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Baseline characteristics, response to and outcome of antiretroviral therapy among patients with HIV-1, HIV-2 and dual infection in Burkina Faso

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ABSTRACT

In an urban district hospital in Burkina Faso we investigated the relative proportions of HIV-1, HIV-2 and HIV-1/2 among those tested, the baseline sociodemographic and clinical characteristics, and the response to and outcome of antiretroviral therapy (ART). A total of 7368 individuals (male = 32%; median age = 34 years) were included in the analysis over a 6 year period (2002–2008). The proportions of HIV-1, HIV-2 and dual infection were 94%, 2.5% and 3.6%, respectively. HIV-1-infected individuals were younger, whereas HIV-2-infected individuals were more likely to be male, have higher CD4 counts and be asymptomatic on presentation. ART was started in 4255 adult patients who were followed up for a total of 8679 person-years, during which time 469 deaths occurred. Mortality differences by serotype were not statistically significant, but were generally worse for HIV-2 and HIV-1/2 after controlling for age, CD4 count and WHO stage. Among severely immunedeficient patients, mortality was higher for HIV-2 than HIV-1. CD4 count recovery was poorest for HIV-2. HIV-2 and dually infected patients appeared to do less well on ART than HIV-1 patients. Reasons may include differences in age at baseline, lower intrinsic immune recovery in HIV-2, use of ineffective ART regimens (inappropriate prescribing) by clinicians, and poor drug adherence.

1. Introduction

HIV type 1 (HIV-1) and type 2 (HIV-2) are very closely related, but differ in their pathogenicity, natural history and susceptibility to therapy. HIV-1 is more easily transmitted, and consequently accounts for the vast majority of global HIV infections; the less transmissible HIV-2 is largely confined to West Africa, where it is thought to have originated.[1,2] As HIV-2 is less pathogenic than HIV-1, HIV-2-infected individuals appear to have a much longer asymptomatic stage, slower progression to AIDS,[3–6] slower decline in CD4 count[3,7,8] and lower mortality[5,9–11] than patients with HIV-1. Serological reactivity to both HIV-1 and HIV-2 (HIV-1/2) exists, and some evidence suggests

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that this serological profile has increased over the past decade in areas previously endemic for HIV-2.[12]

Since the introduction of antiretroviral therapy (ART), many studies from resource-limited settings, particularly in Africa, have described the clinical characteristics, clinical response and treatment outcomes of HIV-1-infected patients on ART.[13–20] However, there is a dearth of similar published information for HIV-2[21,22] and dual HIV-1/2, probably because these infections are less prevalent and are concentrated in West Africa. Although individuals infected with HIV-2 and HIV-1/2 are a considerable minority compared with HIV-1, assessing their baseline characteristics and their response to and outcomes on ART remains important.

Among HIV-positive individuals in an urban district hospital in Pissy, Burkina Faso, we report on the relative proportions of HIV-1, HIV-2 and HIV-1/2, baseline sociodemographic and clinical characteristics, and the response to and outcomes of ART in adults.

2. Materials and methods

2.1. Study setting and population

The study was conducted between January 2002 and October 2008 at the district hospital in Pissy, in Burkina Faso's capital city of Ouagadougou, which has a population of approximately 1.2 million inhabitants. HIV testing is offered free of charge at a voluntary counselling and HIV testing unit within the hospital, with or without referral. HIV testing involves a two-rapid-test serial algorithm (patients testing negative on the first test have no further testing, while those testing positive on the first test have this confirmed by a second test) using the Determine HIV-1/2 assay (Abbott Laboratories, Abbott Park, IL, USA) and the Genie II HIV-1/HIV-2 assay (Bio-Rad, Marnes-La-Coquette, France). The Genie II assay was later replaced by the SD Bioline HIV-1/2 3.0 assay (Standard Diagnostics, Kyonggi-do, South Korea).

All HIV-positive individuals underwent a full clinical assessment, were categorized according to the four WHO clinical stages of HIV, and where possible had their baseline CD4 count measured. The study population for determining the relative proportions of each HIV type included all individuals who tested HIV positive; the response to ART and treatment outcomes were assessed among those adults starting ART.

