Addison’s disease associated with advanced HIV may explain the high mortality

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# Baseline table

\*\*Baseline table\*\*

| Variable | **N** | **N = 554**1 |
| --- | --- | --- |
| **Age at enrolment, median (IQR) (years)** | 552 | 36.0 (31.0, 43.0) |
| **Gender, n(%)** | 553 |  |
| Female |  | 282 (51.0%) |
| Male |  | 271 (49.0%) |
| **Ethnicity, n(%)** | 554 |  |
| Black African |  | 433 (78.2%) |
| Other |  | 121 (21.8%) |
| **Duration of current illness, median (IQR) (days)** | 519 | 14.0 (12.0, 21.0) |
| **Weight loss** | 530 | 457 (86.2%) |
| **Viral load, log10 copies/ml** | 124 | 10.7 (7.2, 12.3) |
| **Tuberculosis** | 554 | 465 (83.9%) |
| **PTB** | 554 | 351 (63.4%) |
| **EPTB** | 554 | 110 (19.9%) |
| **Cryptococcus neoformans** | 554 | 30 (5.4%) |
| **Pneumonia** | 554 | 62 (11.2%) |
| **Staph aureus** | 554 | 1 (0.2%) |
| **Kaposis sarcoma** | 554 | 6 (1.1%) |
| **Cytomegalovirus** | 554 | 1 (0.2%) |
| **HSV** | 554 | 8 (1.4%) |
| **HepB** | 554 | 18 (3.2%) |
| **Candida** | 554 | 35 (6.3%) |
| **GE/c diff** | 554 | 23 (4.2%) |
| **Parvo B19** | 554 | 1 (0.2%) |
| **Syphilis** | 554 | 18 (3.2%) |
| **B menigitis** | 554 | 6 (1.1%) |
| **UTI / Leptospirosis** | 554 | 7 (1.3%) |
| **PCP** | 554 | 5 (0.9%) |
| **COVID-19** | 554 | 2 (0.4%) |
| **Neurocysticercosis** | 554 | 2 (0.4%) |
| **Total CD4 count** | 548 | 34.0 (15.0, 63.0) |
| **White cell count X109** | 544 | 5.5 (3.7, 8.2) |
| **Lymphocyte count X109** | 125 | 0.8 (0.4, 1.8) |
| **Neutrophils** | 128 | 3.4 (1.5, 8.3) |
| **ART exposure** | 554 | 207 (37.4%) |
| **Kidney medication** | 554 | 52 (9.4%) |
| **Rifampicin** | 554 | 45 (8.1%) |
| **Fluconazole** | 554 | 74 (13.4%) |
| **Opiates** | 554 | 126 (22.7%) |
| 1Median (IQR); n (%) | | |

# Table 1

Table 2: ARV status

| Variable | **No**, N = 3461 | **Yes**, N = 2071 | **p-value**2 |
| --- | --- | --- | --- |
| **Age at enrolment** | 36.0 (31.0, 43.0) | 36.0 (32.0, 43.0) | 0.7 |
| **Gender, n(%)** |  |  | 0.3 |
| Female | 171 (49.4%) | 111 (53.6%) |  |
| Male | 175 (50.6%) | 96 (46.4%) |  |
| **Ethnicity, n(%)** |  |  | 0.14 |
| Asian | 1 (0.3%) | 0 (0.0%) |  |
| Black African | 261 (75.4%) | 172 (83.1%) |  |
| Coloured | 80 (23.1%) | 34 (16.4%) |  |
| White | 4 (1.2%) | 1 (0.5%) |  |
| **Duration of current illness, median (IQR) (days)** | 14.0 (12.0, 21.0) | 14.0 (10.0, 21.0) | 0.6 |
| **Weight loss** | 284 (86.9%) | 172 (85.1%) | 0.6 |
| **log10 viral load** | 10.1 (6.1, 12.4) | 10.8 (7.8, 12.3) | 0.5 |
| **Tuberculosis** | 286 (82.7%) | 179 (86.5%) | 0.2 |
| **PTB** | 221 (63.9%) | 130 (62.8%) | 0.8 |
| **EPTB** | 68 (19.7%) | 42 (20.3%) | 0.9 |
| **Cryptococcus neoformans** | 24 (6.9%) | 6 (2.9%) | 0.042 |
| **Pneumonia** | 38 (11.0%) | 24 (11.6%) | 0.8 |
| **Staph aureus** | 1 (0.3%) | 0 (0.0%) | >0.9 |
| **Kaposis sarcoma** | 3 (0.9%) | 3 (1.4%) | 0.7 |
| **Cytomegalovirus** | 1 (0.3%) | 0 (0.0%) | >0.9 |
| **HSV** | 3 (0.9%) | 5 (2.4%) | 0.2 |
| **HepB** | 10 (2.9%) | 8 (3.9%) | 0.5 |
| **Candida** | 24 (6.9%) | 11 (5.3%) | 0.4 |
| **GE/c diff** | 11 (3.2%) | 12 (5.8%) | 0.14 |
| **Parvo B19** | 0 (0.0%) | 1 (0.5%) | 0.4 |
| **Syphilis** | 15 (4.3%) | 3 (1.4%) | 0.064 |
| **B menigitis** | 4 (1.2%) | 2 (1.0%) | >0.9 |
| **UTI / Leptospirosis** | 4 (1.2%) | 3 (1.4%) | 0.7 |
| **PCP** | 5 (1.4%) | 0 (0.0%) | 0.2 |
| **COVID-19** | 2 (0.6%) | 0 (0.0%) | 0.5 |
| **Neurocysticercosis** | 0 (0.0%) | 2 (1.0%) | 0.14 |
| **Total CD4 count** | 33.0 (14.0, 63.3) | 34.0 (16.0, 61.5) | 0.8 |
| **White cell count X109** | 5.3 (3.4, 7.7) | 5.8 (4.0, 8.9) | 0.082 |
| **Lymphocyte count X109** | 0.9 (0.4, 3.4) | 0.7 (0.4, 1.3) | 0.2 |
| **Neutrophils** | 3.6 (1.4, 8.3) | 3.3 (1.7, 7.4) | 0.9 |
| **Kidney medication** | 30 (8.7%) | 22 (10.6%) | 0.4 |
| **Rifampicin** | 22 (6.4%) | 23 (11.1%) | 0.048 |
| **Fluconazole** | 45 (13.0%) | 29 (14.0%) | 0.7 |
| **Opiates** | 97 (28.0%) | 29 (14.0%) | <0.001 |
| 1Median (IQR); n (%) | | | |
| 2Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test | | | |

