

The population-level impact of *Enterococcus faecalis* genetics on intestinal colonisation and extraintestinal infection

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Supplementary Table 1. Relative abundance of *E. faecalis* clades or lineages by individuals' hospitalisation status and isolation source.

| PopPUNK clade | Proportion by isolation source | | Bonferroni adjusted <i>P</i> -value | Proportion by hospitalisation status | | Bonferroni adjusted <i>P</i> -value |
|---------------|--------------------------------|----------------|-------------------------------------|--------------------------------------|------------------|-------------------------------------|
| | Blood | Faeces | | Hospitalised | Non-hospitalised | |
| 1 | 0.11 (55/499) | 0.17 (43/251) | 0.026 | 0.1 (45/452) | 0.18 (53/298) | 0.0027 |
| 11 | 0.016 (8/499) | 0.008 (2/251) | 0.57 | 0.015 (7/452) | 0.01 (3/298) | 0.76 |
| 13 | 0.036 (18/499) | 0.024 (6/251) | 0.5 | 0.035 (16/452) | 0.027 (8/298) | 0.66 |
| 15 | 0.02 (10/499) | 0.012 (3/251) | 0.61 | 0.02 (9/452) | 0.013 (4/298) | 0.7 |
| 16 | 0.012 (6/499) | 0.024 (6/251) | 0.36 | 0.011 (5/452) | 0.023 (7/298) | 0.3 |
| 17 | 0.02 (10/499) | 0.032 (8/251) | 0.46 | 0.022 (10/452) | 0.027 (8/298) | 0.87 |
| 2 | 0.16 (80/499) | 0.024 (6/251) | 6.30E-08 | 0.16 (71/452) | 0.05 (15/298) | 1.20E-05 |
| 20 | 0.02 (10/499) | 0 (0/251) | 0.055 | 0.022 (10/452) | 0 (0/298) | 0.024 |
| 22 | 0.01 (5/499) | 0.02 (5/251) | 0.44 | 0.011 (5/452) | 0.017 (5/298) | 0.73 |
| 3 | 0.082 (41/499) | 0.06 (15/251) | 0.34 | 0.088 (40/452) | 0.054 (16/298) | 0.1 |
| 4 | 0.034 (17/499) | 0.19 (48/251) | 1.40E-12 | 0.033 (15/452) | 0.17 (50/298) | 3.40E-10 |
| 5 | 0.038 (19/499) | 0.048 (12/251) | 0.66 | 0.04 (18/452) | 0.044 (13/298) | 0.95 |
| 6 | 0.12 (58/499) | 0 (0/251) | 4.30E-08 | 0.12 (55/452) | 0.01 (3/298) | 4.80E-08 |
| 7 | 0.056 (28/499) | 0.008 (2/251) | 0.0029 | 0.062 (28/452) | 0.0067 (2/298) | 0.00033 |
| 8 | 0.03 (15/499) | 0.036 (9/251) | 0.84 | 0.029 (13/452) | 0.037 (11/298) | 0.68 |
| 9 | 0.026 (13/499) | 0.028 (7/251) | 1 | 0.02 (9/452) | 0.037 (11/298) | 0.24 |

Supplementary Table 2. Relative abundance of *E. faecalis* sequence types (ST) and virulence factors by individuals' hospitalisation status and isolation source.

| Sequence type (ST) | Proportion by isolation source | | Bonferroni adjusted <i>P</i> -value | Proportion by hospitalisation status | | Bonferroni adjusted <i>P</i> -value |
|--------------------|--------------------------------|----------------|-------------------------------------|--------------------------------------|------------------|-------------------------------------|
| | Blood | Faeces | | Hospitalised | Non-hospitalised | |
| ST16 | 0.076 (38/499) | 0.06 (15/251) | 0.5 | 0.082 (37/452) | 0.054 (16/298) | 0.18 |
| ST179 | 0.026 (13/499) | 0.028 (7/251) | 1 | 0.02 (9/452) | 0.037 (11/298) | 0.24 |
| ST21 | 0.038 (19/499) | 0.06 (15/251) | 0.25 | 0.038 (17/452) | 0.057 (17/298) | 0.28 |
| ST25 | 0.012 (6/499) | 0.068 (17/251) | 7.80E-05 | 0.013 (6/452) | 0.057 (17/298) | 0.0014 |
| ST28 | 0.11 (53/499) | 0 (0/251) | 1.90E-07 | 0.12 (52/452) | 0.0034 (1/298) | 1.20E-08 |
| ST34 | 0.028 (14/499) | 0.02 (5/251) | 0.67 | 0.029 (13/452) | 0.02 (6/298) | 0.62 |
| ST40 | 0.044 (22/499) | 0.092 (23/251) | 0.015 | 0.04 (18/452) | 0.091 (27/298) | 0.0068 |
| ST55 | 0.038 (19/499) | 0.024 (6/251) | 0.42 | 0.033 (15/452) | 0.034 (10/298) | 1 |
| ST6 | 0.15 (76/499) | 0.024 (6/251) | 2.10E-07 | 0.15 (68/452) | 0.047 (14/298) | 1.50E-05 |
| ST64 | 0.024 (12/499) | 0.024 (6/251) | 1 | 0.024 (11/452) | 0.023 (7/298) | 1 |
| ST9 | 0.038 (19/499) | 0.008 (2/251) | 0.034 | 0.042 (19/452) | 0.0067 (2/298) | 0.0082 |

