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Youth, unemployment, and male gender predict mortality in AIDS patients started on HAART in Nigeria

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Abstract

This retrospective study identifies risk factors for mortality in a cohort of HIV-positive adult patients treated with highly active antiretroviral therapy (HAART) in Jos, Nigeria. We analyzed clinical data from a cohort of 1552 patients enrolled in a HIV/acquired immune deficiency syndrome treatment program and started on HAART between December 2004 and 30 April 2006. Death was our study endpoint. Patients were followed in the study until death, being lost to follow-up, or the end of data collection, 1 December 2006. Baseline patient characteristics were compared using Wilcoxon Rank Sum Test for continuous variables and Pearson Chi-Square test for categorical variables to determine if certain demographic factors were associated with more rapid progression to death. The Cox proportional hazard multivariate model analysis was used to find risk factors. As of 1 December 2006, a total of 104 cases progressed to death. In addition to the expected association of CD4 count less than 50 at initiation of therapy and active tuberculosis with mortality, the patient characteristics independently associated with a more rapid progression to death after initiation of HAART were male gender, age less than 30 years old, and unemployment or unknown occupation status. Future research is needed to identify the confounding variables that may be amenable to targeted interventions aimed at ameliorating these health disparities.

Keywords

HIV; mortality; gender; HAART; Nigeria

Introduction

Since the introduction of highly active antiretroviral therapy (HAART) in 1996, progression of HIV infection to acquired immune deficiency syndrome (AIDS) and associated mortality has decreased substantially among those treated with HAART (Badri et al., 2004; Cole, Hernan, Margolick, Cohen, & Robins, 2005; Egger et al., 2002; Hogg et al., 1998; Mayor, Gomez, Rios-Oliveras, & Hunter-Mellado, 2005; Palella et al., 1998). In spite of the progress that has been made in the treatment of HIV, death continues to be a reality for patients in both the developed and developing world. While recent studies show similar efficacy of HAART in the developing World and industrialized nations (Duncombe et al., 2005; Frater et al., 2002; Mills et al., 2006; Stringer et al., 2006), complex social and demographic factors may place certain populations at higher risk for mortality.

Because the majority of reports comparing gender and demographic differences of response to HAART have been conducted in developed countries, the question arises as to whether results from these studies are applicable to patients in the developing World where access to any form of medical care especially HAART is more limited, where patients may have different co-morbid conditions (Nicastri et al., 2005), and where patients typically present at more advanced stages of disease than patients in developed nations (Duncombe et al., 2005). This report examines a cohort of adult, ART-naïve patients started on HAART at the Faith Alive Foundation Hospital (FAFH) in Jos, Nigeria, prior to 1 May 2006. Patient age, gender, education level, occupation, marital status, residence, body mass index (BMI), CD4 cell count prior to initiating therapy, and co-infection with tuberculosis (TB) were compared to evaluate the effect of gender and other variables on mortality in this patient population. The proposed study attempts to determine whether patient gender, education, occupation, and age are associated with increased risk of death in the FAFH clinic population after adjusting for known confounding factors including low initial CD4 cell counts and co-infection with TB. If demographic differences in mortality rates are found, they can be interpreted as health disparities.

Methods

In Nigeria, a country with a population over 130 million people, an estimated3.6 million people were infected with HIV in 2003 (Federal Ministry of Health, 2004). FAFH, located in Jos, Nigeria, is a non-governmental medical and social ministry founded in 1996. Prior to 2005, due to financial restraints, FAFH was only able to supply HAART to a limited number of patients. The US President's Emergency Plan for AIDS Relief (PEPFAR), a global health initiative that began in 2003, aims to increase prevention of HIV infection, access to ART, and care for those infected and affected by HIV/AIDS throughout the world(Office of US Global AIDS Coordinator and the Bureau of Public Affairs, 2006). At the end of 2004, FAFH began receiving PEPFAR funding which enabled the clinic to expand its HIV/AIDS care. In the first 16 months of the FAFH_PEPFAR program, over 7500 people were screened for HIV-1 infection, enrollment in the clinic's HIV/ AIDS care program increased by over 400%, and more than 1300 new patients were enrolled into the program.