# Table 1.2

Table 3: Patient presentation by CD4 count category

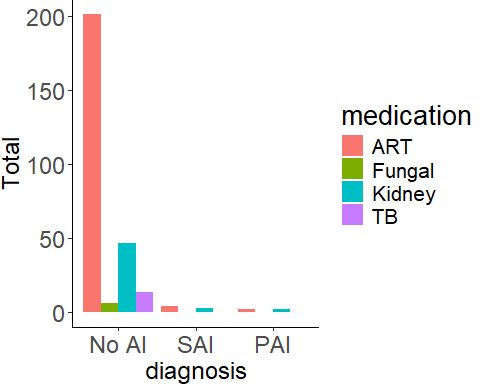
| Variable | **Overall**, N = 5481 | **0 - 33**, N = 2731 | **34 - 66**, N = 1531 | **67 - 100**, N = 1221 | **p-value**2 |
| --- | --- | --- | --- | --- | --- |
| **Age at enrolment, median (IQR) (years)** | 36.0 (31.0, 43.0) | 35.0 (30.0, 42.0) | 37.0 (32.0, 43.0) | 38.0 (33.0, 46.0) | 0.008 |
| **Gender, n(%)** |  |  |  |  | 0.2 |
| Female | 280 (51.2%) | 139 (50.9%) | 86 (56.2%) | 55 (45.5%) |  |
| Male | 267 (48.8%) | 134 (49.1%) | 67 (43.8%) | 66 (54.5%) |  |
| **Ethnicity, n(%)** |  |  |  |  | 0.3 |
| Black African | 429 (78.3%) | 221 (81.0%) | 118 (77.1%) | 90 (73.8%) |  |
| Other | 119 (21.7%) | 52 (19.0%) | 35 (22.9%) | 32 (26.2%) |  |
| **Duration of current illness, median (IQR) (days)** | 14.0 (12.0, 21.0) | 14.0 (14.0, 21.0) | 14.0 (11.8, 21.8) | 14.0 (7.0, 21.0) | 0.036 |
| **Weight loss** | 457 (86.6%) | 233 (87.6%) | 130 (87.2%) | 94 (83.2%) | 0.5 |
| **log10 viral load** | 10.7 (7.2, 12.3) | 11.6 (9.3, 12.8) | 8.9 (6.3, 12.3) | 7.3 (3.9, 10.6) | <0.001 |
| **Tuberculosis** | 463 (84.5%) | 231 (84.6%) | 132 (86.3%) | 100 (82.0%) | 0.6 |
| **PTB** | 349 (63.7%) | 179 (65.6%) | 91 (59.5%) | 79 (64.8%) | 0.4 |
| **EPTB** | 110 (20.1%) | 53 (19.4%) | 40 (26.1%) | 17 (13.9%) | 0.040 |
| **Cryptococcus neoformans** | 30 (5.5%) | 16 (5.9%) | 5 (3.3%) | 9 (7.4%) | 0.3 |
| **Pneumonia** | 62 (11.3%) | 30 (11.0%) | 19 (12.4%) | 13 (10.7%) | 0.9 |
| **Staph aureus** | 1 (0.2%) | 1 (0.4%) | 0 (0.0%) | 0 (0.0%) | >0.9 |
| **Kaposis sarcoma** | 6 (1.1%) | 6 (2.2%) | 0 (0.0%) | 0 (0.0%) | 0.056 |
| **Cytomegalovirus** | 1 (0.2%) | 0 (0.0%) | 1 (0.7%) | 0 (0.0%) | 0.5 |
| **HSV** | 8 (1.5%) | 3 (1.1%) | 4 (2.6%) | 1 (0.8%) | 0.4 |
| **HepB** | 18 (3.3%) | 9 (3.3%) | 8 (5.2%) | 1 (0.8%) | 0.12 |
| **Candida** | 35 (6.4%) | 22 (8.1%) | 11 (7.2%) | 2 (1.6%) | 0.049 |
| **GE/c diff** | 23 (4.2%) | 12 (4.4%) | 7 (4.6%) | 4 (3.3%) | 0.8 |
| **Parvo B19** | 1 (0.2%) | 0 (0.0%) | 1 (0.7%) | 0 (0.0%) | 0.5 |
| **Syphilis** | 17 (3.1%) | 8 (2.9%) | 8 (5.2%) | 1 (0.8%) | 0.11 |
| **B menigitis** | 6 (1.1%) | 3 (1.1%) | 1 (0.7%) | 2 (1.6%) | 0.8 |
| **UTI / Leptospirosis** | 7 (1.3%) | 4 (1.5%) | 0 (0.0%) | 3 (2.5%) | 0.2 |
| **PCP** | 5 (0.9%) | 4 (1.5%) | 1 (0.7%) | 0 (0.0%) | 0.5 |
| **COVID-19** | 2 (0.4%) | 1 (0.4%) | 1 (0.7%) | 0 (0.0%) | >0.9 |
| **Neurocysticercosis** | 2 (0.4%) | 1 (0.4%) | 1 (0.7%) | 0 (0.0%) | >0.9 |
| **White cell count X109** | 5.4 (3.7, 8.2) | 5.1 (2.9, 7.4) | 5.8 (4.2, 8.5) | 6.8 (4.5, 9.7) | <0.001 |
| **Lymphocyte count X109** | 0.8 (0.4, 1.8) | 0.6 (0.3, 1.3) | 0.9 (0.5, 4.9) | 1.3 (0.8, 3.0) | 0.011 |
| **Neutrophils** | 3.4 (1.5, 8.3) | 2.4 (1.0, 5.9) | 6.6 (1.9, 15.2) | 5.1 (2.9, 11.5) | 0.003 |
| **ART exposure** | 207 (37.8%) | 101 (37.0%) | 62 (40.5%) | 44 (36.1%) | 0.7 |
| **Kidney medication** | 52 (9.5%) | 27 (9.9%) | 16 (10.5%) | 9 (7.4%) | 0.7 |
| **TB medication** | 14 (2.6%) | 5 (1.8%) | 3 (2.0%) | 6 (4.9%) | 0.2 |
| **Fungal medication** | 6 (1.1%) | 2 (0.7%) | 1 (0.7%) | 3 (2.5%) | 0.3 |
| **Rifampicin** | 45 (8.2%) | 22 (8.1%) | 11 (7.2%) | 12 (9.8%) | 0.7 |
| **Fluconazole** | 74 (13.5%) | 47 (17.2%) | 17 (11.1%) | 10 (8.2%) | 0.032 |
| **Opiates** | 125 (22.8%) | 63 (23.1%) | 31 (20.3%) | 31 (25.4%) | 0.6 |
| 1Median (IQR); n (%) | | | | | |
| 2Kruskal-Wallis rank sum test; Pearson's Chi-squared test; Fisher's exact test | | | | | |

# A tibble: 3 × 17

Group .y. group1 group2 n1 n2 statistic df p p.adj 1 Random cort… resu… Adren… No Ad… 27 407 -8.91 38.2 7.17e-11 2.15e-10 2 Basal corti… resu… Adren… No Ad… 27 124 -6.51 58.6 1.88e- 8 5.64e- 8 3 Stimulated … resu… Adren… No Ad… 27 121 -14.5 61.7 1.36e-21 4.08e-21 # ℹ 7 more variables: p.adj.signif , y.position , # groups , x , xmin , xmax , p.adj\_1 png 2 # A tibble: 2 × 16 Group .y. group1 group2 n1 n2 statistic df p p.adj p.adj.signif   
1 ART … CD4 … No Yes 341 207 -0.00582 447. 0.995 1 ns  
2 Kidn… CD4 … No Yes 496 52 0.328 61.4 0.744 1 ns  
# ℹ 5 more variables: y.position , groups , x , # xmin , xmax png 2

Table 3.1: addisons disease and medication

| Variable | **Overall**, N = 5541 | **No AI**, N = 5271 | **SAI**, N = 201 | **PAI**, N = 71 | **p-value**2 |
| --- | --- | --- | --- | --- | --- |
| **ART exposure** | 207 (37.4%) | 201 (38.1%) | 4 (20.0%) | 2 (28.6%) | 0.2 |
| **Kidney medication** | 52 (9.4%) | 47 (8.9%) | 3 (15.0%) | 2 (28.6%) | 0.10 |
| **TB medication** | 14 (2.5%) | 14 (2.7%) | 0 (0.0%) | 0 (0.0%) | >0.9 |
| **Fungal medication** | 6 (1.1%) | 6 (1.1%) | 0 (0.0%) | 0 (0.0%) | >0.9 |
| 1n (%) | | | | | |
| 2Fisher's exact test | | | | | |



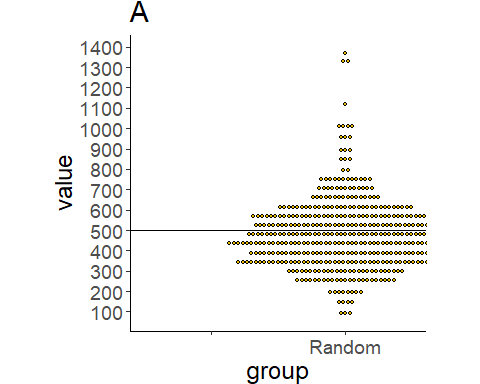
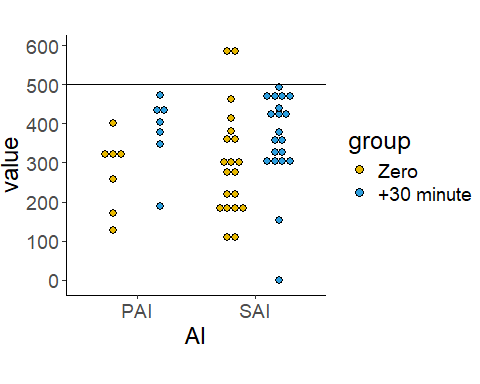
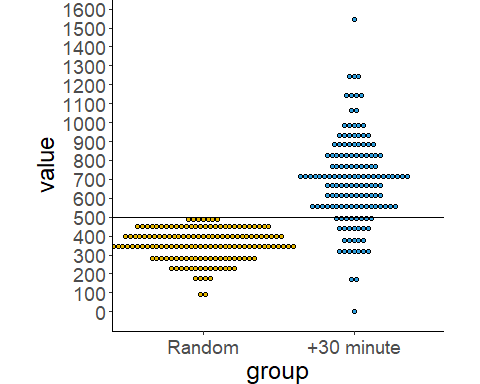
# Table 2: comparing Addisons status with other variables