2.2. Antiretroviral therapy, regimens and outcomes

Apart from pregnant women, HIV-positive individuals are eligible for ART if they present in WHO clinical stage 3 (with a CD4 count $\leq$350 cells/μl), stage 4 (irrespective of CD4 count), or have a CD4 count <200 cells/μl (irrespective of WHO stage). HIV-infected pregnant women are initiated on ART when their CD4 count is $\leq$350 cells/μl, regardless of clinical stage. Once started on ART, patients are reviewed by a clinician 2 weeks later and monthly thereafter, provided there are no complications or drug side effects. Individuals starting ART had WHO clinical stage, CD4 count and weight measured at ART initiation and then at 6 month intervals.

For HIV-1, first-line ART is a fixed-dose combination of stavudine, lamivudine and nevirapine. In cases of stavudine- and nevirapine-related side effects, the alternative treatments are zidovudine and efavirenz, respectively. For HIV-2 and HIV-1/2 coinfection, the first-line treatment is a fixed-dose combination of stavudine and lamivudine plus nelfinavir or lopinavir–ritonavir. The heat-stable form of lopinavir–ritonavir became available much later in the programme.

Standardized treatment outcomes are monitored on a monthly basis using patient cards, and are defined as: alive and on ART (patient alive and on ART at the facility where he/she initially registered); died (patient who died for any reason while on ART); lost to follow-up (patient who did not attend the clinic for 1 month or more after their scheduled follow-up appointment); stopped treatment (patient known to have stopped treatment for any reason); transferred out (patient who permanently transferred to another treatment facility). In the district of Pissy, ART has been offered free of charge since March 2003.

2.3. Data collection and statistical analysis

Structured forms were used to gather information on HIV status, HIV type, WHO clinical stage and CD4 count at presentation. ART outcomes were recorded on a monthly basis. Data were entered and stored in the FUCHIA database system (Epicentre, Paris, France). Data were collated on all patients from January 2002, and were censored on 3 October 2008.

Differences between groups were compared using the χ^2 test for categorical variables and the Wilcoxon rank-sum test for continuous variables. Comparisons of sequential measurements of CD4 count and body weight were performed using the *t* test based on unequal variances. Survival estimates were determined using the Kaplan Meier method and compared using the Cox–Mantel (log-rank) test. A Cox proportional hazard model was constructed to estimate the hazard ratio of mortality according to serotype, adjusting for any variables found to be associated with both mortality and HIV type. The level of significance was set at $P \leq 0.05$ and 95% confidence intervals were used throughout. Data were analysed using STATA/IC 10.0 software (Stata Corp., College Station, TX, USA).

3. Results

3.1. Characteristics of the study population

During the study period, 7548 individuals tested positive for HIV, 180 of whom did not have an HIV type specified and were therefore excluded from further analysis. Among the remaining 7368 individuals included in the analysis, 2333 (32%) were male. Nearly half were housewives (45%), 16% were businessmen/street traders and 22% reported earning a regular income. Table 1 shows their sociodemographic and clinical characteristics according to HIV type.

For HIV-2 and HIV-1/2 there was a significantly higher proportion of infected males than for HIV-1. HIV-1 infected individuals were generally younger at presentation than those with HIV-1/2, who in turn were younger

Table 1
Characteristics of individuals with HIV-1, HIV-2 and HIV-1/2 ($n = 7368$)