This study was conducted using a retrospective cohort study design. All ART-naïve patients over the age of 18, who were enrolled in the PEPFAR-funded HAART program and started on HAART prior to 1 May 2006, were eligible for inclusion in this study. Patients were identified by their HAART start date using the Health Resources and Services Administration (HRSA) CAREWARE medical record system at FAFH. The starting date of HAART was used to define the start of follow-up. Data were gathered by reviewing electronic and paper medical records. All HAART regimens used were first-line with the exception of 10 patients who received the combined lopinavir/ritonavir protease inhibitor as part of their regimen. The most frequently prescribed antiretroviral regimen (n_508) was stavudine 30 mg twice daily, lamivudine 150 mg twice daily, and nevirapine 200 mg twice daily.

Death was our study endpoint. Patients were followed for a mean of 444 days. Date of death was noted when available. When the date of death was unknown but the patient was known to have died, the date of the last encounter with the patient was used as the day of death (Stringer et al., 2006). Patients were classified as lost to follow-up (LTF) if no clinic records existed for them after 30 June 2006, three months prior to the start of data collection. Medical team members typically attempt to contact patients who have been LTF. However, with the rapid increase in the patient population after the beginning of PEPFAR funding, contact was not always possible. The last documented date of a clinic visit was used as their LTF date. Patients were included in the study until death, LTF, or the end of data collection, 1 December 2006. Independent variables included: patient's age, gender, residence, occupation, marital status,

religion, height, initial weight, BMI, baseline CD4 cell count and date, HIV diagnosis date, HAART start date, history of TB, and date of death or date of transfer. Age and initial CD4 count were broken into categories to allow for discovery of nonlinear relationships. History of TB was assessed using patient files and pharmacy records. Patient occupations were divided into nine categories based on modified WHO guidelines (Thacher et al., 2000) with the addition of one category for the inclusion of students. These categories were further condensed so that four occupation categories were used in the final analysis. The hypothesis tested was that male gender was associated with increased risk of death in this clinic population, after adjusting for initial severity of illness, age, and comorbidities.

The follow-up time was calculated from the date of initiation of HAART to the last date of follow-up, that is, the date of death, LTF date, or the end of data collection, 1 December 2006. Only those who died were considered to have experienced an “event” for the purposes of the statistical analysis. The baseline patient characteristics at the initiation of HAART using median and range were compared using Wilcoxon Rank Sum Test for continuous variables and Pearson Chi-Square test for categorical variables. The same method was used to compare males LTF to males not LTF and females LTF to females not LTF. Cox proportional hazard model analysis was used to determine risk factors associated with death. The independent variables described above were used as co-variates in a backwards elimination process. P-values less than 0.05 were considered to be statistically significant.

Results

The analysis included 1552 cases of HIV-infected patients started on HAART. As of 1 December 2006, a total of 104 cases (6.7%) died during the study period from 1 January 2005 to 1 December 2006. Deceased patients were followed for a mean of 126 days prior to death. Table 1 shows the baseline characteristics of patients. The typical patient was a female clerical worker or manual laborer, under 35 years of age with no history of TB, and an initial CD4 count of over 100. Men were significantly older than women, weighed more, had higher levels of education, held higher positions of employment, were more likely to be married, and were more likely to be taking anti-TB medications at the same time as antiretroviral therapy. There were no significant differences between genders regarding CD4 cell count prior to beginning ART, rural or urban residence, and BMI.

The final Cox proportional multivariate model using data from all patients while on treatment is presented in Table 2. This analysis demonstrates statistically significant differences in survival of HIV-infected men and women who prior to initiation of therapy hadCD4 cell counts greater than 50 cells/mL and who while on antiretroviral therapy were not concurrently treated for TB infection. Male gender (HR_1.77, CI_1.15_2.75, P_0.010), age less than 30 years old (HR _1.65, CI 1.07_2.53, P_0.023), CD4 count less than 50 (HR_3.28, CI_2.20_4.89, PB0.0001), co-infection with HIV and TB (HR_3.53, CI_2.36_5.28, PB0.0001), and unemployment/unknown occupation (HR_1.79, CI_1.21_2.66) were significantly associated with increased risk of death. Three hundred and seventy-three patients were listed as unemployed and no occupation was listed for 162 patients. Patients categorized as clerks and manual laborers also were shown to have a lower risk of death than workers in other fields and unemployed patients (HR_0.59, CI_0.40_0.88, P_0.010). Thirty-two percent of males 30 years or older and 40.4% of males less than 30 years are classified as being unemployed/unknown occupation status (P_0.0019). Age less than 30 years old and unemployment/unknown occupation status were tested as a product term in the multivariate analysis and found to have no interaction (HR_1.292, CI_0.571_2.924, P-value_0.5385).