Table 2: Should compare Total AI with Non-AI patients

|  | **Non-AI vs AI** | | | **PAI vs SAI patients** | | |
| --- | --- | --- | --- | --- | --- | --- |
| Variable | **no-AI**, N = 5271 | **AI**, N = 271 | **p-value**2 | **SAI**, N = 201 | **PAI**, N = 71 | **p-value**3 |
| **Age at enrolment, median (IQR) (years)** | 36.0 (31.0, 43.0) | 36.0 (32.0, 47.5) | 0.4 | 36.0 (32.0, 48.5) | 40.0 (35.0, 45.0) | 0.6 |
| **Gender, n(%)** |  |  | >0.9 |  |  | 0.7 |
| Female | 268 (51.0%) | 14 (51.9%) |  | 11 (55.0%) | 3 (42.9%) |  |
| Male | 258 (49.0%) | 13 (48.1%) |  | 9 (45.0%) | 4 (57.1%) |  |
| **Ethnicity, n(%)** |  |  | 0.4 |  |  | >0.9 |
| Black African | 410 (77.8%) | 23 (85.2%) |  | 17 (85.0%) | 6 (85.7%) |  |
| Other | 117 (22.2%) | 4 (14.8%) |  | 3 (15.0%) | 1 (14.3%) |  |
| **Duration of current illness, median (IQR) (days)** | 14.0 (12.0, 21.0) | 14.0 (14.0, 27.8) | 0.4 | 21.0 (14.0, 30.0) | 10.0 (7.0, 12.5) | 0.019 |
| **Weight loss** | 435 (86.5%) | 22 (81.5%) | 0.4 | 15 (75.0%) | 7 (100.0%) | 0.3 |
| **Viral load (log10 Copies/mL)** | 10.7 (7.1, 12.4) | 11.0 (10.7, 11.3) | 0.9 | 10.5 (10.5, 10.5) | 11.6 (11.6, 11.6) | >0.9 |
| **Tuberculosis** | 444 (84.3%) | 21 (77.8%) | 0.4 | 16 (80.0%) | 5 (71.4%) | 0.6 |
| **PTB** | 340 (64.5%) | 11 (40.7%) | 0.012 | 8 (40.0%) | 3 (42.9%) | >0.9 |
| **EPTB** | 100 (19.0%) | 10 (37.0%) | 0.022 | 8 (40.0%) | 2 (28.6%) | 0.7 |
| **Cryptococcus neoformans** | 20 (3.8%) | 10 (37.0%) | <0.001 | 7 (35.0%) | 3 (42.9%) | >0.9 |
| **Pneumonia** | 59 (11.2%) | 3 (11.1%) | >0.9 | 3 (15.0%) | 0 (0.0%) | 0.5 |
| **Staph aureus** | 0 (0.0%) | 1 (3.7%) | 0.049 | 1 (5.0%) | 0 (0.0%) | >0.9 |
| **Kaposis sarcoma** | 5 (0.9%) | 1 (3.7%) | 0.3 | 1 (5.0%) | 0 (0.0%) | >0.9 |
| **Cytomegalovirus** | 0 (0.0%) | 1 (3.7%) | 0.049 | 1 (5.0%) | 0 (0.0%) | >0.9 |
| **HSV** | 7 (1.3%) | 1 (3.7%) | 0.3 | 1 (5.0%) | 0 (0.0%) | >0.9 |
| **HepB** | 16 (3.0%) | 2 (7.4%) | 0.2 | 2 (10.0%) | 0 (0.0%) | >0.9 |
| **Candida** | 34 (6.5%) | 1 (3.7%) | >0.9 | 1 (5.0%) | 0 (0.0%) | >0.9 |
| **GE/c diff** | 23 (4.4%) | 0 (0.0%) | 0.6 | 0 (0.0%) | 0 (0.0%) |  |
| **Parvo B19** | 0 (0.0%) | 1 (3.7%) | 0.049 | 0 (0.0%) | 1 (14.3%) | 0.3 |
| **Syphilis** | 18 (3.4%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **B menigitis** | 6 (1.1%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **UTI / Leptospirosis** | 7 (1.3%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **PCP** | 5 (0.9%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **COVID-19** | 2 (0.4%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **Neurocysticercosis** | 2 (0.4%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **Total CD4 count** | 34.0 (15.0, 63.0) | 28.0 (13.5, 49.5) | 0.4 | 19.0 (10.0, 48.8) | 46.0 (25.5, 61.0) | 0.2 |
| **White cell count X109** | 5.6 (3.8, 8.2) | 5.2 (2.8, 8.9) | 0.5 | 5.3 (2.8, 11.9) | 3.5 (3.0, 5.5) | 0.4 |
| **Lymphocyte count X109** | 0.8 (0.4, 1.9) | 0.9 (0.5, 1.2) | 0.7 | 0.7 (0.5, 1.0) | 1.3 (1.3, 1.3) | 0.6 |
| **Neutrophils** | 3.7 (1.5, 8.7) | 1.3 (0.9, 1.6) | 0.039 | 1.5 (1.0, 1.7) | 0.9 (0.9, 0.9) | 0.7 |
| **Sodium mmol/L** | 133.0 (130.0, 137.0) | 135.0 (133.0, 137.5) | 0.033 | 135.5 (134.0, 137.3) | 133.0 (131.5, 136.5) | 0.2 |
| **Potassium mmol/L** | 4.1 (3.6, 4.6) | 3.9 (3.3, 4.3) | 0.069 | 4.0 (3.3, 4.5) | 3.6 (3.3, 3.9) | 0.4 |
| **Haemoglobin g/dL** | 8.7 (7.4, 10.3) | 8.7 (7.6, 10.4) | 0.6 | 8.7 (7.6, 10.7) | 10.2 (7.9, 10.3) | 0.7 |
| **BP (systolic)** | 112.0 (102.0, 125.0) | 120.0 (102.5, 128.5) | 0.4 | 118.0 (99.5, 129.3) | 120.0 (120.0, 123.5) | 0.7 |
| **BP (diastolic)** | 70.0 (60.0, 79.0) | 71.0 (66.5, 80.0) | 0.080 | 72.0 (60.0, 80.0) | 70.0 (70.0, 82.0) | 0.8 |
| **Heart rate** | 91.0 (79.0, 108.5) | 87.0 (78.5, 107.0) | 0.7 | 85.0 (76.8, 102.3) | 97.0 (88.0, 111.0) | 0.10 |
| **Hypotension** | 47 (9.4%) | 1 (3.7%) | 0.5 | 1 (5.0%) | 0 (0.0%) | >0.9 |
| **Weakness** | 427 (85.2%) | 21 (77.8%) | 0.3 | 17 (85.0%) | 4 (57.1%) | 0.3 |
| **Tiredness** | 428 (85.3%) | 23 (85.2%) | >0.9 | 18 (90.0%) | 5 (71.4%) | 0.3 |
| **Poor appetite** | 379 (76.1%) | 22 (81.5%) | 0.5 | 16 (80.0%) | 6 (85.7%) | >0.9 |
| **Increased pigmentation of the skin** | 251 (51.1%) | 9 (37.5%) | 0.2 | 6 (31.6%) | 3 (60.0%) | 0.3 |
| **Nausea** | 267 (53.3%) | 16 (59.3%) | 0.5 | 11 (55.0%) | 5 (71.4%) | 0.7 |
| **Vomiting** | 139 (27.8%) | 9 (33.3%) | 0.5 | 5 (25.0%) | 4 (57.1%) | 0.2 |
| **Liking for salt** | 265 (53.1%) | 19 (70.4%) | 0.080 | 14 (70.0%) | 5 (71.4%) | >0.9 |
| **Hypoglycaemia** | 11 (2.2%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **Loss of consciousness** | 7 (1.4%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **Diarrhoea** | 224 (45.1%) | 8 (29.6%) | 0.12 | 7 (35.0%) | 1 (14.3%) | 0.6 |
| **Dizziness** | 241 (48.3%) | 13 (50.0%) | 0.9 | 9 (45.0%) | 4 (66.7%) | 0.6 |
| **Shock** | 5 (1.0%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **Anorexia** | 239 (47.8%) | 8 (29.6%) | 0.065 | 4 (20.0%) | 4 (57.1%) | 0.14 |
| **Loss of axillary and pubic hair, if female** |  |  | 0.5 |  |  | 0.8 |
| No | 160 (31.5%) | 11 (40.7%) |  | 9 (45.0%) | 2 (28.6%) |  |
| Not applicable | 251 (49.4%) | 13 (48.1%) |  | 9 (45.0%) | 4 (57.1%) |  |
| Yes | 97 (19.1%) | 3 (11.1%) |  | 2 (10.0%) | 1 (14.3%) |  |
| **Any postural drop in blood pressure** | 21 (4.2%) | 2 (7.4%) | 0.3 | 2 (10.0%) | 0 (0.0%) | >0.9 |
| **Presence of anaemia** | 297 (59.6%) | 13 (50.0%) | 0.3 | 9 (47.4%) | 4 (57.1%) | >0.9 |
| **mortality** | 62 (44.3%) | 6 (50.0%) | 0.7 | 4 (44.4%) | 2 (66.7%) | >0.9 |
| **ART exposure** | 201 (38.1%) | 6 (22.2%) | 0.10 | 4 (20.0%) | 2 (28.6%) | 0.6 |
| **Kidney medication** | 47 (8.9%) | 5 (18.5%) | 0.2 | 3 (15.0%) | 2 (28.6%) | 0.6 |
| **Rifampicin** | 44 (8.3%) | 1 (3.7%) | 0.7 | 1 (5.0%) | 0 (0.0%) | >0.9 |
| **Fluconazole** | 63 (12.0%) | 11 (40.7%) | <0.001 | 8 (40.0%) | 3 (42.9%) | >0.9 |
| **Opiates** | 114 (21.6%) | 12 (44.4%) | 0.006 | 10 (50.0%) | 2 (28.6%) | 0.4 |
| 1Median (IQR); n (%) | | | | | | |
| 2Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test | | | | | | |
| 3Wilcoxon rank sum test; Fisher's Exact Test for Count Data; Wilcoxon rank sum exact test; Fisher's Exact Test for Count Data with simulated p-value  (based on 2000 replicates) | | | | | | |