Supplementary Table 3. Relative abundance of *E. faecalis* virulence factors by individuals' hospitalisation status and isolation source.

| Gene | Type | Proportion by isolation source | | Bonferroni adjusted <i>P</i> -value | Proportion by hospitalisation status | | Bonferroni adjusted <i>P</i> -value |
|------------------|-----------|--------------------------------|----------------|-------------------------------------|--------------------------------------|------------------|-------------------------------------|
| | | Blood | Faeces | | Hospitalised | Non-hospitalised | |
| <i>ace</i> | Adherence | 1.00 (439/440) | 1.00 (296/296) | 1 | 1.00 (484/485) | 1.00 (251/251) | 1 |
| <i>ebpA</i> | Adherence | 0.99 (437/440) | 1.00 (296/296) | 0.4 | 0.99 (482/485) | 1.00 (251/251) | 0.52 |
| <i>ebpB</i> | Adherence | 1.00 (438/440) | 1.00 (296/296) | 0.66 | 1.00 (483/485) | 1.00 (251/251) | 0.79 |
| <i>ebpC</i> | Adherence | 1.00 (438/440) | 1.00 (296/296) | 0.66 | 1.00 (483/485) | 1.00 (251/251) | 0.79 |
| <i>ecbA_fss3</i> | Adherence | 0.55 (240/440) | 0.38 (113/296) | 1.80E-05 | 0.55 (268/485) | 0.34 (85/251) | 5.70E-08 |
| EF0149 | Adherence | 0.68 (297/440) | 0.55 (163/296) | 0.00084 | 0.67 (323/485) | 0.55 (137/251) | 0.0019 |
| EF0485 | Adherence | 0.68 (297/440) | 0.55 (164/296) | 0.0012 | 0.67 (323/485) | 0.55 (138/251) | 0.0026 |
| <i>efaA</i> | Adherence | 1.00 (440/440) | 1.00 (296/296) | 1 | 1.00 (485/485) | 1.00 (251/251) | 1 |
| <i>srtC</i> | Adherence | 1.00 (438/440) | 1.00 (296/296) | 0.66 | 1.00 (483/485) | 1.00 (251/251) | 0.79 |
| <i>bopD</i> | Biofilm | 1.00 (440/440) | 1.00 (296/296) | 1 | 1.00 (485/485) | 1.00 (251/251) | 1 |
| <i>fsrA</i> | Biofilm | 0.57 (249/440) | 0.51 (152/296) | 0.19 | 0.57 (276/485) | 0.50 (125/251) | 0.079 |
| <i>fsrB</i> | Biofilm | 0.58 (254/440) | 0.52 (154/296) | 0.15 | 0.58 (281/485) | 0.51 (127/251) | 0.069 |
| <i>fsrC</i> | Biofilm | 0.86 (378/440) | 0.77 (229/296) | 0.0038 | 0.86 (416/485) | 0.76 (191/251) | 0.0015 |