A second multivariate analysis was conducted which excluded patients with initial CD4 counts less than 50 or any one who were concurrently being treated for TB infection. This analysis

included1303 patients. The results of this multivariate analysis are shown in Table 3. After removing patients with CD4 counts less than 50 or those were being treated for TB, age less than 30 (HR_2.715, CI_1.363_5.408, P_0.0045) and primary education (HR_2.064, CI_1.043_4.085, P_0.0376) were the only significant predictors for increased risk of death.

Although our cohort of patients on HAART experienced a high drop-out rate, the difference in gender mortality rate is not explained by drop-out bias. One hundred and thirty-seven patients (8.8%) were listed as LTF, 95 (8.64%) females and 42 (9.29%) males. This is a high percentage that reflects barriers to access and resource challenges inherent in this study environment. Table 4 divides the patients who were LTF into categories based on gender and then compares the LTF patients to males or females who were not LTF to determine if drop-out bias influenced our results. Significant differences were found to exist in education level and occupation, however, there were no significant differences detected between the LTF group and others when comparing age, weight, BMI, initial CD4 cell count, residence, marital status, or concurrent infection with TB.

Of note, both LTF male and female patients were more likely to have experienced less improvement in their CD4 count on HAART than non-LTF patients. However, in both LTF female and male groups, there was a non-statistically significant trend toward improvement in the last CD4 cell count taken prior to loss of contact. The median increase in CD4 cell counts from the initial CD4 count in the LTF female group was greater than the median increase in CD4 cell counts of the LTF male group. LTF patients as a whole were more likely to have had active TB than those who had complete follow-up. LTF males were much more likely than LTF females to have active TB during HAART treatment. Together, these findings strongly suggest that patients LTF did not introduce bias into our results by removing sicker women from the completed study.

Discussion

The results of studies addressing the issue of differences in progression of HIV with relation to gender have been variable. Comparing males to females, the rate of clinical progression, defined as either development of AIDS or death, has been reported to be either the same (Braitstein et al., 2006; Duncombe et al., 2005; Garcia de la Hera et al., 2004; Hogg et al., 2001; Mayor et al., 2005; Moore, Sabin, Johnson, & Phillips, 2002; Moore, Cheever, Keruly, & Chaisson, 1999; Napravnik, Poole, Thomas, & Eron, 2002), higher (Collazos, Asensi, & Carton, 2007; Lucas et al., 1993; Sani et al., 2006; Spino, Kahn, Dolin, & Phair, 1997), or lower (Melnick et al., 1994). Because of the varying results, further investigation to definitively answer questions about gender differences in HIV infection is necessary. The profiles of patients presenting to clinics in the developing world are different from those in developed nations (Braitstein et al., 2006). In many African clinics, more female patients present for HIV/AIDS therapy than men (Stringer et al., 2006). Related to this, more patients acquire HIV through heterosexual transmission in sub-Saharan Africa than in developed nations where male-to-male sexual transmission and injection drug use predominate (Boerma, Nunn, & Whitworth, 1998). Thus, African-specific mortality studies are important because of the differences in HIV epidemiology, socio-cultural differences, and impaired access to health care (Boerma et al., 1998). Despite these differences, few previous studies have examined the relationship between gender and mortality in African settings (Boerma et al., 1998; Lucas et al., 1993; Sani et al., 2006).

Our results demonstrate that men, the unemployed, and younger adults have a worse clinical outcome than women even after controlling for coinfection with TB and initial CD4 count, two known risk factors for increased mortality (Boerma et al., 1998; Duncombe et al., 2005; Hogg et al., 2001; Lemp, Payne, Neal, Temelso, & Rutherford, 1990; Lucas et al., 1993; Moore et

al., 2002; Nicastri et al., 2005; Saah, Hoover, He, Kingsley, & Phair, 1994; Shafer et al., 1996). However, our results are different when we use the full sample of patients or restrict the sample based on certain variables. After removing patients with initial CD4 counts less than 50 or who were concurrently taking anti-TB therapy and antiretroviral therapy from the multivariate analysis, unemployment and primary education were shown to be significantly associated with increased mortality. This difference suggests that males who begin ARV treatment with CD4 counts above 50 or who are not co-infected with TB have similar mortality outcomes to females with similar demographics.

