 (28) | 34 (33) |
| Asian | 15 (4) | 2 (3) | 10 (5) | 8 (3) | 5 (3) | 2 (7) | 4 (4) | 2 (2) |
| Other | 81 (23) | 18 (31) | 44 (22) | 49 (21) | 44 (27) | 8 (30) | 29 (29) | 26 (25) |
| **Ethnicity** |  |  |  |  |  |  |  |  |
| Hispanic | 51 (14) | 10 (17) | 25 (13) | 31 (13) | 19 (12) | 3 (11) | 12 (12) | 10 (10) |
| Non-Hispanic | 307 (86) | 49 (83) | 171 (87) | 206 (87) | 142 (88) | 23 (85) | 87 (87) | 92 (90) |
| Unknown | 1 (0) | 0 (0) | 1(1) | 1 (0) | 1 (1) | 1 (4) | 1 (1) | 0 (0) |
| **≥1 Complex Chronic Condition** | 286 (80) | 47 (80) | 158 (80) | 188 (79) | 132 (81) | 17 (63)\* | 77 (77) | 88 (86) |
| **Immunocompromise** | 146 (41) | 29 (49) | 78 (40) | 82 (34) | 72 (44) | 10 (37) | 43 (43) | 43 (42) |
| **Documented adverse reaction to β-lactam antibiotic** | 47 (13) | 13 (22) | 26 (13) | 26 (11) | 10 (6) | 1 (4) | 8 (8) | 5 (5) |
| **Length of stay (days) prior to study day 0** | 2 (0, 19) | 1 (0, 12) | 1 (0, 19) | 2.5 (0, 19) | 1 (0, 14) | 1 (0, 21) | 1 (0, 12) | 7 (0, 17) |
| **Central venous catheter present on study day 0** | 210 (59) | 34 (58) | 115 (58) | 120 (50) | 109 (67) | 15 (56) | 63 (63) | 77 (75) |
| **Intensive care on study day 0, 1, or 2** | 116 (32) | 11 (19)\* | 62 (31) | 79 (33) | 65 (40) | 7 (26) | 40 (40) | 52 (51) |
| **Infectious diseases consult note on day of or following culture positivity** | 165 (46) | 33 (56) | 107 (54) | 109 (46) | 78 (48) | 17 (63) | 55 (55) | 46 (45) |
| **Contaminant** | 78 (22) |  |  | 71 (30)\* |  |  |  |  |
| **Gram-positive organism type** |  |  |  |  |  |  |  |  |
| *Staphylococcus aureus* | 108 (30) | 16 (27) | 89 (45)\* | 72 (30) |  |  |  |  |
| *Staphylococcus epidermidis* | 96 (27) | 17 (29) | 28 (14)\* | 45 (19)\* |  |  |  |  |
| Coagulase-negative staphylococcus | 30 (8) | 0 (0)\* | 0 (0)\* | 26 (11) |  |  |  |  |
| Beta-hemolytic streptococcus | 17 (5) | 0 (0) | 15 (8) | 15 (6) |  |  |  |  |
| Other *Streptococcus* spp. | 65 (18) | 14 (24) | 39 (20) | 50 (21) |  |  |  |  |
| *Enterococcus faecalis* or *faecium* | 24 (7) | 9 (15)\* | 21 (11) | 21 (9) |  |  |  |  |
| Organism that can be detected by BC-GP | 343 (96) | 57 (97) | 194 (98) | 231 (97) |  |  |  |  |
| Organism with potential resistance marker that can be detected by BC-GP | 228 (64) | 42 (71) | 138 (70) | 138 (58) |  |  |  |  |

BC-GP: VERIGENE® Gram-Positive Blood Culture Test. IQR: Interquartile range.

Comparison of characteristics between the primary analytic cohort for time to optimal therapy [TOT] and subgroups for secondary endpoints (time to effective therapy [TET], time to definitive therapy [TDT], and time to stopping vancomycin [TSV]) stratified by gram-positive (GP) and gram-negative (GN) isolates. \**P*<0.05 for comparisons between GP/GN subgroups and corresponding TOT-GP or TOT-GN cohort.