Variable	HIV-1 *n* (%)	HIV-2 *n* (%)	*P*-value[a,b]	HIV-1/2 *n* (%)	*P*-value[a,c]
Total	6921 (93.9)	185 (2.5)	–	262 (3.6)	–
Gender					
Female	4756 (68.7)	114 (61.6)	0.04	165 (63.0)	0.05
Male	2165 (31.3)	71 (38.4)		97 (37.0)	
Age (years)					
<15	300 (4.3)	2 (1.1)	0.03	3 (1.1)	0.01
15–29	1967 (28.4)	16 (8.6)	<0.001	42 (16.0)	<0.001
30–44	3865 (55.8)	87 (47.0)	0.02	154 (58.8)	0.35
≥45	789 (11.4)	80 (43.2)	<0.001	63 (24.0)	<0.001
Median age (years); IQR	34; 28–40	44; 37–50[d]	<0.001	39; 32–45[d]	<0.001
Marital status					
Single	1700 (24.6)	16 (8.6)	<0.001	36 (13.7)	<0.001
Married	3569 (51.6)	124 (67.0)	<0.001	149 (56.9)	0.09
Widowed	1281 (18.5)	33 (17.8)	0.82	62 (23.7)	0.04
Divorced/separated	371 (5.4)	12 (6.5)	0.50	15 (5.7)	0.80
CD4 count (cells/μl)					
<50	667 (13.7)	15 (11.1)	0.38	19 (10.9)	0.29
50–199	1950 (40.2)	48 (35.6)	0.28	63 (36.2)	0.29
200–349	1178 (24.3)	28 (20.7)	0.34	45 (25.9)	0.63
≥350	1057 (21.8)	44 (32.6)	0.003	47 (27.0)	0.10
Median CD4 count; IQR ($n = 5161$)	183; 91–324 ($n = 4852$)	208; 103–459 ($n = 135$)	0.01	210; 102–373 ($n = 174$)	0.16
WHO clinical stage					
Stage 1	1131 (16.3)	49 (26.5)	0.006	50 (19.1)	0.24
Stage 2	1349 (19.5)	24(13.0)	0.03	48 (18.3)	0.64
Stage 3	3430 (49.6)	92 (49.7)	0.96	124 (47.3)	0.50
Stage 4	1011 (14.6)	20 (10.8)	0.15	40 (15.3)	0.77

IQR: interquartile range.
[a] χ^2 test for categorical variables and Wilcoxon rank-sum test for continuous variables.
[b] Comparing HIV-1 with HIV-2.
[c] Comparing HIV-1 with HIV-1/2.
[d] Comparing HIV-2 with HIV-1/2; $P < 0.001$.

than HIV-2-infected individuals. Probably associated with age, a significantly greater proportion of HIV-1-infected individuals were unmarried than those with HIV-2 or dual HIV-1/2. The proportion of children (<15 years) with HIV-1 was significantly greater than for either HIV-2 or dual infection. HIV-2-infected individuals tended to present with a significantly higher CD4 count than HIV-1-infected individuals, and a significantly greater proportion of those with HIV-2 were asymptomatic on presentation (WHO stage 1) than those with HIV-1. Among adults in WHO stage 3 or 4, the proportions with CD4 counts >350 cells/μl at presentation were 9%, 15% and 11% for HIV-1, HIV-2 and HIV-1/2, respectively. Among adults, a significantly higher proportion of HIV-1-infected individuals had started ART (61%) than those with HIV-2 (50%) or HIV-1/2 (47%).

3.2. Characteristics of adult patients on ART and treatment outcomes

Among the 7363 HIV-positive individuals with HIV type classified, 4255 adults had started ART. Table 2 shows the sociodemographic and clinical characteristics, and treatment outcomes of patients on ART by HIV type. Mirroring the trend seen at baseline, HIV-1 patients were generally younger at ART initiation than HIV-1/2 patients, who in turn were younger than HIV-2 patients. Twenty-nine per cent of HIV-2 patients and 27% of HIV-1/2 patients had been started on a regimen of two nucleoside reverse transcriptase inhibitors (NRTI) plus one non-nucleoside reverse transcriptase inhibitor (NNRTI), which is not a recommended regimen for these infections.

3.3. Clinical and immunological response to ART

Figure 1 shows mean CD4 cell counts since starting ART, for adults by HIV type. In the first 6 months the mean increase in CD4 count was similar for HIV-1 and HIV-2 patients, whereas between 6 and 12 months increases in CD4 count were significantly greater for HIV-1 than for HIV-2 patients. Thereafter, mean changes in CD4 count were not significantly different between these two groups, but CD4 count for HIV-2 patients reached a plateau and never recovered to the same level as for HIV-1 patients. Comparing HIV-1 with HIV-1/2, the mean increase in CD4 count in the first 6 months of starting ART was significantly greater for HIV-1 patients, but thereafter there was no significant difference between the serotypes.

Figure 2 shows mean body weight since starting ART, for adults by HIV type. Mean body weight among HIV-1 patients increased by 2.7 kg more than for HIV-2 patients in the first 6 months ($P < 0.001$). However, beyond this time a comparison of HIV types showed no distinct trends in body weight change.