Variables not measured in our study that might possibly increase mortality among younger adults, the unemployed, and males as compared to patients over the age of 30, the employed, and females include the following: medication noncompliance (not accurately measured in our clinic population and more likely among the poorer, unemployed patients (Hardon et al., 2007), higher risk behaviors (more exposure to opportunistic infections), access to good nutrition, and inaccurately recorded cause of death (assumed to be due to HIV in those LTF but possibly due to some other cause, for example, trauma among younger males). While the male patients in our clinic population appear to present later for care, stage of disease was controlled for by including CD4 count in the multivariate analysis. The reasons for late presentation of male patients may be related to social stigma associated with HIV infection (Alubo, Zwandor, Jolayemi, & Omudu, 2002), other factors which impair access to care, or lack of knowledge about self-risk for HIV infection (St Lawrence et al., 1995). The higher prevalence of TB in the male cohort of our study population suggests that as a group, males receiving care at Faith Alive may present at more advanced stages of disease than females, but does not explain their more rapid mortality when controlling for stage of disease at initiation of HAART.

Our findings are similar to other studies of mortality in HIV-infected patients in Africa which show that the rate of mortality is higher in men than in women (Lucas et al., 1993; Sani et al., 2006). Despite these previous results, many HIV/AIDS prevention and treatment programs continue to focus on women and children. One study from Ghana suggests that because of a lack of a specific focus on men and an increased focus on women, men may have a false impression that their relative risk for HIV infection is lower (Luginaah, Yiridoe, & Taabazuing, 2005). This false sense of security may result in fewer men presenting to clinics for HIV testing thus delaying initiation of HIV treatment and possibly contributing to the risk of death that male gender seems to independently confer.

Our study differs from those of Boerma (Boerma et al., 1998), Sani (Sani et al., 2006), and Lucas (Lucas et al., 1993) in that the majority of patients in their studies were not receiving HAART while all of the patients in our study cohort were receiving HAART. In addition, the patient populations of both the Sani and Lucas studies were made up entirely of hospitalized patients. This implies that their patients were likely at more advanced stages of disease compared to the typical patient in our study cohort. It is interesting to note that even with these differences in study design, our study had similar gender-related results to these two studies. Boerma et al., Sani et al., and Lucas et al. do not address mortality associated with distinct age categories or occupation status.

Limitations of our study include some elements common to research in resource-limited countries. There is some uncertainty about the cause of a few deaths. When AIDS patients died outside of FAFH, death was assumed to be due to complications of HIV. It is therefore possible that some patient deaths were due to causes other than HIV. If there was systematic gender-associated bias in assigning cause of death among males as due to HIV when the true cause of death was unknown (e.g., trauma, as discussed above) or bias in not recording the cause of death in women as due to HIV, more males may have incorrectly appeared to have died of

HIV. Our study has limited generalizability since it has been noted that causes of mortality may differ by region, by country, and even within countries (Boerma et al., 1998). Our study population was from a single medical facility and a particular geographical area of Nigeria.

As noted above, one of the variables not measured well in our clinic population which may confound the results is treatment compliance. While our data set had clear information about treatment compliance for some patients, it is conceivable that some or all of the difference in gender-associated outcomes is due to poorer medication compliance among males. However, the partial information we have about treatment compliance does not suggest a gender difference; and a prior study noted neither gender differences nor differences between developing and developed nations in medication compliance (Mills et al., 2006). Further research on this subject should include compliance as a variable. In addition to treatment compliance, access to appropriate nutrition is an important factor that determines the outcome of ART. Our study did not measure patient nutrition. If found to be a confounders, social science research would be useful to determine gender-related causes of differences in medication compliance and nutrition that may be alleviated through program design.

Individual/household income has a strong correlation with predictors like “youth” and “unemployment”. Although we attempted to control for economic differences between patients by using employment status as a proxy for socioeconomic status, we realize that this has limited value. In cultures where extended families live together, household income, rather than individual employment status, is a stronger predictor of socioeconomic status.