**Supplementary Table 3.** Unadjusted Time-to-Therapy Outcomes Before and After BC-GP Implementation, Stratified by Organism

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Organism | Outcome | Pre-Implementation | | Post-Implementation | | *P* (log-rank test) |
| median (IQR) | *n* | median (IQR) | *n* |
| *S. aureus* (all isolates)  *n*=108 | TOT | 35.1 (26.0, 48.4) | 59 | 18.1 (6.8, 26.2) | 49 | 0.0000\* |
| TET | 2.3 (1.5, 3.7) | 11 | 2.6 (1.1, 3.2) | 5 | 0.3556 |
| TDT | 36.0 (29.2, 47.7) | 45 | 9.2 (6.0, 21.0) | 44 | 0.0000\* |
| TSV | 35.7 (23.9, 44.3) | 40 | 8.3 (2.6, 24.4) | 32 | 0.0000\* |
| Methicillin-susceptible *S. aureus*  *n*=86 | TOT | 39.2 (29.9, 49.6) | 44 | 17.5 (6.8, 25.8) | 42 | 0.0000\* |
| TET | 3.5 (1.9, 21.6) | 8 | 2.6 (1.1, 3.2) | 5 | 0.1392 |
| TDT | 36.0 (29.8, 47.7) | 41 | 9.2 (6.0, 18.3) | 40 | 0.0000\* |
| TSV | 33.9 (23.8, 43.8) | 38 | 7.4 (2.6, 23.1) | 31 | 0.0000\* |
| Methicillin-resistant  *S. aureus*  *n*=22 | TOT | 26.0 (9.6, 41.7) | 15 | 20.2 (4.25, 56.2) | 7 | 0.4349 |
| TET | 1.8 (0.7, 2) | 3 | -- | 0 | -- |
| TDT | 22.0 (1.4, 48.8) | 4 | 31.2 (4.7, 59.7) | 4 | 0.2082 |
| TSV | 46.1 (40.1, 52.2) | 2 | 55.2 | 1 | 0.2253 |
| *S. epidermidis*  (all isolates)  *n*=96 | TOT | 33.8 (22.1, 48.1) | 47 | 19.7 (7.0, 33.1) | 49 | 0.0008\* |
| TET | 2.4 (1.6, 4.4) | 9 | 2.1 (1.5, 4.1) | 8 | 0.9555 |
| TDT | 6.5 (1.9, 45.5) | 14 | 4.2 (1.6, 16.2) | 14 | 0.3886 |
| TSV | 42.9 (26.7, 49.4) | 23 | 21.4 (15.8, 37.9) | 22 | 0.0014\* |
| *S. epidermidis*  (pathogens)  *n*=61 | TOT | 32.7 (10.2, 46.5) | 31 | 19.3 (4.8, 33.1) | 30 | 0.0268\* |
| TET | 2.4 (1.6, 4.4) | 9 | 2.1 (1.5, 4.1) | 8 | 0.9555 |
| TDT | 6.5 (1.9, 45.5) | 14 | 4.2 (1.6, 16.2) | 14 | 0.3886 |
| TSV | 44.9 (35.6, 59.6) | 8 | 36.8 (33.5, 39.6) | 4 | 0.0983 |
| *S. epidermidis*  (contaminants)  *n*=35 | TOT | 42.7 (26.8, 52.3) | 16 | 19.7 (7.0, 37.4) | 19 | 0.0047\* |
| TET | -- | 0 | -- | 0 | -- |
| TDT | -- | 0 | -- | 0 | -- |
| TSV | 42.6 (26.3, 49.4) | 15 | 19.1 (7.3, 37.4) | 18 | 0.0086\* |
| Other coagulase-negative staphylococci  *n*=30 | TOT | 35.3 (28.0, 45.3) | 16 | 20.5 (5.6, 34.5) | 14 | 0.1536 |
| TET | -- | 0 | -- | 0 | -- |
| TDT | -- | 0 | -- | 0 | -- |
| TSV | 39.1 (30.1, 44.6) | 14 | 19.8 (6.3, 32.0) | 12 | 0.1116 |
| All coagulase-negative staphylococci (including *S. epidermidis*)  (all isolates) *n*=126 | TOT | 35.1 (23.8, 47.5) | 63 | 20.0 (5.7, 34.5) | 63 | 0.0002\* |
| TET | 2.4 (1.6, 4.4) | 9 | 2.1 (1.5, 4.1) | 8 | 0.9555 |