# Table 2.2: Cause of moratlity

# Dotplot

png 2 png 2 png 2

# Table 3: Bivariate table

# Table 3a: Deep dive on Addison’s disease patients

Mortality: Non-AI vs AI

| Variable | **AI deaths**, N = 101 | **Alive without AI**, N = 2751 | **p-value**2 |
| --- | --- | --- | --- |
| **Age at enrolment, median (IQR) (years)** | 42 (39, 48) | 35 (31, 42) | 0.049 |
| **Gender, n(%)** |  |  | >0.9 |
| Female | 5 (50.0%) | 133 (48.4%) |  |
| Male | 5 (50.0%) | 142 (51.6%) |  |
| **Ethnicity, n(%)** |  |  | >0.9 |
| Black African | 8 (80.0%) | 221 (80.4%) |  |
| Other | 2 (20.0%) | 54 (19.6%) |  |
| **Duration of current illness, median (IQR) (days)** | 14 (10, 14) | 14 (14, 21) | 0.2 |
| **Weight loss** | 8 (80.0%) | 245 (92.1%) | 0.2 |
| **Viral load (log10 Copies/mL)** | NA (NA, NA) | 10.14 (8.01, 12.12) |  |
| **Tuberculosis** | 8 (80.0%) | 240 (87.3%) | 0.6 |
| **Cryptococcus neoformans** | 5 (50.0%) | 9 (3.3%) | <0.001 |
| **Pneumonia** | 0 (0.0%) | 40 (14.5%) | 0.4 |
| **Staph aureus** | 0 (0.0%) | 0 (0.0%) |  |
| **Kaposis sarcoma** | 0 (0.0%) | 2 (0.7%) | >0.9 |
| **Cytomegalovirus** | 1 (10.0%) | 0 (0.0%) | 0.035 |
| **HSV** | 0 (0.0%) | 4 (1.5%) | >0.9 |
| **HepB** | 1 (10.0%) | 8 (2.9%) | 0.3 |
| **Candida** | 1 (10.0%) | 14 (5.1%) | 0.4 |
| **GE/c diff** | 0 (0.0%) | 12 (4.4%) | >0.9 |
| **Parvo B19** | 0 (0.0%) | 0 (0.0%) |  |
| **Syphilis** | 0 (0.0%) | 9 (3.3%) | >0.9 |
| **B menigitis** | 0 (0.0%) | 1 (0.4%) | >0.9 |
| **UTI / Leptospirosis** | 0 (0.0%) | 3 (1.1%) | >0.9 |
| **PCP** | 0 (0.0%) | 1 (0.4%) | >0.9 |
| **COVID-19** | 0 (0.0%) | 2 (0.7%) | >0.9 |
| **Neurocysticercosis** | 0 (0.0%) | 0 (0.0%) |  |
| **Total CD4 count** | 33 (17, 55) | 36 (15, 63) | >0.9 |
| **White cell count X109** | 6.1 (5.3, 27.5) | 5.3 (3.8, 8.2) | 0.14 |
| **Lymphocyte count X109** | NA (NA, NA) | 0.7 (0.3, 1.8) |  |
| **Neutrophils** | NA (NA, NA) | 4 (1, 8) |  |
| **Sodium mmol/L** | 136.5 (133.0, 139.0) | 134.0 (130.0, 137.0) | 0.10 |
| **Potassium mmol/L** | 3.85 (3.62, 4.00) | 4.15 (3.80, 4.60) | 0.2 |
| **Haemoglobin g/dL** | 9.45 (7.65, 10.47) | 8.90 (7.50, 10.60) | 0.8 |
| **BP (systolic)** | 128 (120, 130) | 111 (101, 127) | 0.12 |
| **BP (diastolic)** | 78 (65, 80) | 68 (60, 76) | 0.10 |
| **Heart rate** | 87 (70, 104) | 92 (80, 111) | 0.5 |
| **Hypotension** | 0 (0.0%) | 21 (8.0%) | >0.9 |
| **Weakness** | 8 (80.0%) | 228 (86.4%) | 0.6 |
| **Tiredness** | 10 (100.0%) | 237 (89.1%) | 0.6 |
| **Poor appetite** | 10 (100.0%) | 200 (76.3%) | 0.12 |
| **Increased pigmentation of the skin** | 3 (37.5%) | 122 (47.5%) | 0.7 |
| **Nausea** | 8 (80.0%) | 135 (50.9%) | 0.11 |
| **Vomiting** | 4 (40.0%) | 79 (29.9%) | 0.5 |
| **Liking for salt** | 8 (80.0%) | 166 (62.9%) | 0.3 |
| **Hypoglycaemia** | 0 (0.0%) | 7 (2.7%) | >0.9 |
| **Loss of consciousness** | 0 (0.0%) | 1 (0.4%) | >0.9 |
| **Diarrhoea** | 2 (20.0%) | 110 (42.0%) | 0.2 |
| **Dizziness** | 4 (40.0%) | 124 (46.8%) | 0.8 |
| **Shock** | 0 (0.0%) | 3 (1.1%) | >0.9 |
| **Anorexia** | 3 (30.0%) | 122 (46.2%) | 0.4 |
| **Loss of axillary and pubic hair, if female** |  |  | 0.8 |
| No | 4 (40.0%) | 84 (31.1%) |  |
| Not applicable | 5 (50.0%) | 141 (52.2%) |  |
| Yes | 1 (10.0%) | 45 (16.7%) |  |
| **Any postural drop in blood pressure** | 0 (0.0%) | 9 (3.4%) | >0.9 |
| **Presence of anaemia** | 5 (50.0%) | 143 (54.4%) | >0.9 |
| **ART exposure** | 1 (10.0%) | 105 (38.2%) | 0.10 |
| **Kidney medication** | 2 (20.0%) | 23 (8.4%) | 0.2 |
| **Rifampicin** | 0 (0.0%) | 24 (8.7%) | >0.9 |
| **Fluconazole** | 6 (60.0%) | 33 (12.0%) | <0.001 |
| **Opiates** | 3 (30.0%) | 77 (28.0%) | >0.9 |
| **incremental\_cortisol** | 32 (17, 107) | 283 (194, 383) | <0.001 |
| 1Median (IQR); n (%) | | | |
| 2Wilcoxon rank sum test; Fisher's exact test | | | |