Differences in health outcomes between demographic groups are by definition health disparities. Our results show that even when controlling for more advanced HIV illness by including initial CD4 count, active TB, and socio-demographic risk factors in the multivariate equation, younger adults, the unemployed or those with unknown employment, and men started on HAART have a poorer clinical outcome than women, the employed, and older adults. Are these results applicable to populations living in other areas of Nigeria and the African continent? Are there biological factors involved or is the differential rate of progression due to socio-cultural factors not included in our multivariate model such as medication compliance, higher risk behaviors, and unknown or inaccurate causes of death? The results of this study prompt a call for further investigation to confirm our findings. If our findings are verified by other studies, further research will be needed to determine the reasons for cultural and/or biological explanations for these disparities.

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Table 1

Comparison of 1552 HIV-positive patients receiving HAART at Faith Alive Clinic.

Variable	Overall (*N* = 1552)	Females (*N* = 1100)	Males (*N* = 452)	Wilcoxon Rank Sum *P*-value
Age, Median (Min, Max)	34 (17.0, 76.0)	32 (17.0, 76.0)	38 (21.0, 75.0)	<0.001
Initial weight, Median (Min, Max)	55 (17.0, 113.0)	54 (29.0, 113.0)	60 (17.0, 91.0)	<0.001
Height, Median (Min, Max)	161 (104.0, 198.0)	159 (104.0, 191.0)	169 (118.0, 198.0)	<0.001
BMI, Median (Min, Max)	21.1 (6.0, 47.2)	21.3 (11.1, 47.2)	20.8 (6.0, 40.6)	0.34
CD4 cell count prior to starting HAART, Median (Min, Max)	112 (1.0, 1314.0)	113 (1.0, 631.0)	109 (1.0, 1314.0)	0.9
Residence, No. (%)				Pearson *P* 0.92
R	615 (40%)	435 (40%)	180 (40%)	
U	937 (60%)	665 (60%)	272 (60%)	
Education, No. (%)				<0.001
None/Unknown	214 (14%)	171 (16%)	43 (10%)	
Post-Secondary	453 (29%)	277 (25%)	176 (39%)	
Primary	357 (23%)	267 (24%)	90 (20%)	
Secondary	528 (34%)	385 (35%)	143 (32%)	
Occupation, No. (%)				<0.001
Professionals	535 (34%)	334 (30%)	201 (44%)	
Clerks/Manual	415 (27%)	287 (26%)	128 (28%)	
Student	67 (4%)	63 (6%)	4 (1%)	
Unemployed/Unknown occupation	535 (34%)	416 (38%)	119 (26%)	
Marital status, No. (%)				<0.001
Married	771 (50%)	444 (40%)	327 (72%)	
Single	380 (24%)	301 (27%)	79 (17%)	
Unknown	7 (0%)	4 (0%)	3 (1%)	
Widowed	394 (25%)	351 (32%)	43 (10%)	
Active TB infection, No. (%)				0.016
No	1301 (84%)	938 (85%)	363 (80%)	
Yes	251 (16%)	162 (15%)	89 (20%)	

Note: Occupation categories: professional =professionals, senior officials, managers, associate professionals; clerks/manual = junior non-manual, clerks, skilled manual, semi-skilled manual, unskilled manual, farmers; students; unemployed/unknown.

Table 2

Results of Cox proportional hazard analysis showing the risk of mortality related to specific demographic factors for HIV-infected patients at Faith Alive during treatment (*N* = 1552).

		95% CI		
Variable*	**Hazard ratio**	**Lower**	**Upper**	***P*-value**
Male gender	1.756	1.135	2.715	0.0114
Age <30 years old	1.707	1.114	2.616	0.0141
Active TB infection	3.617	2.418	5.410	<0.0001
CD4 cell count < 50	3.277	2.198	4.886	<0.0001
Unemployed/Unknown occupation	1.792	1.208	2.660	0.0038

* Original variables considered in the above multivariate model which are not included in the final model: age less than 30 and unemployed/unknown occupation status, marital status, urban versus rural residence, secondary education, post-secondary education, religion, and drop in CD4 count after initiation of therapy.

Table 3

Results of Cox proportional hazard model analysis which does not include patients with CD4 counts less than 50 or taking anti-TB therapy at the same time as antiretroviral therapy (N = 1303).

