

Online Supplemental Material

Supplemental Table 1. Modification of the associations of iron deficiency anemia¹ categories with mortality in HIV-infected patients initiating HAART (n = 27,569)

| Exposure status | Baseline anemia and early mortality ² | | Anemia during follow up and overall mortality | |
|----------------------|--|---------|---|---------|
| | Multivariate RR ³ (95% CI) | P-value | Multivariate RR ⁴ (95% CI) | P-value |
| Sex | | 0.03 | | < 0.001 |
| Male | | | | |
| No anemia or ID | 1.00 (Ref) | | 1.00 (Ref) | |
| ID without anemia | 1.00 (0.54, 1.84) | | 1.00 (0.71, 1.41) | |
| Anemia without ID | 1.96 (1.47, 2.63) | | 1.97 (1.67, 2.33) | |
| IDA | 2.67 (2.00, 3.58) | | 2.43 (2.05, 2.88) | |
| Female | | | | |
| No anemia or ID | 1.00 (Ref) | | 1.00 (Ref) | |
| ID without anemia | 1.25 (0.86, 1.82) | | 0.96 (0.76, 1.20) | |
| Anemia without ID | 1.58 (1.24, 2.02) | | 1.39 (1.21, 1.60) | |
| IDA | 1.86 (1.46, 2.36) | | 1.54 (1.33, 1.77) | |
| BMI category | | < 0.001 | | 0.03 |
| Obese | | | | |
| No anemia or ID | 1.00 (Ref) | | 1.00 (Ref) | |
| ID without anemia | 2.20 (0.20, 24.31) | | 0.67 (0.26, 1.75) | |
| Anemia without ID | 6.45 (1.50, 27.81) | | 1.67 (1.03, 2.66) | |
| IDA | 5.27 (1.19, 23.37) | | 1.46 (0.87, 2.43) | |
| Overweight | | | | |
| No anemia or ID | 1.00 (Ref) | | 1.00 (Ref) | |
| ID without anemia | 1.36 (0.27, 6.74) | | 1.11 (0.64, 1.93) | |
| Anemia without ID | 3.74 (1.60, 8.71) | | 1.79 (1.30, 2.47) | |
| IDA | 4.61 (1.99, 10.67) | | 2.01 (1.45, 2.79) | |
| Normal weight | | | | |
| No anemia or ID | 1.00 (Ref) | | 1.00 (Ref) | |
| ID without anemia | 1.87 (1.13, 3.07) | | 1.05 (0.79, 1.40) | |
| Anemia without ID | 2.32 (1.66, 3.24) | | 1.64 (1.39, 1.93) | |
| IDA | 3.19 (2.30, 4.44) | | 2.02 (1.72, 2.38) | |

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| Exposure status | Baseline anemia and early mortality ² | | Anemia during follow up and overall mortality | |
|--|--|---------|---|---------|
| | Multivariate RR ³ (95% CI) | P-value | Multivariate RR ⁴ (95% CI) | P-value |
| Underweight | | | | |
| No anemia or ID | 1.00 (Ref) | | 1.00 (Ref) | |
| ID without anemia | 0.89 (0.57, 1.38) | | 0.93 (0.68, 1.28) | |
| Anemia without ID | 1.16 (0.91, 1.50) | | 1.43 (1.19, 1.73) | |
| IDA | 1.41 (1.10, 1.81) | | 1.60 (1.33, 1.93) | |
| Zidovudine use⁵ | | - | | 0.004 |
| Yes | | | | |
| No anemia or ID | - | | 1.00 (Ref) | |
| ID without anemia | - | | 0.99 (0.72, 1.37) | |
| Anemia without ID | - | | 1.23 (1.03, 1.47) | |
| IDA | - | | 1.48 (1.23, 1.77) | |
| No | | | | |
| No anemia or ID | - | | 1.00 (Ref) | |
| ID without anemia | - | | 0.99 (0.75, 1.31) | |
| Anemia without ID | - | | 1.88 (1.61, 2.19) | |
| IDA | - | | 2.06 (1.77, 2.40) | |
| CD4 cell count | | - | | 0.04 |
| < 350 cells/μL | | | | |
| No anemia or ID | - | | 1.00 (Ref) | |
| ID without anemia | - | | 1.10 (0.89, 1.37) | |
| Anemia without ID | - | | 1.78 (1.57, 2.02) | |
| IDA | - | | 1.98 (1.74, 2.25) | |
| \geq 350 cells/μL | | | | |
| No anemia or ID | - | | 1.00 (Ref) | |
| ID without anemia | - | | 0.63 (0.40, 1.01) | |
| Anemia without ID | - | | 1.28 (1.01, 1.62) | |
| IDA | - | | 1.43 (1.11, 1.83) | |

¹ Iron deficiency anemia defined as follows: anemia as hemoglobin < 12 g/dL for women or hemoglobin < 13 g/dL for men, and iron deficiency as mean corpuscular volume < 80 fL. Anemia and iron deficiency exposures were cross classified to define each individual's exposure status.