| TDT | 6.5 (1.9, 45.5) | 14 | 4.2 (1.6, 16.2) | 14 | 0.3886 |
| TSV | 42.8 (28.8, 47.5) | 37 | 20.5 (7.3, 37.4) | 34 | 0.0007\* |
| All coagulase-negative staphylococci (including *S. epidermidis*)  (pathogens) *n*=65 | TOT | 31.2 (15.2, 45.5) | 33 | 24 (6, 36.8) | 32 | 0.0392\* |
| TET | 2.4 (1.6, 4.4) | 9 | 2.1 (1.5, 4.1) | 8 | 0.9555 |
| TDT | 6.5 (1.9, 45.5) | 14 | 4.2 (1.6, 16.2) | 14 | 0.3886 |
| TSV | 44.9 (35.6, 59.6) | 8 | 36.8 (31.1, 40.5) | 6 | 0.0507 |
| All coagulase-negative staphylococci (including *S. epidermidis*)  (contaminants) *n*=61 | TOT | 42.7 (28.4, 47.6) | 30 | 19.7 (5.7, 34.5) | 31 | 0.0031\* |
| TET | -- | 0 | -- | 0 | -- |
| TDT | -- | 0 | -- | 0 | -- |
| TSV | 42.6 (27.2, 46.3) | 29 | 19.6 (6.4, 33.3) | 28 | 0.0106\* |
| Vancomycin-susceptible *Enterococcus faecalis/faecium*  *n*=22 | TOT | 48.7 (44.3, 55.8) | 10 | 43.2 (34.5, 50.1) | 11 | 0.5541 |
| TET | 3.3 (1.3, 5.3) | 2 | 1.5 (1.3, 1.9) | 5 | 0.3384 |
| TDT | 47.6 (44.3, 52.5) | 9 | 45.3 (38.3, 50.1) | 9 | 0.8564 |
| TSV | 39.8 (30.7, 45.5) | 10 | 37.1 (34.1, 41.3) | 9 | 0.7922 |
| Vancomycin-resistant *Enterococcus faecalis/faecium*  *n*=2 | TOT | 41.8 | 1 | 7.7 | 1 | 0.3173 |
| TET | 41.8 | 1 | 7.7 | 1 | 0.3173 |
| TDT | 41.8 | 1 | 7.7 | 1 | 0.3173 |
| TSV | 31.1 | 1 | 1.3 | 1 | 0.3173 |
| β-hemolytic streptococci  *n*=17 | TOT | 40.8 (25.9, 49.7) | 11 | 28.6 (27, 56.3) | 5 | 0.8829 |
| TET | -- | 0 | -- | 0 | -- |
| TDT | 36.5 (25.9, 49.1) | 9 | 28.6 (27.0, 56.3) | 5 | 0.5972 |
| TSV | 28.0 (16.5, 42.3) | 10 | 15.2 (9.9, 37.5) | 4 | 0.9393 |
| Other *Streptococcus* spp.  *n*=65 | TOT | 56.3 (51.5, 62.8) | 34 | 55.8 (48, 69.6) | 31 | 0.9121 |
| TET | 2.8 (1.6, 4.7) | 6 | 2.8 (0.8, 6.5) | 8 | 0.4990 |
| TDT | 58.6 (52.8, 78.2) | 24 | 55.8 (14.1, 72.7) | 15 | 0.6624 |
| TSV | 53.2 (46.8, 60.8) | 25 | 48.9 (43.2, 56.6) | 25 | 0.2285 |
| Organism for which BC-GP tests for resistance marker  *n*=228 | TOT | 38.9 (26.0, 49.0) | 117 | 20.1 (6.8, 35.3) | 110 | 0.0000\* |
| TET | 2.4 (1.6, 5.3) | 23 | 1.9 (1.3, 3.6) | 19 | 0.1341 |
| TDT | 39.6 (26.8, 48.1) | 69 | 9.9 (5.6, 36.8) | 68 | 0.0004\* |
| TSV | 38.2 (26.3, 46.3) | 74 | 5.2 (20.2, 34.4) | 64 | 0.0000\* |
| Organism for which BC-GP does not test for resistance marker  *n*=131 | TOT | 49.0 (31.4, 58.9) | 72 | 48.1 (23.5, 58.7) | 58 | 0.9373 |
| TET | 2.9 (1.6, 4.7) | 9 | 2.8 (0.8, 6.5) | 8 | 0.7371 |
| TDT | 55.5 (33.5, 62.8) | 37 | 55.4 (27.0, 69.6) | 21 | 0.9628 |
| TSV | 45.5 (55.3, 31.1) | 55 | 41.8 (19.6, 49.5) | 44 | 0.3386 |