Table 2.2.1: Mortality; PAI SAI

| Variable | **PAI**, N = 41 | **SAI**, N = 61 | **p-value**2 |
| --- | --- | --- | --- |
| **mortality with Addisons disease** |  |  |  |
| Die | 4 (100.0%) | 6 (100.0%) |  |
| **Age at enrolment median (IQR) (years)** | 39.5 (37.0, 41.8) | 45.0 (41.3, 49.5) | 0.3 |
| **Gender, n(%)** |  |  | >0.9 |
| Female | 2 (50.0%) | 3 (50.0%) |  |
| Male | 2 (50.0%) | 3 (50.0%) |  |
| **Ethnicity, n(%)** |  |  | 0.5 |
| Black African | 4 (100.0%) | 4 (66.7%) |  |
| Other | 0 (0.0%) | 2 (33.3%) |  |
| **Duration of current illness, median (IQR) (days)** |  |  | >0.9 |
| 4 | 1 (33.3%) | 0 (0.0%) |  |
| 7 | 0 (0.0%) | 1 (16.7%) |  |
| 9 | 0 (0.0%) | 1 (16.7%) |  |
| 23 | 1 (33.3%) | 0 (0.0%) |  |
| 236 | 1 (33.3%) | 0 (0.0%) |  |
| 1812 | 0 (0.0%) | 1 (16.7%) |  |
| 3630 | 0 (0.0%) | 1 (16.7%) |  |
| 5528 | 0 (0.0%) | 1 (16.7%) |  |
| 7754 | 0 (0.0%) | 1 (16.7%) |  |
| **Random cortisol** | 312.5 (263.0, 359.0) | 293.5 (252.0, 335.8) | 0.8 |
| **Basal cortisol** | 243.5 (161.0, 336.3) | 283.5 (237.5, 361.0) | 0.6 |
| **Stimulated cortisol** | 375.0 (307.5, 409.3) | 376.5 (320.8, 427.8) | 0.8 |
| **ACTH** | 115.6 (83.8, 185.8) | 25.0 (22.7, 34.0) | 0.010 |
| **incremental\_cortisol** |  |  | >0.9 |
| 3 | 1 (25.0%) | 0 (0.0%) |  |
| 15 | 0 (0.0%) | 1 (20.0%) |  |
| 17 | 1 (25.0%) | 0 (0.0%) |  |
| 30 | 0 (0.0%) | 1 (20.0%) |  |
| 32 | 1 (25.0%) | 0 (0.0%) |  |
| 50 | 0 (0.0%) | 1 (20.0%) |  |
| 107 | 0 (0.0%) | 1 (20.0%) |  |
| 246 | 0 (0.0%) | 1 (20.0%) |  |
| 300 | 1 (25.0%) | 0 (0.0%) |  |
| **BP (systolic)** |  |  | 0.2 |
| 95 | 0 (0.0%) | 1 (16.7%) |  |
| 100 | 0 (0.0%) | 1 (16.7%) |  |
| 120 | 2 (50.0%) | 0 (0.0%) |  |
| 127 | 1 (25.0%) | 0 (0.0%) |  |
| 128 | 0 (0.0%) | 2 (33.3%) |  |
| 130 | 0 (0.0%) | 1 (16.7%) |  |
| 134 | 1 (25.0%) | 0 (0.0%) |  |
| 140 | 0 (0.0%) | 1 (16.7%) |  |
| **BP (diastolic)** |  |  | 0.5 |
| 55 | 0 (0.0%) | 1 (16.7%) |  |
| 60 | 0 (0.0%) | 1 (16.7%) |  |
| 63 | 1 (25.0%) | 0 (0.0%) |  |
| 71 | 0 (0.0%) | 1 (16.7%) |  |
| 76 | 0 (0.0%) | 1 (16.7%) |  |
| 79 | 1 (25.0%) | 0 (0.0%) |  |
| 80 | 0 (0.0%) | 2 (33.3%) |  |
| 85 | 1 (25.0%) | 0 (0.0%) |  |
| 86 | 1 (25.0%) | 0 (0.0%) |  |
| **Heart rate** | 111.0 (101.8, 122.5) | 72.0 (65.8, 80.5) | 0.019 |
| **Hypotension** | 0 (0.0%) | 0 (0.0%) |  |
| **Weakness** | 3 (75.0%) | 5 (83.3%) | >0.9 |
| **Tiredness** | 4 (100.0%) | 6 (100.0%) |  |
| **Poor appetite** | 4 (100.0%) | 6 (100.0%) |  |
| **Weight loss** | 4 (100.0%) | 4 (66.7%) | 0.5 |
| **Increased pigmentation of the skin** | 3 (100.0%) | 0 (0.0%) | 0.018 |
| **Nausea** | 4 (100.0%) | 4 (66.7%) | 0.5 |
| **Vomiting** | 3 (75.0%) | 1 (16.7%) | 0.2 |
| **Liking for salt** | 3 (75.0%) | 5 (83.3%) | >0.9 |
| **Hypoglycaemia** | 0 (0.0%) | 0 (0.0%) |  |
| **Loss of consciousness** | 0 (0.0%) | 0 (0.0%) |  |
| **Diarrhoea** | 1 (25.0%) | 1 (16.7%) | >0.9 |
| **Dizziness** | 3 (75.0%) | 1 (16.7%) | 0.2 |
| **Shock** | 0 (0.0%) | 0 (0.0%) |  |
| **Anorexia** | 3 (75.0%) | 0 (0.0%) | 0.033 |
| **Loss of axillary and pubic hair, if female** |  |  | 0.7 |
| No | 1 (25.0%) | 3 (50.0%) |  |
| Not applicable | 2 (50.0%) | 3 (50.0%) |  |
| Yes | 1 (25.0%) | 0 (0.0%) |  |
| **Any postural drop in blood pressure** | 0 (0.0%) | 0 (0.0%) |  |
| **Presence of anaemia** | 3 (75.0%) | 2 (33.3%) | 0.5 |
| **Tuberculosis** | 3 (75.0%) | 5 (83.3%) | >0.9 |
| **PTB** | 2 (50.0%) | 2 (33.3%) | >0.9 |
| **EPTB** | 1 (25.0%) | 3 (50.0%) | 0.6 |
| **Cryptococcus neoformans** | 2 (50.0%) | 3 (50.0%) | >0.9 |
| **Pneumonia** | 0 (0.0%) | 0 (0.0%) |  |
| **Staph aureus** | 0 (0.0%) | 0 (0.0%) |  |
| **Kaposis sarcoma** | 0 (0.0%) | 0 (0.0%) |  |
| **Cytomegalovirus** | 0 (0.0%) | 1 (16.7%) | >0.9 |
| **HSV** | 0 (0.0%) | 0 (0.0%) |  |
| **HepB** | 0 (0.0%) | 1 (16.7%) | >0.9 |
| **Candida** | 0 (0.0%) | 1 (16.7%) | >0.9 |
| **GE/c diff** | 0 (0.0%) | 0 (0.0%) |  |
| **Parvo B19** | 0 (0.0%) | 0 (0.0%) |  |
| **Syphilis** | 0 (0.0%) | 0 (0.0%) |  |
| **B menigitis** | 0 (0.0%) | 0 (0.0%) |  |
| **UTI / Leptospirosis** | 0 (0.0%) | 0 (0.0%) |  |
| **PCP** | 0 (0.0%) | 0 (0.0%) |  |
| **COVID-19** | 0 (0.0%) | 0 (0.0%) |  |
| **Neurocysticercosis** | 0 (0.0%) | 0 (0.0%) |  |
| **Viral load (log10 Copies/mL)** | NA (NA, NA) | NA (NA, NA) |  |
| **Total CD4 count** |  |  | 0.5 |
| 13 | 0 (0.0%) | 1 (16.7%) |  |
| 15 | 1 (25.0%) | 0 (0.0%) |  |
| 17 | 0 (0.0%) | 2 (33.3%) |  |
| 23 | 1 (25.0%) | 0 (0.0%) |  |
| 43 | 0 (0.0%) | 1 (16.7%) |  |
| 46 | 1 (25.0%) | 0 (0.0%) |  |
| 58 | 0 (0.0%) | 1 (16.7%) |  |
| 76 | 1 (25.0%) | 0 (0.0%) |  |
| 98 | 0 (0.0%) | 1 (16.7%) |  |
| **Sodium mmol/L** |  |  | 0.8 |
| 131 | 0 (0.0%) | 2 (33.3%) |  |
| 133 | 1 (25.0%) | 1 (16.7%) |  |
| 134 | 1 (25.0%) | 0 (0.0%) |  |
| 139 | 2 (50.0%) | 1 (16.7%) |  |
| 141 | 0 (0.0%) | 1 (16.7%) |  |
| 150 | 0 (0.0%) | 1 (16.7%) |  |
| **Potassium mmol/L** |  |  | 0.5 |
| 2.79999995231628 | 0 (0.0%) | 1 (16.7%) |  |
| 3.29999995231628 | 1 (25.0%) | 0 (0.0%) |  |
| 3.59999990463257 | 1 (25.0%) | 0 (0.0%) |  |
| 3.70000004768372 | 1 (25.0%) | 0 (0.0%) |  |
| 3.79999995231628 | 0 (0.0%) | 1 (16.7%) |  |
| 3.90000009536743 | 0 (0.0%) | 1 (16.7%) |  |
| 4 | 0 (0.0%) | 2 (33.3%) |  |
| 5.40000009536743 | 1 (25.0%) | 0 (0.0%) |  |
| 32 | 0 (0.0%) | 1 (16.7%) |  |
| **Haemoglobin g/dL** | 10.3 (9.7, 11.2) | 8.1 (6.4, 10.0) | 0.4 |
| **White cell count X109** | 5.5 (4.6, 5.9) | 21.9 (6.8, 37.5) | 0.2 |
| **Lymphocyte count X109** | NA (NA, NA) | NA (NA, NA) |  |
| **Addisons disease** |  |  | >0.9 |
| 0 | 0 (0.0%) | 0 (0.0%) |  |
| 1 | 4 (100.0%) | 6 (100.0%) |  |
| **ART exposure** | 0 (0.0%) | 1 (16.7%) | >0.9 |
| **Kidney medication** | 1 (25.0%) | 1 (16.7%) | >0.9 |
| **Rifampicin** | 0 (0.0%) | 0 (0.0%) | >0.9 |
| **Fluconazole** | 2 (50.0%) | 4 (66.7%) | >0.9 |
| **Opiates** | 1 (25.0%) | 2 (33.3%) | >0.9 |
| 1n (%); Median (IQR) | | | |
| 2Wilcoxon rank sum exact test; Fisher's exact test | | | |