Table 2
Characteristics and treatment outcomes of adult patients on antiretroviral therapy (ART) according to HIV type ($n = 4255$)

Variable	HIV-1 *n* (%)	HIV-2 *n* (%)	*P*-value[a,b]	HIV-1/2 *n* (%)	*P*-value[a,c]
Total	4043 (95.0)	91 (2.1)	–	121 (2.8)	–
Gender					
Female	2818 (69.7)	58 (63.7)	0.22	80 (66.1)	0.71
Male	1225 (30.3)	33 (36.3)		41 (33.9)	
Age (years)					
15–29	921 (22.8)	4 (4.4)	<0.001	12 (9.9)	0.001
30–44	2538 (62.8)	42 (46.2)	0.001	73 (60.3)	0.58
≥45	584 (14.4)	45 (49.5)	<0.001	36 (29.8)	<0.001
Median age (years); IQR	35; 30–41	45; 39–50	<0.001	41; 34–46	<0.001
WHO clinical stage					
Stage 1 or 2 (CD4 <250 cells/μl)	613 (15.2)	13 (14.3)	0.82	16 (13.2)	0.56
Stage 3	2323 (57.5)	53 (58.2)	0.88	68 (56.2)	0.78
Stage 4	1107 (27.4)	25 (27.5)	0.98	37 (30.6)	0.44
CD4 count (cells/μl)					
<50	626 (15.5)	13 (14.3)	0.76	16 (13.2)	0.50
50–199	1880 (46.5)	45 (49.5)	0.58	59 (48.8)	0.62
200–349	496 (12.3)	8 (8.8)	0.32	17 (14.0)	0.56
≥350	88 (2.2)	2 (2.2)	0.99	4 (3.3)	0.41
Unknown	953 (23.6)	23 (25.3)	0.71	25 (20.7)	0.46
Median CD4 count; IQR	128; 60–187	111; 61–171		128; 79–178	
Median duration on ART (months); IQR	23; 8–40	23; 8–34	0.39	17; 5–35	0.03
ART regimen					
2 NRTIs + 1 NNRTI	4009 (99.2)	26 (28.6)	<0.001	33 (27.3)	<0.001
3 NRTIs	2 (0.1)	1 (1.1)	<0.001	1 (0.8)	0.002
2 NRTIs + IDV	12 (0.3)	12 (13.2)	<0.001	14 (11.6)	<0.001
2 NRTIs + LPV/r	10 (0.2)	17 (18.7)	<0.001	28 (23.1)	<0.001
2 NRTIs + NFV	10 (0.2)	35 (38.5)	<0.001	45 (37.2)	<0.001
ART outcomes					
Alive on ART	3135 (77.6)	68 (74.7)	0.44	91 (75.2)	0.45
Dead	439 (10.9)	14 (15.4)	0.17	16 (13.2)	0.41
Lost to follow-up	320 (7.9)	6 (6.6)	0.64	10 (8.3)	0.89
Transferred out	148 (3.7)	3 (3.3)	0.86	4 (3.3)	0.84

IQR: interquartile range; NRTI: nucleoside reverse transcriptase inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor; IDV: indinavir; LPV/r: lopinavir/ritonavir; NFV: nelfinavir.
[a] χ^2 test for categorical variables and Wilcoxon rank-sum test for continuous variables.
[b] Comparing HIV-1 with HIV-2.
[c] Comparing HIV-1with HIV-1/2.

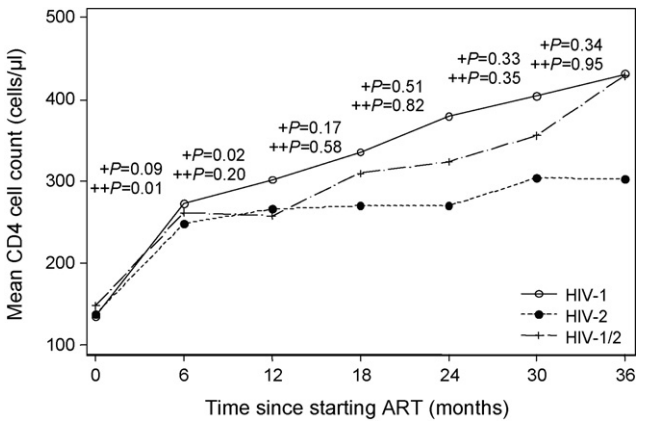

Figure 1. Mean CD4 counts in adult patients on antiretroviral therapy (ART) during follow-up, according to HIV type. *P*-values represent comparisons of mean change in CD4 count from one time point to another, between HIV-1 and HIV-2 (+*P*-values) and HIV-1 and HIV-1/2 (++*P*-values) (log-rank test).