BC-GP: VERIGENE® Gram-Positive Blood Culture Test

IQR: Interquartile range

TOT: time to optimal therapy

TET: time to effective therapy

TDT: time to definitive therapy

TSV: time to stopping vancomycin

\**P*<0.05

**Supplementary Table 4.** Factors associated with time-to-therapy outcomes

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Outcome | Cohort | Factor | Hazard ratio | *P* value | 95% CI |
| Time to optimal therapy | Gram-positive | Post-intervention period | 1.71 | 0.021\* | 1.08, 2.69 |
| Month of enrollment (1 to 24) | 0.99 | 0.655 | 0.95, 1.03 |
| Month of enrollment following intervention (13 to 24) | 1.00 | 0.877 | 0.94, 1.06 |
| Contaminant | 1.30 | 0.056 | 0.99, 1.70 |
| Male sex | 1.14 | 0.227 | 0.92, 1.42 |
| Age category  <6 months  6 months – 4 years  5 – 10 years  11 – 21 years | *-ref-*  0.84  0.76  0.82 | ----  0.264  0.102  0.198 | ----  0.62, 1.14  0.55, 1.05  0.60, 1.11 |
| Race  White  Black  Asian  Other | *-ref-*  0.92  1.76  1.06 | ----  0.543  0.049\*  0.669 | ----  0.71, 1.20  1.00, 3.08  0.80, 1.40 |
| ≥1 complex chronic condition | 0.87 | 0.352 | 0.64, 1.17 |
| Positive culture obtained within 3 days of admission | 1.32 | 0.022\* | 1.04, 1.67 |
| β-lactam allergy | 1.18 | 0.318 | 0.85, 1.65 |
| ID consult at culture positivity | 1.31 | 0.016\* | 1.05, 1.64 |
| Gram-negative | Post-intervention period | 1.54 | 0.219 | 0.77, 3.05 |
| Month of enrollment (1 to 24) | 0.91 | 0.021\* | 0.84, 0.97 |
| Month of enrollment following intervention (13 to 24) | 1.12 | 0.031\* | 1.01, 1.24 |
| Ethnicity  Non-Hispanic  Hispanic | *-ref-*  0.98 | ----  0.937 | ----  0.60, 1.61 |
| ≥1 complex chronic condition | 0.82 | 0.407 | 0.50, 1.32 |
| CVC at enrollment | 0.86 | 0.471 | 0.58, 1.28 |
| Time to effective therapy | Gram-positive | Post-intervention period | 2.49 | 0.164 | 0.69, 9.05 |
| Month of enrollment (1 to 24) | 0.95 | 0.374 | 0.84, 1.07 |
| Month of enrollment following intervention (13 to 24) | 1.03 | 0.708 | 0.87, 1.22 |
| Race  White  Black  Asian  Other | *-ref-*  0.63  4.26  1.30 | ----  0.233  0.072  0.433 | ----  0.29, 1.35  0.88, 20.66  0.67, 2.53 |
| Gram-negative | Post-intervention period | 252.41 | 0.004\* | 5.81, 10 973.5 |
| Month of enrollment (1 to 24) | 0.58 | 0.006\* | 0.40, 0.86 |
| Month of enrollment following intervention (13 to 24) | 1.39 | 0.083 | 0.96, 2.02 |
| Medicaid (vs. private insurance) | 1.90 | 0.286 | 0.58, 6.18 |
| ≥1 complex chronic condition | 1.29 | 0.754 | 0.26, 6.44 |
| Immunocompromised | 0.16 | 0.015\* | 0.04, 0.70 |