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² Early mortality defined as mortality in the first three months of follow up.

³ Baseline exposure model adjusted for sex, age, facility level, BMI, CD4 cell count, WHO disease stage, alanine aminotransferase, HAART regimen, iron use, tuberculosis history, tuberculosis treatment, oral candidiasis, diarrhea, and calendar year of HAART initiation.

⁴ Anemia during follow up model also adjusted for sex, facility level, calendar year of HAART initiation, and time-varying values of age, BMI and CD4 cell count splines, WHO disease stage, alanine aminotransferase, HAART regimen, iron use, tuberculosis treatment, oral candidiasis, diarrhea, and season of visit.

HAART, highly active antiretroviral therapy; ID, iron deficiency; IDA, iron deficiency anemia; Ref, reference.

⁵ Model also included interaction terms for missing categories of the effect modifier but the results are not shown.

Supplemental Table 2. Associations of anemia¹ with mortality in HIV-infected patients without iron deficiency at the time of initiation of HAART (n=14223)

| Exposure status | Deaths/person-months | Univariate RR (95% CI) | Trend test P-value | Multivariate RR ² (95% CI) | Trend test P-value |
|--|----------------------|------------------------|--------------------|---------------------------------------|--------------------|
| Baseline anemia and early mortality⁴ | 1,290/21,053 | | | | |
| No anemia | 122/4,716 | 1.00 (Ref) | < 0.001 | 1.00 (Ref) | < 0.001 |
| Mild anemia | 395/9,506 | 1.59 (1.29, 1.94) | | 1.29 (1.05, 1.58) | |
| Moderate anemia | 570/6,059 | 3.34 (2.74, 4.06) | | 2.06 (1.68, 2.52) | |
| Severe anemia | 203/772 | 7.57 (6.05, 9.48) | | 3.34 (2.64, 4.24) | |
| Anemia during follow up and overall mortality | 2,416/452,048 | | | | |
| No anemia | 352/182,514 | 1.00 (Ref) | < 0.001 | 1.00 (Ref) | < 0.001 |
| Mild anemia | 833/202,420 | 1.46 (1.28, 1.65) | | 1.30 (1.15, 1.48) | |
| Moderate anemia | 892/61,042 | 3.13 (2.75, 3.56) | | 2.23 (1.95, 2.54) | |
| Severe anemia | 339/6,072 | 8.11 (6.95, 9.47) | | 4.13 (3.51, 4.87) | |

¹ Anemia defined as: mild (hemoglobin 10-< 12 g/dL in women or 10-< 13 g/dL in men), moderate (hemoglobin 7.0-< 10 g/dL), and severe (hemoglobin < 7 g/dL). No anemia was defined as hemoglobin ≥ 12 g/dL in women or hemoglobin ≥ 13 g/dL in men.

² Baseline anemia model adjusted for sex, age, facility level, BMI and CD4 cell count splines, WHO disease stage, alanine aminotransferase, HAART regimen, iron supplement use, tuberculosis history, tuberculosis treatment, oral candidiasis, diarrhea, season of HAART initiation, and calendar year since HAART initiation. Anemia during follow up model adjusted for sex, tuberculosis history, calendar year of HAART initiation, and time-varying values of age, facility level, BMI and CD4 cell count splines, WHO disease stage, alanine aminotransferase, HAART regimen, iron supplement use, oral candidiasis, diarrhea, and season of visit.

³ Early mortality defined as mortality in the first three months of follow up.

HAART, highly active antiretroviral therapy; Ref, reference.