3.4. ART outcomes and survival

Treatment outcomes censored on 3 October 2008 included 3294 (77.4%) alive and on ART, 469 (11.0) deaths, 336 (7.9%) lost to follow-up and 155 (3.6%) transferred out (Table 2). A higher proportion of HIV-2 (15.4%) and HIV-1/2 patients (13.2%) had died than HIV-1 patients (10.9%), but differences were not

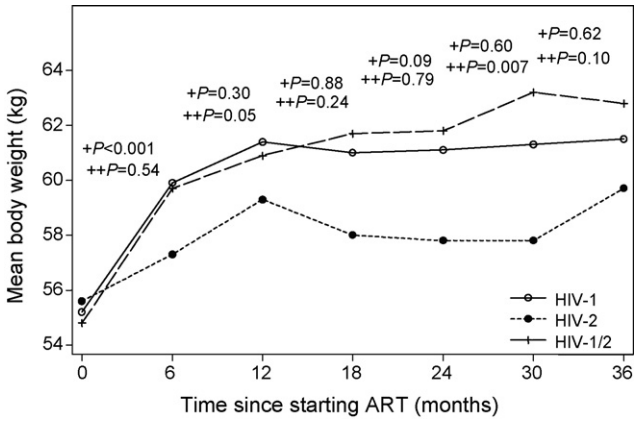

Figure 2. Mean body weight of adult patients on antiretroviral therapy (ART) during follow-up, according to HIV-type. *P*-values represent comparisons of mean change in body weight from one time point to another, between HIV-1 and HIV-2 (+*P*-values) and HIV-1 and HIV-1/2 (++*P*-values) (log-rank test).

statistically significant. Other outcomes were similar by HIV type.

Patients on ART were followed up for a total of 8679 person-years [median 22.6 months; interquartile range (IQR) 7.7–39.4 months], during which time the cumulative incidence of death per 100 person-years of follow-up was 5.4 (95% CI 4.9–5.9). Mortality hazard ratios comparing HIV-2 with HIV-1 and HIV-1/2 with HIV-1 were 1.41 (95% CI 0.83–2.41) and 1.32 (95% CI 0.80–2.17), respectively. Adjusting for different background variables showed that the mortality differences by HIV serotype were partly explained by age, CD4 count and WHO stage at ART initiation. After adjusting for these variables, mortality hazard ratios comparing HIV-2 with HIV-1 and HIV-1/2 with HIV-1 were 1.38 (95% CI 0.80–2.37) and 1.26 (95% CI 0.76–2.07), respectively. These differences in mortality were not statistically significant.

For patients with CD4 count <100 cells/μl at ART initiation, mortality hazard ratios comparing HIV-2 with HIV-1 and HIV-1/2 with HIV-1 were 2.05 (95% CI 0.99–4.25) and 1.12 (95% CI 0.46–2.74), respectively, after adjusting for age and CD4 count at ART initiation.

Figure 3 shows the cumulative survival probability on ART, for adults by HIV type. Survival over total follow-up time and in the first 3 months (early mortality) did not differ significantly by HIV type.

4. Discussion

This is one of the few studies to report on the baseline characteristics, response to ART and outcome of ART in patients with HIV-1, HIV-2 and dual HIV-1/2 in the routine setting of a district hospital in West Africa. Although the proportion of patients with HIV-2 and dual HIV-1/2 infections was low, there were significant age and gender differences between the different serotypes; the immunological response to ART was poorer for adults with HIV-2, and ART outcomes tended to be worse for HIV-2 and dually infected adults than for HIV-1 patients. The findings of this analysis raise a number of points that merit discussion.

First, the ratio of men to women was higher for HIV-2 and dual infection than for HIV-1. Does this reflect better healthcare access for male HIV-2 and dually infected individuals, or are there sociobehavioural and biological factors associated with male gender that predispose males to become infected with HIV-2? This would require specific investigations and studies.