| CVC at enrollment | 0.77 | 0.760 | 0.15, 4.07 |
| ID consult at culture positivity | 4.89 | 0.023\* | 1.25, 19.18 |
| Time to definitive therapy | Gram-positive | Post-intervention period | 1.76 | 0.083 | 0.93, 3.33 |
| Month of enrollment (1 to 24) | 0.96 | 0.146 | 0.90, 1.02 |
| Month of enrollment following intervention (13 to 24) | 1.07 | 0.138 | 0.98, 1.17 |
| Race  White  Black  Asian  Other | *-ref-*  0.87  2.53  1.26 | ----  0.432  0.007\*  0.225 | ----  0.61, 1.24  1.28, 4.97  0.87, 1.84 |
| β-lactam allergy | 1.60 | 0.035\* | 1.03, 2.47 |
| ID consult at culture positivity | 1.55 | 0.004\* | 1.15, 2.09 |
| Gram-negative | Post-intervention period  Main  Time-varying† | 2.20  0.99 | 0.243  0.213 | 0.59, 8.22  0.97, 1.01 |
| Month of enrollment (1 to 24) | 0.88 | 0.007\* | 0.80, 0.97 |
| Month of enrollment following intervention (13 to 24) | 1.21 | 0.006\* | 1.06, 1.38 |
| Age category  <6 months  6 months – 4 years  5 – 10 years  11 – 21 years | *-ref-*  1.80  0.99  0.80 | ----  0.034\*  0.978  0.459 | ----  1.05, 1.38  0.52, 1.90  0.44, 1.44 |
| Positive culture obtained within 3 days of admission | 1.68 | 0.019\* | 1.09, 2.59 |
| Time to stopping vancomycin | Gram-positive | Post-intervention period  Main  Time-varying† | 5.62  0.97 | <0.001\*  <0.001\* | 2.58, 12.23  0.96, 0.98 |
| Month of enrollment (1 to 24) | 1.00 | 0.939 | 0.95, 1.05 |
| Month of enrollment following intervention (13 to 24) | 0.97 | 0.412 | 0.90, 1.04 |
| Contaminant | 1.24 | 0.187 | 0.90, 1.72 |
| Age category  <6 months  6 months – 4 years  5 – 10 years  11 – 21 years | *-ref-*  0.83  0.74  0.80 | ----  0.330  0.152  0.308 | ----  0.57, 1.20  0.48, 1.12  0.53, 1.22 |
| ≥1 complex chronic condition | 1.06 | 0.755 | 0.73, 1.55 |
| Immunocompromised  Main  Time-varying† | 0.40  1.02 | 0.007\*  0.015\* | 0.20, 0.77  1.00, 1.04 |
| Positive culture obtained within 3 days of admission | 1.54 | 0.011\* | 1.10, 2.15 |
| CVC at enrollment | 1.09 | 0.632 | 0.76, 1.56 |
| β-lactam allergy | 1.16 | 0.527 | 0.73, 1.85 |
| ID consult at culture positivity | 1.70 | <0.001\* | 1.27, 2.29 |
| Gram-negative | Post-intervention period | 1.17 | 0.733 | 0.48, 2.83 |
| Month of enrollment (1 to 24) | 0.96 | 0.447 | 0.88, 1.06 |
| Month of enrollment following intervention (13 to 24) | 1.06 | 0.347 | 0.94, 1.20 |

ID: Infectious diseases. CVC: Central venous catheter.

\**P*<0.05

†Time-varying covariates were added when proportional hazards assumptions were not met by individual covariates