		95% CI		
Variable*	**Hazard ratio**	**Lower**	**Upper**	***P*-value**
Male gender	1.185	0.533	2.636	0.6769
Age < 30 years old	2.715	1.363	5.408	0.0045
Unemployed/Unknown occupation	1.062	0.532	2.120	0.8643
Primary education	2.064	1.043	4.085	0.0376

Note: The results show the risk of mortality related to specific demographic factors for a subset of HIV-infected patients at Faith Alive during treatment.

* Original variables considered in the above multivariate model which are not included in the final model: age less than 30 and unemployed/unknown occupation status, marital status, urban versus rural residence, secondary education, post-secondary education, religion, and drop in CD4 count after initiation of therapy.

Table 4

Gender-differentiated comparisons of lost-to-follow-up patients with patients for whom complete data sets are available, for HIV-positive patients receiving HAART at Faith Alive Clinic.

	Female patients			Male patients		
Variable	**Others (*N* = 1005)**	**LTF (*N*=95)**	***P*-value**	**Others (*N*=410)**	**LTF (*N*=42)**	***P*-value**
Age, Median (Min, Max)	32 (19.0, 73.0)	31 (17.0, 76.0)	0.14	38 (21.0, 75.0)	38 (24.0, 70.0)	0.68
Initial weight, Median (Min, Max)	54 (29.0, 113.0)	50 (30.0, 105.0)	0.047	60 (17.0, 91.0)	57 (39.0, 80.0)	0.22
Height, Median (Min, Max)	159 (104.0, 191.0)	158 (115.0, 190.0)	0.23	169 (118.0, 198.0)	167.3 (150.0, 179.0)	0.11
BMI, Median (Min, Max)	21.4 (11.1 , 47.2)	20.1 (13.3, 44.3)	0.09	20.9 (6.0, 40.6)	20.1 (16.3 , 29.1)	0.66
CD4 count prior to starting HAART, Median (Min, Max)	116.5 (1.0, 631.0)	94.5 (3.0, 583.0)	0.25	109 (1.0, 1314.0)	106 (2.0, 426.0)	0.79
Patient's most recent CD4 count, Median (Min, Max)	326 (2.0, 1239.0)	124 (3.0, 723.0)	<0.001	265 (3.0, 1468.0)	117 (2.0, 426.0)	<0.001
Residence, No. (%)			0.92			0.81
Rural	397 (40%)	38 (40%)		164 (40%)	16 (38%)	
Urban	608 (60%)	57 (60%)		246 (60%)	26 (62%)	
Education, No. (%)			0.002			0.26
None/Unknown	157 (16%)	14 (15%)		40 (10%)	3 (7%)	
Post-Secondary	265 (26%)	12 (13%)		163 (40%)	13 (31%)	
Primary	247 (25%)	20 (21%)		83 (20%)	7 (17%)	
Secondary	336 (33%)	49 (52%)		124 (30%)	19 (45%)	
Occupation, No. (%)			<0.001			0.017
Professionals	314 (31%)	20 (21%)		190 (46%)	11 (26%)	
Clerks/Manual	274 (27%)	13 (14%)		116 (28%)	12 (29%)	
Student	60 (6%)	3 (3%)		4 (1%)	0 (0%)	
Unemployed/Unknown occupation	357 (36%)	59 (62%)		100 (24%)	19 (45%)	
Marital status, No.(%)			0.32			0.44
Married	413 (41%)	31 (33%)		295 (72%)	32 (76%)	
Single	269 (27%)	32 (34%)		73 (18%)	6 (14%)	

	Female patients			Male patients		
Variable	**Others (*N* = 1005)**	**LTF (*N*=95)**	***P*-value**	**Others (*N*=410)**	**LTF (*N*=42)**	***P*-value**
Unknown	4 (0%)	0 (0%)		2 (0%)	1 (2%)	
Widowed	319 (32%)	32 (34%)		40 (10%)	3 (7%)	
Active TB infection, No. (%)			0.22			0.05
No	861 (86%)	77 (81%)		334 (81%)	29 (69%)	
Yes	144 (14%)	18 (19%)		76 (19%)	13 (31%)	

Note: Occupation categories: professional =professionals, senior officials, managers, associate professionals; clerks/manual =junior non-manual, clerks, skilled manual, semi-skilled manual, unskilled manual, farmers; students; unemployed/unknown.