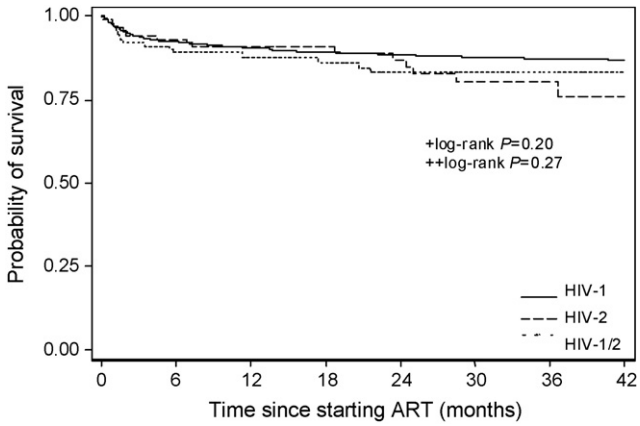

Figure 3. Kaplan-Meier survival estimates among adults on antiretroviral therapy (ART), by HIV type. +Log-rank test comparing HIV-1 with HIV-2; ++log-rank test comparing HIV-1 with HIV-1/2.

Second, HIV-1-infected individuals tended to initiate ART at a much earlier age than those with HIV-2 or dual infection, a finding probably explained by the slower progression of disease with HIV-2,[3–6,8] and an HIV-2 protective effect conferred in dual infection.[23] The fact that median baseline CD4 counts were higher for HIV-2 and dual infection than HIV-1 is further evidence that HIV-2 and dual infection are associated with slower progression and probably lower virulence. The finding that the proportion of children among those with HIV-2 was smaller than for HIV-1 corroborates the finding of previous studies that rates of vertical transmission of HIV-2 are much lower than for HIV-1 (20–30 times lower in some studies).[24–28]

Third, just over 1 in 6 HIV-2 patients assessed as being in WHO stage 3 or 4 at presentation had CD4 counts >350 cells/μl. This is slightly higher than one might expect, and may reflect a problem with the quality of staging, which could be improved by training. Furthermore, if this is the case among patients at baseline before ART, it may be reasonable to assume that among patients started on ART in the absence of a known CD4 count, with eligibility based purely on the basis of WHO stage (25% of all HIV-2 patients started on ART), a considerable proportion may have CD4 counts >350 cells/μl and could thus be being placed unnecessarily on ART. This would be associated with all the usual public health implications of unnecessary treatment, including drug toxicity and potential burnout of first-line regimens so they are not available later, when ART is most needed. This emphasizes the need for access to point-of-care CD4 counting technology in such settings.

Fourth, despite baseline CD4 counts at ART initiation being similar for the different serotypes, CD4 recovery appeared to be poorer for HIV-2 than HIV-1 patients, increasing in the first 6 months, but quickly tapering off after this. Possible reasons may include the use of ineffective ART regimens for HIV-2, poorer ART adherence related to the greater complexity of a protease inhibitor-containing ART regimen, and/or possibly a biological phenomenon related to older age (HIV-2 patients generally being older than HIV-1 patients on ART). Furthermore, this immunological difference between HIV-1 and HIV-2 has been previously reported in France,[29,30] and it has been suggested that although disease progression with HIV-2 is slower, there may be a lower intrinsic immune recovery in HIV-2 patients with severe immune deficiency than in HIV-1 patients.[29] If the difference seen in our study is underpinned by permanent immune damage occurring in severely immune-deficient HIV-2 patients, it would justify the need for earlier ART initiation in these patients. It would also imply that many HIV-2 patients who do not achieve threshold-level increases in CD4 counts would need indefinitely to continue adjunctive trimethoprim–sulfamethoxazole and other prophylaxis against opportunistic infections.

Fifth, although not statistically significant, mortality rates for patients on ART were higher for HIV-1/2, and even higher for HIV-2, than for HIV-1 after controlling for age, CD4 count and WHO stage at ART initiation. There are a number of possible reasons for this: (1) although the confounding effects of CD4 count were controlled for as far as possible, between 20 and 25% of patients were started on ART in the absence of a known CD4 count, and therefore there may be residual confounding by CD4 count that explains some of the difference, (2) the administration of inappropriate ART regimens for HIV-2, (3) poorer ART adherence among HIV-2 patients. The latter two reasons may also explain why HIV-2 patients with severe immune deficiency had higher mortality than severely immune-deficient HIV-1 patients. Alternatively, this finding supports the hypothesis that in severely immune-deficient HIV-2 patients permanent immune damage may have occurred, and thus immune recovery, even with the use of ART, is lower.