Mortality: Non-AI vs AI

|  | **Mortality: Non-AI vs AI** | | | **Mortality among only Addisons disease patients** | | |
| --- | --- | --- | --- | --- | --- | --- |
| Variable | **1**, N = 1411 | **2**, N = 101 | **p-value**2 | **Alive**, N = 151 | **Died**, N = 101 | **p-value**3 |
| **Age at enrolment, median (IQR) (years)** | 37 (32, 44) | 42 (39, 48) | 0.11 |  |  |  |
| **Gender, n(%)** |  |  | >0.9 |  |  | 0.7 |
| Female | 76 (53.9%) | 5 (50.0%) |  | 9 (60.0%) | 5 (50.0%) |  |
| Male | 65 (46.1%) | 5 (50.0%) |  | 6 (40.0%) | 5 (50.0%) |  |
| **Ethnicity, n(%)** |  |  | >0.9 |  |  | 0.5 |
| Black African | 115 (81.6%) | 8 (80.0%) |  | 14 (93.3%) | 8 (80.0%) |  |
| Other | 26 (18.4%) | 2 (20.0%) |  | 1 (6.7%) | 2 (20.0%) |  |
| **Duration of current illness, median (IQR) (days)** | 14 (14, 21) | 14 (10, 14) | 0.13 | 1,610.0 (286.5, 3,356.0) | 236.0 (9.0, 3,630.0) | 0.6 |
| **Random cortisol** | 508 (405, 636) | 307 (252, 342) | <0.001 | 294.0 (243.0, 382.0) | 306.5 (252.0, 342.3) | 0.8 |
| **Basal cortisol** | 483 (408, 608) | 284 (201, 365) | <0.001 | 300.0 (197.0, 339.0) | 283.5 (201.0, 364.5) | >0.9 |
| **Stimulated cortisol** | 768 (624, 908) | 375 (321, 426) | <0.001 | 379.0 (334.0, 467.5) | 375.0 (320.8, 425.5) | 0.4 |
| **ACTH** | 33 (22, 56) | 42 (25, 84) | 0.3 | 25.3 (13.6, 56.1) | 42.4 (24.9, 83.8) | 0.3 |
| **Weight loss** | 116 (89.2%) | 8 (80.0%) | 0.3 | 12 (80.0%) | 8 (80.0%) | >0.9 |
| **Viral load (log10 Copies/mL)** | 10.8 (7.6, 12.6) | NA (NA, NA) |  |  |  |  |
| 11.60516730587 |  |  |  | 1 (100.0%) | 0 (NA%) |  |
| **Tuberculosis** | 120 (85.1%) | 8 (80.0%) | 0.6 | 11 (73.3%) | 8 (80.0%) | >0.9 |
| **PTB** | 92 (65.2%) | 4 (40.0%) | 0.2 | 5 (33.3%) | 4 (40.0%) | >0.9 |
| **EPTB** | 26 (18.4%) | 4 (40.0%) | 0.11 | 6 (40.0%) | 4 (40.0%) | >0.9 |
| **Cryptococcus neoformans** | 6 (4.3%) | 5 (50.0%) | <0.001 | 5 (33.3%) | 5 (50.0%) | 0.4 |
| **Pneumonia** | 14 (9.9%) | 0 (0.0%) | 0.6 | 3 (20.0%) | 0 (0.0%) | 0.3 |
| **Staph aureus** | 0 (0.0%) | 0 (0.0%) |  | 1 (6.7%) | 0 (0.0%) | >0.9 |
| **Kaposis sarcoma** | 1 (0.7%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **Cytomegalovirus** | 0 (0.0%) | 1 (10.0%) | 0.066 | 0 (0.0%) | 1 (10.0%) | 0.4 |
| **HSV** | 2 (1.4%) | 0 (0.0%) | >0.9 | 1 (6.7%) | 0 (0.0%) | >0.9 |
| **HepB** | 5 (3.5%) | 1 (10.0%) | 0.3 | 1 (6.7%) | 1 (10.0%) | >0.9 |
| **Candida** | 7 (5.0%) | 1 (10.0%) | 0.4 | 0 (0.0%) | 1 (10.0%) | 0.4 |
| **GE/c diff** | 3 (2.1%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **Parvo B19** | 0 (0.0%) | 0 (0.0%) |  | 1 (6.7%) | 0 (0.0%) | >0.9 |
| **Syphilis** | 4 (2.8%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **B menigitis** | 1 (0.7%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **UTI / Leptospirosis** | 2 (1.4%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **PCP** | 2 (1.4%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **COVID-19** | 0 (0.0%) | 0 (0.0%) |  | 0 (0.0%) | 0 (0.0%) |  |
| **Neurocysticercosis** | 0 (0.0%) | 0 (0.0%) |  | 0 (0.0%) | 0 (0.0%) |  |
| **Total CD4 count** | 28 (12, 57) | 33 (17, 55) | 0.5 | 28.0 (9.0, 49.5) | 33.0 (17.0, 55.0) | 0.5 |
| **White cell count X109** | 5.6 (3.8, 8.2) | 6.1 (5.3, 27.5) | 0.2 | 3.5 (2.5, 5.7) | 6.1 (5.3, 27.5) | 0.026 |
| **Lymphocyte count X109** | 0.9 (0.4, 1.7) | NA (NA, NA) |  |  |  | >0.9 |
| 0.360000014305115 |  |  |  | 1 (20.0%) | 0 (NA%) |  |
| 0.490000009536743 |  |  |  | 1 (20.0%) | 0 (NA%) |  |
| 1.10000002384186 |  |  |  | 1 (20.0%) | 0 (NA%) |  |
| 1.30999994277954 |  |  |  | 1 (20.0%) | 0 (NA%) |  |
| 33.5999984741211 |  |  |  | 1 (20.0%) | 0 (NA%) |  |
| **Neutrophils** | 3 (2, 8) | NA (NA, NA) |  |  |  |  |
| **Sodium mmol/L** | 133.0 (129.0, 137.0) | 136.5 (133.0, 139.0) | 0.063 | 135.0 (134.0, 136.0) | 136.5 (133.0, 139.0) | 0.6 |
| **Potassium mmol/L** | 3.90 (3.50, 4.60) | 3.85 (3.62, 4.00) | 0.7 | 3.5 (3.0, 4.1) | 3.9 (3.6, 4.0) | 0.4 |
| **Haemoglobin g/dL** | 8.35 (7.10, 9.60) | 9.45 (7.65, 10.47) | 0.4 | 8.4 (7.6, 9.9) | 9.4 (7.7, 10.5) | 0.7 |