Supplemental Table 3. Modification of the associations of anemia¹ with mortality in HIV-infected patients without iron deficiency at HAART initiation (n = 14,223)

| Exposure status | Baseline anemia and early mortality ² | | Anemia during follow up and overall mortality | |
|----------------------|--|---------|---|---------|
| | Multivariate RR ³ (95% CI) | P-value | Multivariate RR ⁴ (95% CI) | P-value |
| Sex | | - | | 0.005 |
| Male | | | | |
| No anemia | - | | 1.00 (Ref) | |
| Mild anemia | - | | 1.65 (1.37, 2.00) | |
| Moderate anemia | - | | 2.73 (2.24, 3.33) | |
| Severe anemia | - | | 4.89 (3.85, 6.22) | |
| Female | | | | |
| No anemia | - | | 1.00 (Ref) | |
| Mild anemia | - | | 1.05 (0.88, 1.25) | |
| Moderate anemia | - | | 1.88 (1.58, 2.23) | |
| Severe anemia | - | | 3.59 (2.91, 4.42) | |
| BMI category | | < 0.001 | | < 0.001 |
| Obese | | | | |
| No anemia | 1.00 (Ref) | | 1.00 (Ref) | |
| Mild anemia | 3.57 (0.74, 17.22) | | 0.91 (0.49, 1.69) | |
| Moderate anemia | 12.98 (2.80, 60.18) | | 3.90 (2.12, 7.20) | |
| Severe anemia | 14.91 (2.08, 106.9) | | 7.28 (2.90, 18.27) | |
| Overweight | | | | |
| No anemia | 1.00 (Ref) | | 1.00 (Ref) | |
| Mild anemia | 2.53 (1.03, 6.22) | | 1.30 (0.88, 1.92) | |
| Moderate anemia | 6.93 (2.86, 16.81) | | 3.95 (2.66, 5.87) | |
| Severe anemia | 5.07 (1.02, 25.31) | | 6.21 (3.01, 12.79) | |
| Normal weight | | | | |
| No anemia | 1.00 (Ref) | | 1.00 (Ref) | |
| Mild anemia | 1.59 (1.12, 2.28) | | 1.36 (1.12, 1.64) | |
| Moderate anemia | 2.91 (2.04, 4.14) | | 2.44 (2.00, 2.98) | |
| Severe anemia | 6.20 (4.13, 9.31) | | 5.82 (4.53, 7.49) | |
| Underweight | | | | |
| No anemia | 1.00 (Ref) | | 1.00 (Ref) | |
| Mild anemia | 0.93 (0.71, 1.23) | | 1.15 (0.93, 1.43) | |

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|----------------------------|-------------------|-------------------|-------|
| Moderate anemia | 1.30 (1.00, 1.69) | 1.65 (1.34, 2.04) | |
| Severe anemia | 2.02 (1.49, 2.74) | 2.91 (2.29, 3.70) | |
| Iron supplement use | - | | 0.003 |
| Yes | | | |
| No anemia | - | 1.00 (Ref) | |
| Mild anemia | - | 1.09 (0.54, 2.21) | |
| Moderate anemia | - | 1.04 (0.53, 2.02) | |
| Severe anemia | - | 1.53 (0.78, 3.01) | |
| No | | | |
| No anemia | - | 1.00 (Ref) | |
| Mild anemia | - | 1.36 (1.13, 1.65) | |
| Moderate anemia | - | 2.27 (1.87, 2.75) | |
| Severe anemia | - | 4.44 (3.45, 5.71) | |

¹ Baseline anemia defined as: mild (hemoglobin 10-< 12 g/dL in women or 10-< 13 g/dL in men), moderate (hemoglobin 7.0-< 10 g/dL), and severe (hemoglobin < 7 g/dL). No anemia was defined as hemoglobin \geq 12 g/dL in women or hemoglobin \geq 13 g/dL in men.

² Early mortality defined as mortality in the first three months of follow up.

³ Baseline anemia model adjusted for sex, age, facility level, BMI and CD4 cell count splines, WHO disease stage, alanine aminotransferase, HAART regimen, iron supplement use, tuberculosis history, tuberculosis treatment, oral candidiasis, diarrhea, season of HAART initiation, and calendar year since HAART initiation. Anemia during follow up model adjusted for sex, tuberculosis history, calendar year of HAART initiation, and time-varying values of age, facility level, BMI and CD4 cell count splines, WHO disease stage, alanine aminotransferase, HAART regimen, iron supplement use, oral candidiasis, diarrhea, and season of visit.

HAART, highly active antiretroviral therapy; Ref, reference.