Sixth, although NNRTI regimens have been shown to be ineffective in the treatment of HIV-2 (because HIV-2 is naturally resistant to NNRTI[31,32]), about a quarter of these patients were started on an ART regimen incorporating NNRTI. Although this important clinical error was recognized and corrected over time, efforts are being put in place to avoid the same mistakes in the future. Possible reasons for these errors include shortcomings in clinician training and supervision, HIV status designation errors, lack of stock of discriminatory HIV test kits and/or initiation of an ART regimen based on an initial HIV-1 diagnosis that was not amended later, and lack of stock of recommended treatment options. Approximately 38% of HIV-2 patients were also placed on a nelfinavir-containing regimen that has limited virological benefit in HIV-2 patients compared with other protease inhibitors (indinavir–ritonavir and lopinavir–ritonavir).[33–35] This may explain the less favourable overall outcomes seen in HIV-2 and dual infection. Initial operational obstacles linked to access issues, cost, and conservation at high temperatures were the reason for the use of nelfinavir, and most of these patients were offered a change to lopinavir–ritonavir when the thermostable formulation became available and nelfinavir was recalled by the manufacturer because of contamination.

Finally, misdiagnosis of HIV-1/2 might have been a problem, although to what extent we do not yet know, and this is currently being investigated. Accurate identification of dual HIV-1/2 infection remains a diagnostic challenge. Discriminating between HIV-1 and HIV-2 is relatively simple, as the rapid HIV-detection assays used in the programme setting are sensitive and specific for HIV-1 and HIV-2. However, these assays lack specificity for dual HIV-1/2 infection. Different studies have shown that among individuals diagnosed as dually seropositive, often only HIV-1 or HIV-2 DNA is isolated (more often HIV-1), a phenomenon commonly thought to be explained by crossreactivity.[12,36–41] In our study it is therefore possible that dual infection was overestimated, although to what extent is uncertain. Diagnosis of dual infection would ideally require the isolation of both viruses from an individual through the use of PCR techniques. Implementing such techniques in Burkina Faso is currently not feasible. Meanwhile, we have embarked on crosschecking all reported dual infections by ELISA, which is more accurate than rapid tests.[37]

The strengths of this study are that a relatively large number of individuals were included and recruited over a period of nearly 7 years, loss to follow-up was relatively low (7.9%) and the data come from a programme setting

and thus probably reflect the operational reality on the ground. The findings of this analysis also highlight a number of highly relevant programme-related shortcomings that need urgently to be addressed and prevented in the future. The limitations of the study are that: (1) no data were collected for those testing HIV negative, and therefore we cannot report on the prevalence of the different HIV serotypes, (2) height was not systematically recorded, and thus we are unable to report on changes in body mass index over time, (3) patients lost to follow-up may include unascertained deaths not accounted for in the study, (4) the power of the study to detect statistically significant differences was limited because of the relatively small number of HIV-2 and HIV-1/2 patients, and (5) the proportion of HIV-1/2 infected individuals may have been overestimated.

In a district setting in urban Burkina Faso, HIV-2 and dually infected patients may not be benefiting from ART as favourably as HIV-1 patients. The reasons for this are not clear, but it may result from slower intrinsic immune recovery in HIV-2, older age, use of ineffective ART regimens by clinicians, and poor drug adherence. Further research to understand why this is so and to provide further therapeutic guidance is needed. The findings of this study also highlight a number of operational shortcomings that clinicians and programme managers in similar programmes with dual infections need to remain alert to.

Authors' contributions: KH, RZ, MM, PF, JD and GO were involved with the study conception and design; MM, RM JD and GO were involved with the field implementation and supervision; KH, RZ, MM and LA were involved with data analysis and interpretation, which were improved by AH; KH and RZ drafted the first version of the manuscript and all co-authors were involved with critical revision; AH and LA considerably improved the intellectual content. All authors read and approved the final version. RZ is guarantor of the paper.

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Conflicts of interest: None declared.

Ethical approval: General measures are provided in the district hospital to ensure patient confidentiality, consent for HIV testing, and counselling and support for those who receive a positive HIV test result. The data in this study did not include patient identifiers. The analysis used routine programmatic data collected for monitoring purposes, and was conducted as part of a formal project collaboration and operational support agreement with the Ministry of Health of Burkina Faso. Ethics clearance was thus not required.

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