| **BP (systolic)** | 110 (100, 122) | 128 (120, 130) | 0.052 | 120.0 (108.0, 125.0) | 127.5 (120.0, 129.5) | 0.3 |
| **BP (diastolic)** | 70 (60, 80) | 78 (65, 80) | 0.4 | 71.0 (70.0, 79.0) | 77.5 (65.0, 80.0) | 0.7 |
| **Heart rate** | 93 (80, 108) | 87 (70, 104) | 0.4 | 87.0 (83.5, 111.5) | 87.0 (70.0, 103.8) | 0.4 |
| **Hypotension** | 16 (12.3%) | 0 (0.0%) | 0.6 | 0 (0.0%) | 0 (0.0%) |  |
| **Weakness** | 114 (87.7%) | 8 (80.0%) | 0.6 | 12 (80.0%) | 8 (80.0%) | >0.9 |
| **Tiredness** | 115 (89.1%) | 10 (100.0%) | 0.6 | 12 (80.0%) | 10 (100.0%) | 0.3 |
| **Poor appetite** | 107 (82.3%) | 10 (100.0%) | 0.4 | 11 (73.3%) | 10 (100.0%) | 0.12 |
| **Increased pigmentation of the skin** | 77 (60.6%) | 3 (37.5%) | 0.3 | 5 (35.7%) | 3 (37.5%) | >0.9 |
| **Nausea** | 78 (60.0%) | 8 (80.0%) | 0.3 | 7 (46.7%) | 8 (80.0%) | 0.2 |
| **Vomiting** | 37 (28.5%) | 4 (40.0%) | 0.5 | 5 (33.3%) | 4 (40.0%) | >0.9 |
| **Liking for salt** | 78 (60.5%) | 8 (80.0%) | 0.3 | 9 (60.0%) | 8 (80.0%) | 0.4 |
| **Hypoglycaemia** | 3 (2.3%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **Loss of consciousness** | 4 (3.1%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **Diarrhoea** | 66 (50.8%) | 2 (20.0%) | 0.10 | 5 (33.3%) | 2 (20.0%) | 0.7 |
| **Dizziness** | 68 (52.7%) | 4 (40.0%) | 0.5 | 8 (57.1%) | 4 (40.0%) | 0.4 |
| **Shock** | 2 (1.5%) | 0 (0.0%) | >0.9 | 0 (0.0%) | 0 (0.0%) |  |
| **Anorexia** | 68 (52.7%) | 3 (30.0%) | 0.2 | 4 (26.7%) | 3 (30.0%) | >0.9 |
| **Loss of axillary and pubic hair, if female** |  |  | 0.5 |  |  | >0.9 |
| No | 35 (26.3%) | 4 (40.0%) |  | 7 (46.7%) | 4 (40.0%) |  |
| Not applicable | 64 (48.1%) | 5 (50.0%) |  | 6 (40.0%) | 5 (50.0%) |  |
| Yes | 34 (25.6%) | 1 (10.0%) |  | 2 (13.3%) | 1 (10.0%) |  |
| **Any postural drop in blood pressure** | 7 (5.5%) | 0 (0.0%) | >0.9 | 1 (6.7%) | 0 (0.0%) | >0.9 |
| **Presence of anaemia** | 82 (63.6%) | 5 (50.0%) | 0.5 | 7 (50.0%) | 5 (50.0%) | >0.9 |
| **ART exposure** | 61 (43.3%) | 1 (10.0%) | 0.048 | 4 (26.7%) | 1 (10.0%) | 0.6 |
| **Kidney medication** | 14 (9.9%) | 2 (20.0%) | 0.3 | 3 (20.0%) | 2 (20.0%) | >0.9 |
| **incremental\_cortisol** | 260 (175, 356) | 32 (17, 107) | <0.001 | 122.0 (95.0, 179.0) | 32.0 (17.0, 107.0) | 0.2 |
| **Rifampicin** | 16 (11.3%) | 0 (0.0%) | 0.6 | 1 (6.7%) | 0 (0.0%) | >0.9 |
| **Fluconazole** | 21 (14.9%) | 6 (60.0%) | 0.002 | 4 (26.7%) | 6 (60.0%) | 0.12 |
| **Opiates** | 21 (14.9%) | 3 (30.0%) | 0.2 | 9 (60.0%) | 3 (30.0%) | 0.2 |
| **Age at enrolment median (IQR) (years)** |  |  |  | 35.0 (29.5, 39.5) | 41.5 (39.3, 47.8) | 0.13 |
| **Addisons disease** |  |  |  |  |  | 0.4 |
| PAI |  |  |  | 3 (20.0%) | 4 (40.0%) |  |
| SAI |  |  |  | 12 (80.0%) | 6 (60.0%) |  |
| 1Median (IQR); n (%) | | | | | | |
| 2Wilcoxon rank sum test; Fisher's exact test; Wilcoxon rank sum exact test | | | | | | |
| 3Wilcoxon rank sum test; Fisher's exact test; Wilcoxon rank sum exact test; Pearson's Chi-squared test | | | | | | |

# Table 4: Multivariate table mortality

iter imp variable 1 1 Age\_at\_enrolment Gender Duration\_of\_current\_illness cd4 Sodium Potassium\_mmol\_L Haemoglobin White\_cell\_count Random\_cortisol ACTH BP\_systolic BP\_diastolic Heart\_rate Hypotension Weakness Poor\_appetite Weight\_loss Increased\_pigmentation\_skin Nausea Vomiting Liking\_for\_salt Hypoglycaemia Loss\_of\_consciousness Diarrhoea Shock Any\_postural\_drop\_in\_blood\_pressure Presence\_of\_anaemia 1 2 Age\_at\_enrolment Gender Duration\_of\_current\_illness cd4 Sodium Potassium\_mmol\_L Haemoglobin White\_cell\_count Random\_cortisol ACTH BP\_systolic BP\_diastolic Heart\_rate Hypotension Weakness Poor\_appetite Weight\_loss Increased\_pigmentation\_skin Nausea Vomiting Liking\_for\_salt Hypoglycaemia Loss\_of\_consciousness Diarrhoea Shock Any\_postural\_drop\_in\_blood\_pressure Presence\_of\_anaemia 1 3 Age\_at\_enrolment Gender Duration\_of\_current\_illness cd4 Sodium Potassium\_mmol\_L Haemoglobin White\_cell\_count Random\_cortisol ACTH BP\_systolic 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Call: NULL