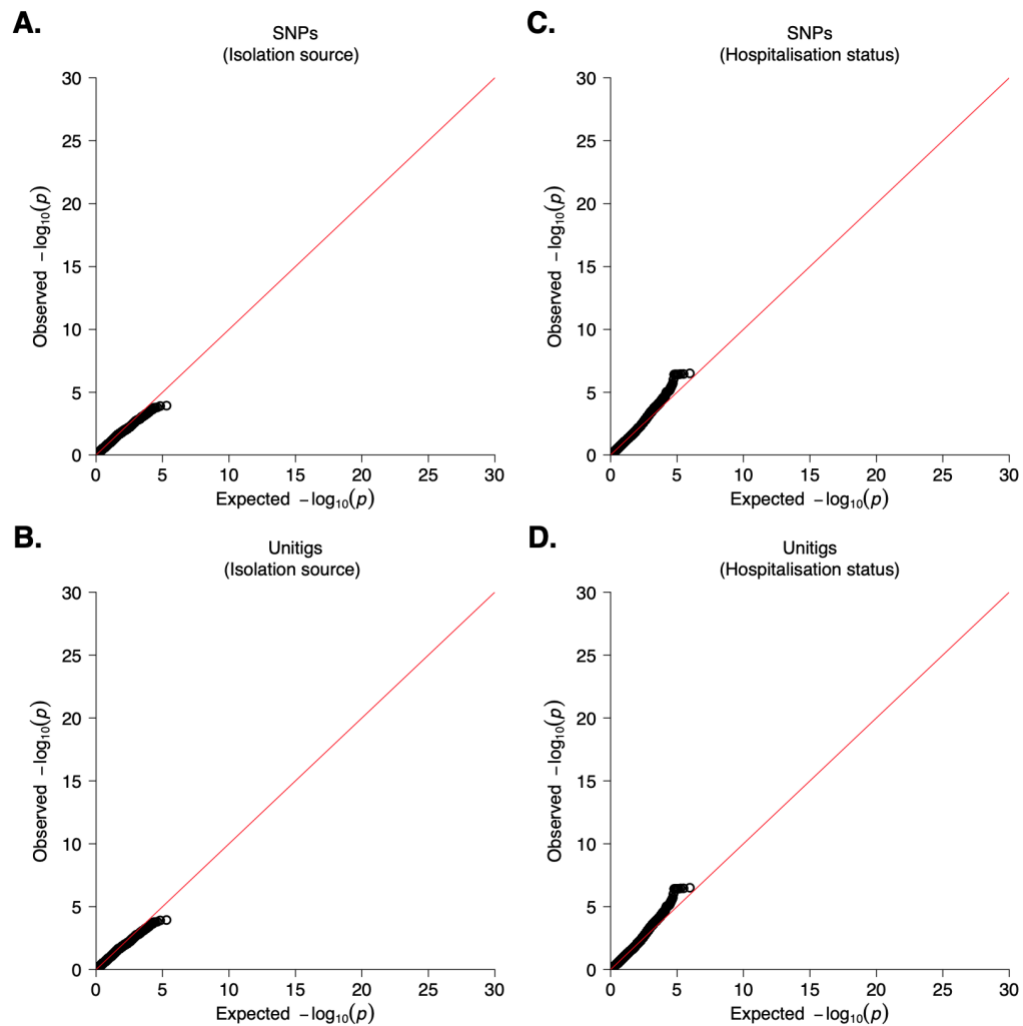
| | | | | | | | |
|---------------|-------------------|----------------|----------------|----------|----------------|----------------|----------|
| EF0818 | Exoenzyme | 0.68 (297/440) | 0.61 (180/296) | 0.074 | 0.68 (331/485) | 0.58 (146/251) | 0.0085 |
| EF3023 | Exoenzyme | 0.79 (349/440) | 0.86 (255/296) | 0.023 | 0.79 (385/485) | 0.87 (219/251) | 0.011 |
| <i>gelE</i> | Exoenzyme | 0.86 (379/440) | 0.78 (232/296) | 0.0081 | 0.86 (418/485) | 0.77 (193/251) | 0.0021 |
| <i>sprE</i> | Exoenzyme | 0.88 (388/440) | 0.81 (240/296) | 0.01 | 0.88 (428/485) | 0.80 (200/251) | 0.0027 |
| <i>cylL-l</i> | Exotoxin | 0.37 (163/440) | 0.23 (67/296) | 5.00E-05 | 0.37 (181/485) | 0.20 (49/251) | 1.20E-06 |
| <i>cylL-s</i> | Exotoxin | 0.37 (163/440) | 0.23 (67/296) | 5.00E-05 | 0.37 (181/485) | 0.20 (49/251) | 1.20E-06 |
| <i>cylM</i> | Exotoxin | 0.37 (163/440) | 0.23 (67/296) | 5.00E-05 | 0.37 (181/485) | 0.20 (49/251) | 1.20E-06 |
| <i>cylR2</i> | Exotoxin | 0.37 (163/440) | 0.23 (67/296) | 5.00E-05 | 0.37 (181/485) | 0.20 (49/251) | 1.20E-06 |
| <i>cpsA</i> | Immune modulation | 1.00 (440/440) | 1.00 (296/296) | 1 | 1.00 (485/485) | 1.00 (251/251) | 1 |
| <i>cpsB</i> | Immune modulation | 1.00 (440/440) | 1.00 (296/296) | 1 | 1.00 (485/485) | 1.00 (251/251) | 1 |
| <i>cpsC</i> | Immune modulation | 0.63 (276/440) | 0.41 (120/296) | 5.10E-09 | 0.61 (298/485) | 0.39 (98/251) | 1.20E-08 |
| <i>cpsD</i> | Immune modulation | 0.63 (276/440) | 0.40 (119/296) | 3.00E-09 | 0.61 (298/485) | 0.39 (97/251) | 6.60E-09 |
| <i>cpsE</i> | Immune modulation | 0.63 (276/440) | 0.40 (119/296) | 3.00E-09 | 0.61 (298/485) | 0.39 (97/251) | 6.60E-09 |
| <i>cpsF</i> | Immune modulation | 0.44 (194/440) | 0.27 (79/296) | 2.40E-06 | 0.44 (211/485) | 0.25 (62/251) | 8.40E-07 |
| <i>cpsG</i> | Immune modulation | 0.63 (276/440) | 0.40 (119/296) | 3.00E-09 | 0.61 (298/485) | 0.39 (97/251) | 6.60E-09 |

| | | | | | | | |
|-------------|-------------------|----------------|----------------|----------|----------------|---------------|----------|
| <i>cpsH</i> | Immune modulation | 0.63 (276/440) | 0.40 (119/296) | 3.00E-09 | 0.61 (298/485) | 0.39 (97/251) | 6.60E-09 |
| <i>cpsI</i> | Immune modulation | 0.63 (276/440) | 0.41 (120/296) | 5.10E-09 | 0.61 (298/485) | 0.39 (98/251) | 1.20E-08 |
| <i>cpsJ</i> | Immune modulation | 0.63 (276/440) | 0.41 (120/296) | 5.10E-09 | 0.61 (298/485) | 0.39 (98/251) | 1.20E-08 |
| <i>cpsK</i> | Immune modulation | 0.63 (276/440) | 0.41 (120/296) | 5.10E-09 | 0.61 (298/485) | 0.39 (98/251) | 1.20E-08 |

Supplementary Table 4. The abundance of *E. faecalis* antibiotic resistance genes by individuals' hospitalisation status and isolation source.

| Antibiotic | Body isolation source | | Bonferroni adjusted P-value | Hospitalisation status | | Bonferroni adjusted P-value |
|----------------|-----------------------|----------------|-----------------------------|------------------------|------------------|-----------------------------|
| | Blood | Faeces | | Hospitalised | Non-hospitalised | |
| Aminoglycoside | 0.51 (225/440) | 0.28 (84/296) | 5.51E-09 | 0.51 (247/485) | 0.25 (62/251) | 5.69E-11 |
| Linezolid | 0 (0/440) | 0 (0/296) | 1 | 0 (0/485) | 0 (0/251) | 1 |
| Macrolide | 0.53 (233/440) | 0.3 (88/296) | 3.77E-09 | 0.53 (256/485) | 0.26 (65/251) | 2.70E-11 |
| Phenicol | 0.29 (127/440) | 0.16 (46/296) | 8.59E-05 | 0.28 (136/485) | 0.15 (37/251) | 0.00016145 |
| Tetracycline | 0.75 (328/440) | 0.59 (176/296) | 6.75E-05 | 0.75 (364/485) | 0.56 (140/251) | 4.52E-07 |
| Vancomycin | 0.0091 (4/440) | 0.027 (8/296) | 0.11246715 | 0.016 (8/485) | 0.016 (4/251) | 1 |

*All the values in the contingency table were increased by a value of 1 to avoid division by zero when calculating the *P*-values.



Supplementary Figure 1. Quantile-quantile plots for the genome-wide association (GWA) of *E. faecalis* body isolation site and hospitalisation status. (A) QQ-plot of GWA based on SNPs for the isolation source phenotype. (B) QQ-plot of GWA based on unitigs for the isolation source phenotype. (C) QQ-plot of GWA based on SNPs for the hospitalisation status phenotype. (D) QQ-plot of GWA based on unitigs for the hospitalisation status phenotype.