Coefficients: Estimate Std. Error z value Pr(>|z|)  
(Intercept) -3.8291438 1.4689621 -2.607 0.009142 \*\* Random\_cortisol 0.0023018 0.0006231 3.694 0.000221  ***BP\_systolic -0.0258304 0.0077709 -3.324 0.000887***  Loss\_of\_consciousness 1.3385296 0.8940006 1.497 0.134332  
Opiates -0.4990573 0.2630541 -1.897 0.057806 .  
discharged 1.4076597 0.6380137 2.206 0.027362 \*  
BP\_diastolic 0.0310194 0.0104035 2.982 0.002867 \*\* Liking\_for\_salt 0.2469938 0.2092821 1.180 0.237922  
Nausea 0.3870176 0.2117475 1.828 0.067590 .  
— Signif. codes: 0 ‘***’ 0.001 ’****’ 0.01 ’*’ 0.05 ‘.’ 0.1 ’ ’ 1

(Dispersion parameter for binomial family taken to be 1)

Null deviance: 649.06 on 553 degrees of freedom

Residual deviance: 593.27 on 545 degrees of freedom AIC: 611.27

Number of Fisher Scoring iterations: 5

Generalized Linear Model

554 samples 8 predictor

No pre-processing Resampling: Cross-Validated (5 fold) Summary of sample sizes: 443, 443, 443, 443, 444 Resampling results:

RMSE Rsquared MAE  
0.4286379 0.08454833 0.3616647

# Table 5 univariate analysis for addisson’s disease

| **Characteristic** | **N** | **OR**1 | **95% CI**1 | **p-value** |
| --- | --- | --- | --- | --- |
| Age at enrolment | 547 | 1.02 | 0.98, 1.07 | 0.2 |
| Gender, n(%) | 548 |  |  |  |
| Female |  | — | — |  |
| Male |  | 0.97 | 0.44, 2.11 | >0.9 |
| Ethnicity, n(%) | 549 | 0.62 | 0.18, 1.64 | 0.4 |
| Duration of current illness, median (IQR) (days) | 514 | 1.00 | 0.98, 1.00 | 0.7 |
| Weight loss | 525 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.70 | 0.27, 2.13 | 0.5 |
| log10 viral load | 121 | 1.11 | 0.75, 1.84 | 0.6 |
| Tuberculosis | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.65 | 0.27, 1.82 | 0.4 |
| PTB | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.38 | 0.17, 0.82 | 0.015 |
| EPTB | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 2.51 | 1.08, 5.57 | 0.026 |
| Cryptococcus neoformans | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 14.8 | 5.88, 36.1 | <0.001 |
| Pneumonia | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.98 | 0.23, 2.92 | >0.9 |
| Staph aureus | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 42,526,536 | 0.00, NA | >0.9 |
| Kaposis sarcoma | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 3.98 | 0.20, 25.9 | 0.2 |
| Cytomegalovirus | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 42,526,536 | 0.00, NA | >0.9 |
| HSV | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 2.83 | 0.15, 16.8 | 0.3 |
| HepB | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 2.53 | 0.39, 9.57 | 0.2 |
| Candida | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.57 | 0.03, 2.82 | 0.6 |
| GE/c diff | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.00 |  | >0.9 |
| Parvo B19 | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 42,526,536 | 0.00, NA | >0.9 |
| Syphilis | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.00 |  | >0.9 |
| B menigitis | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.00 |  | >0.9 |
| UTI / Leptospirosis | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.00 |  | >0.9 |
| PCP | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.00 |  | >0.9 |
| COVID-19 | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.00 |  | >0.9 |
| Neurocysticercosis | 549 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.00 |  | >0.9 |
| Total CD4 count | 542 | 0.99 | 0.98, 1.01 | 0.4 |
| White cell count X109 | 538 | 1.00 | 1.00, 1.00 | 0.4 |
| Lymphocyte count X109 | 124 | 1.00 |  | 0.9 |
| Neutrophils | 126 | 0.24 | 0.02, 0.82 | 0.2 |
| Sodium mmol/L | 518 | 1.23 | 0.97, 1.54 | 0.089 |
| Potassium mmol/L | 516 | 0.96 | 0.55, 1.13 | 0.8 |
| Haemoglobin g/dL | 542 | 1.00 |  | 0.9 |
| BP (systolic) | 538 | 1.00 | 0.98, 1.02 | 0.7 |
| BP (diastolic) | 538 | 1.02 | 0.99, 1.05 | 0.2 |
| Any postural drop in blood pressure | 521 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 1.80 | 0.28, 6.63 | 0.4 |
| Heart rate | 537 | 1.00 | 0.98, 1.01 | 0.7 |
| Hypotension | 522 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.38 | 0.02, 1.83 | 0.3 |
| Weakness | 523 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.61 | 0.25, 1.72 | 0.3 |
| Tiredness | 524 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 1.01 | 0.37, 3.50 | >0.9 |
| Poor appetite | 520 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 1.40 | 0.56, 4.25 | 0.5 |
| Increased pigmentation of the skin | 510 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.58 | 0.24, 1.33 | 0.2 |
| Nausea | 523 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 1.29 | 0.59, 2.91 | 0.5 |
| Vomiting | 522 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 1.10 | 0.44, 2.49 | 0.8 |
| Liking for salt | 521 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 2.10 | 0.93, 5.18 | 0.085 |
| Hypoglycaemia | 521 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.00 |  | >0.9 |
| Loss of consciousness | 520 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.00 |  | >0.9 |
| Diarrhoea | 519 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.52 | 0.21, 1.18 | 0.13 |
| Dizziness | 520 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 1.09 | 0.49, 2.43 | 0.8 |
| Shock | 524 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.00 |  | >0.9 |
| Anorexia | 522 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.47 | 0.19, 1.06 | 0.079 |
| Presence of anaemia | 519 |  |  |  |
| FALSE |  | — | — |  |
| TRUE |  | 0.70 | 0.32, 1.56 | 0.4 |
| ART exposure | 549 |  |  |  |
| No |  | — | — |  |
| Yes |  | 0.46 | 0.17, 1.08 | 0.10 |
| Kidney medication | 549 |  |  |  |
| No |  | — | — |  |
| Yes |  | 2.30 | 0.74, 5.91 | 0.11 |
| mortality | 150 |  |  |  |
| no |  | — | — |  |
| yes |  | 1.30 | 0.39, 4.35 | 0.7 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | | |

iter imp variable 1 1 BP\_diastolic Weakness Diarrhoea Sodium Lymphocyte\_count Weight\_loss Anorexia Neutrophils Total.CD4.count Potassium Duration\_of\_current\_illness Age\_at\_enrolment Gender 1 2 BP\_diastolic Weakness Diarrhoea Sodium Lymphocyte\_count Weight\_loss Anorexia Neutrophils Total.CD4.count Potassium Duration\_of\_current\_illness Age\_at\_enrolment Gender 1 3 BP\_diastolic Weakness Diarrhoea Sodium Lymphocyte\_count Weight\_loss Anorexia Neutrophils Total.CD4.count Potassium Duration\_of\_current\_illness Age\_at\_enrolment Gender 1 4 BP\_diastolic Weakness Diarrhoea Sodium Lymphocyte\_count Weight\_loss Anorexia Neutrophils Total.CD4.count Potassium Duration\_of\_current\_illness Age\_at\_enrolment Gender 1 5 BP\_diastolic Weakness Diarrhoea Sodium Lymphocyte\_count Weight\_loss Anorexia Neutrophils Total.CD4.count Potassium Duration\_of\_current\_illness Age\_at\_enrolment Gender 2 1 BP\_diastolic Weakness Diarrhoea Sodium Lymphocyte\_count Weight\_loss Anorexia 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| **Characteristic** | **OR**1 | **95% CI**1 | **p-value** |
| --- | --- | --- | --- |
| Potassium | 0.99 | 0.56, 1.17 | >0.9 |
| Neutrophils | 0.92 | 0.73, 1.05 | 0.4 |
| CD4\_count | 0.99 | 0.98, 1.01 | 0.4 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |