

1 ***New-Onset Type 2 Diabetes Mellitus Among Patients Receiving HIV Care At***  
2 ***Newlands Clinic, Harare, Zimbabwe. A Retrospective Cohort Analysis***

3 Cleophas Chimbetete<sup>1, 2, 3</sup>, Catrina Mugglin<sup>1</sup>, Tinei Shamu<sup>2</sup>, Bindu Kalesan<sup>4</sup>, Barbara  
4 Bertisch<sup>1,3,4,5</sup>, Matthias Egger<sup>1</sup>, Olivia Keiser<sup>1,3</sup>

5 1 Institute of Social and Preventive Medicine (ISPM), University of Bern, Switzerland

6 2 Newlands Clinic, Harare, Zimbabwe

7 3 Institute of Global Health, University of Geneva

8 4 Center for Translational Epidemiology and Comparative Effectiveness Research  
9 Boston University School of Medicine, USA

10 5 Checkpoint Zuerich, Zuerich, Switzerland

11

12 Corresponding Author: Cleophas Chimbetete

13 56 Enterprise Road

14 Harare, Zimbabwe

15 Phone number: +263 772 572 877

16 E-mail: [docchimbetete@gmail.com](mailto:docchimbetete@gmail.com)

17

18 E-mail addresses of authors:

19 CM: [catrina.mugglin@ispm.unibe.ch](mailto:catrina.mugglin@ispm.unibe.ch)

20 TS: [TineiS@newlandsclinic.org.zw](mailto:TineiS@newlandsclinic.org.zw)

21 BK: [kalesan@bu.edu](mailto:kalesan@bu.edu)

22 BB: [barbara.bertisch@unige.ch](mailto:barbara.bertisch@unige.ch)

23 ME: [matthias.egger@ispm.unibe.ch](mailto:matthias.egger@ispm.unibe.ch)

24 OK: [olivia.keiser@unige.ch](mailto:olivia.keiser@unige.ch)

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26 Keywords: Type 2 Diabetes Mellitus, HIV Infection, Zimbabwe

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28

29 **Abstract**

30 **Background**

31 Diagnosing and managing Type 2 Diabetes Mellitus (T2DM) among people living with HIV  
32 (PLHIV) is becoming more important as the HIV-infected population ages and becomes  
33 increasingly comorbid. Data on incidence of T2DM in PLHIV in Sub-Saharan Africa is  
34 scarce.

35 **Methods**

36 We analyzed data for all HIV-infected patients older than 16 years who attended Newlands  
37 Clinic between March 1, 2004 and April 29, 2015. The clinic considers patients whose  
38 random blood sugar is higher than 11.1 mmol/L and which is confirmed by a fasting blood  
39 sugar higher than 7.0 mmol/L to have T2DM. T2DM is also diagnosed in symptomatic  
40 patients who have a RBS >11.0 mmol/l. Risk factors for developing T2DM were identified  
41 using Cox proportional hazard models adjusted for confounding. Missing baseline BMI data  
42 were multiply imputed. Results are presented as adjusted hazard ratios (aHR) with 95%  
43 confidence intervals (95%CI).

44 **Results**

45 Data for 4,110 participants were included: 67.2% were women; median age was 37 (IQR:31-  
46 43) years. Median baseline CD4 count was 197 (IQR: 95-337) cells/mm<sup>3</sup>. The proportion of  
47 participants with hypertension at baseline was 15.5% (n=638). Over a median follow-up time  
48 of 4.7 (IQR:2.1-7.2) years, 57 patients developed T2DM; the overall incidence rate was 2.8  
49 (95%CI: 2.1 – 3.6) per 1000 person-years of follow up. Exposure to PIs was associated with  
50 T2DM (HR: 1.80, 95%CI: 1.04-3.09). In the multivariable analysis, obesity (BMI>30kg/m<sup>2</sup>)  
51 (aHR=2.26, 95%CI: 1.17-4.36), age >40yrs (aHR=2.16, 95%CI: 1.22-3.83) and male gender,  
52 (aHR=2.13, 95%CI: 1.22-3.72) were independently associated with the risk of T2DM. HIV

53 related factors (baseline CD4 cell count and baseline WHO clinical stage) were not  
54 independent risk factors for developing T2DM.

## 55 **Conclusion**

56 Even though the incidence of T2DM in this HIV cohort was lower than has been observed in  
57 other cohorts, our results show that risk factors for developing T2DM among HIV infected  
58 people are similar to the general population. HIV-infected patients in sub-Saharan Africa  
59 need a comprehensive approach to care that includes better health services for prevention,  
60 early detection and treatment of chronic diseases especially among the elderly and obese.

61 **Key words:** Type 2 Diabetes mellitus, Zimbabwe, HIV infection

62

## 63 **Background**

64 Access to antiretroviral therapy (ART) has reduced the Human Immunodeficiency Virus (HIV)  
65 associated morbidity and mortality among people living with HIV (PLHIV). However, access to  
66 long term ART may be associated with toxicities including hyperglycaemia and diabetes  
67 mellitus [1]. As PLHIV live longer, they are likely to develop comorbidities such as Type 2  
68 Diabetes Mellitus (T2DM). Furthermore, the prevalence of noncommunicable diseases is  
69 increasing in low and middle income countries [2], hence PLHIV in these countries are faced  
70 with a dual burden of disease as they grow older. Traditional and well established risk factors  
71 of development of T2DM in non HIV infected patients include older age, hypertension, obesity  
72 and physical inactivity [3]. Factors associated with the occurrence of T2DM in HIV-infected  
73 patients are complex. They include the effects of HIV itself, which is a chronic inflammatory  
74 and insulin-resistant condition, genetics, cigarette smoking, physical inactivity, obesity, aging  
75 and the toxic effects of ART [4]. As persons infected with HIV are surviving longer due to ART  
76 uptake, T2DM and cardiovascular diseases are increasingly noted [5], [6]. The WHO  
77 STEPwise chronic disease risk factor surveillance programme (STEPS) quantifies the burden  
78 of diabetes in sub-Saharan Africa, which varies widely; it is 6.1% in Cameroon, over 7.1% in  
79 Congo, and 10.2% in Zimbabwe [7]. In a recent cross sectional facility based study, 2.1%  
80 (95%CI:1.3-3.2%) of people living with HIV in Zimbabwe had comorbid T2DM [8]. Results from  
81 the phase 3 HPTN 052 randomised controlled trial done in Uganda and Zimbabwe showed a  
82 very low event rate for diabetes mellitus (9 new cases in 1761 patients) among HIV infected  
83 patients on ART [9].

84 There is documented evidence of an increase in the burden of T2DM in Zimbabwe [10]. In  
85 2015, 209,800 cases of diabetes were recorded in the country and these contributed to the  
86 national adult prevalence of 2.9% [11]. However, the incidence of T2DM among HIV  
87 infected individuals in Zimbabwe is unknown. The increasing burden of non-communicable  
88 diseases among PLHIV will increase the costs of comprehensive healthcare provision  
89 especially in resource limited settings. Despite this double burden, there is a dearth of

90 literature surrounding diabetes and HIV research in Zimbabwe. Given the evidence  
91 concerning HIV's role (via ART mediated pathways) as a potential risk factor for diabetes,  
92 there is a need for this research to be carried out in Zimbabwe. The objective of this study  
93 was to assess the incidence and associated risk factors of new onset T2DM in a cohort of  
94 HIV infected individuals receiving ART at an outpatient clinic in Zimbabwe.

## 95 **Methods**

### 96 ***Study setting***

97 Newlands Clinic (NC) is a family-centered, nurse-based and doctor supervised HIV  
98 treatment center in Harare, Zimbabwe. Nurses provide routine HIV care to patients and  
99 doctors consult all patients with new clinical complains and / or abnormal laboratory results.  
100 It is a part of the coordinated public-private partnership between the Ministry of Health and  
101 Child Care and several private organisations that provide HIV treatment in Zimbabwe. NC  
102 provides access to care and treatment to approximately 5,500 HIV-1 infected paediatric,  
103 adolescent and adult patients. Patient care follows the Zimbabwe national guidelines [12].  
104 Patients enrolled at NC have similar demographic and socio-economic characteristics to  
105 those in the national OI / ART program [13]. NC uses the same guidelines for initiation of  
106 ART as the national program. As part of routine HIV care, the following laboratory test are  
107 done at least once every year: Full Blood Count (FBC), serum creatinine clearance, liver  
108 function tests, CD4 cell count, HIV viral load and urinalysis (since 2013). The clinic does not  
109 offer routine testing for lipids and HbA1c.

### 110 **Study Procedures / Methods**

111 The clinic includes a laboratory and a pharmacy with quick turnaround times for laboratory  
112 investigations and convenient drug pick-up after consultations. These services are provided  
113 free to patients. All clinic patients are screened for T2DM with random venous blood  
114 glucose measurements performed at baseline and routinely once a year by the laboratory.

115 Diagnosis of T2DM was based on two different criteria defined by the American Diabetes  
116 Association [14]. 1) If a patient had an elevated random blood glucose measurement  
117 of >11.0 mmol/l, a fasting plasma glucose (FPG) test was done to screen for T2DM. Fasting  
118 blood sugar is measured after the patient has not consumed food or drink (except water) for  
119 at least 8 hours. If the FPG value was >7.0 mmol/l, the patient was diagnosed with T2DM. 2)  
120 Patients who presented with clinical signs and symptoms of hyperglycemia, such as thirst,  
121 polyuria, weight loss and blurred vision were screened immediately by measuring random  
122 blood sugar; if sugar was elevated (>11.1 mmol/l), they were diagnosed as T2DM. All  
123 patients had access to blood sugar measurements. Screening and diagnosis of T2DM is  
124 done by a doctor. There has not been any patient diagnosed of type 1 diabetes mellitus at  
125 the clinic to date and hence type 1 diabetes mellitus was not part of this analysis. All patient  
126 data are entered into an electronic medical record system since the clinic was started in  
127 2004.

## 128 **Ethical Approval**

129 Newlands Clinic is part of the International epidemiologic Databases to Evaluate AIDS-  
130 Southern African Region (IeDEA-SA) [15]. Patients provided written informed consent  
131 allowing their clinic data to be used for research analysis to answer epidemiological  
132 questions. This study was approved by the Medical Research Council of Zimbabwe  
133 (Approval number: MRCZ/A/1336).

## 134 ***Inclusion criteria and definitions***

135 All patients aged 16 years and above at ART commencement receiving care at Newlands  
136 Clinic in the period 01 March 2004 to 29 April 2015 were eligible for analysis. Baseline  
137 values / variables were at commencement of ART. Patients who were diagnosed with T2DM  
138 before or at the time they started ART were excluded from this analysis. Incident T2DM was  
139 defined as a documented new diagnosis of T2DM after ART commencement. Hypertension  
140 was defined as a documented systolic pressure greater than 140 mm Hg and / or diastolic

141 pressure greater than 90 mm Hg measured on at least 2 different days or receiving  
142 antihypertensive medicines. All patients with a diagnosis of hypertension are on anti-  
143 hypertensive medicines such as atenolol, enalapril, spironolactone, amlodipine and  
144 antihypertensive medicines are not used for non-hypertensive heart diseases at NC.  
145 Baseline values of CD4 and BMI were the closest values, within 3 months before or after  
146 start of ART. ART was defined as a regimen of at least three antiretroviral drugs from any  
147 drug class. Loss-to-follow-up (LTFU) was defined as failing to attend a scheduled clinic  
148 appointment for at least 90 days without documentation of death or transfer to another clinic.

### 149 ***Statistical analysis***

150 The overall and stratified incidence rates of T2DM were calculated as the number of new-  
151 onset T2DM cases, divided by the total number of person-years (PY) of follow-up. We  
152 calculated T2DM incidence rates for the whole observation period and did not consider  
153 interruptions or treatment changes to ART. Data was complete for all variables except  
154 baseline BMI where 8.7% (n=357) were missing. We imputed these missing BMI values  
155 based on the other characteristics at baseline, and whether the patient developed T2DM or  
156 not. Analyses were done for each of the 20 imputed datasets and we used Rubin's rule to  
157 combine results [16]. We also did a complete case analysis.

158 We used crude and adjusted Cox proportional hazards models to describe risk factors for  
159 incident T2DM and checked for proportional hazard assumptions using Schoenfeld  
160 residuals. Use of protease inhibitors (PI) was assessed in the univariable analysis only and  
161 not in multivariable analysis because it is in the causal pathway for T2DM. We measured  
162 follow-up time from day of ART initiation until the date of T2DM diagnosis, the last follow-up  
163 visit, or death, whichever occurred first. We considered the following explanatory variables at  
164 start of antiretroviral therapy: age (<40 and  $\geq$ 40 years); gender; baseline CD4 count category  
165 (<200 and  $\geq$ 200 cell/ mm<sup>3</sup>); baseline BMI (<30 and  $\geq$ 30 kg/ m<sup>2</sup>, missing baseline BMI data  
166 was imputed as a continuous variable); hypertension; and, WHO clinical stage (stages 1

167 and 2 vs stages 3 and 4). Results are presented as incidence rates per 1000 person years,  
168 crude and adjusted hazard ratios (HR) with 95% confidence intervals (CI). All statistical  
169 analyses were performed in Stata version 13.0. (StataCorp, College Station, Texas, USA).



170 **Results**

171 ***Patient characteristics***

172 The Clinic database had 5,467 patient records. We excluded 42 patients who had prevalent  
173 T2DM, 6 participants who had not started ART and 1,309 who were children <16 years old.  
174 We analysed data for 4,110 patients, of whom 67.2% (n=2,761) were women. The  
175 characteristics of the participants at start of ART are shown in Table 1. Median age of  
176 participants was 37 years (IQR: 31-43); median baseline CD4 count was 197 cells/mm<sup>3</sup>  
177 (IQR: 95-337). Overall 46.6% (n=1,917) participants were in WHO stage 3 or 4. Prevalence  
178 of obesity was 9.6% (n=3753). Among the 16% (n=638) patients with hypertension,  
179 prevalence of obesity was almost twice as high (30.2%; n=110) when compared to those  
180 without hypertension. Median follow-up time for study participants was 4.7 years (IQR 2.1 -  
181 7.2). At the time of data abstraction (29 April 2015), 78% (n= 3,208) participants were still in  
182 care, 8.9% (n=364) had died, 5.3% (n=217) were LTFU and 7.8% (n=321) were transferred  
183 to other HIV treatment centres.

184

185 ***Incidence of T2DM***

186 The number of new T2DM diagnoses over the 20,504 PY of follow-up was 57; overall  
187 incidence rate was 2.8 per 1000 PY (95% CI: 2.1-3.6). There were 5 new T2DM diagnoses  
188 among patients who deceased and 4 among patients transferred out. None of the new  
189 T2DM diagnoses were diagnosed in pregnancy. The incidence rate of T2DM was higher in  
190 men than in women. The incidence rate of T2DM increased with age from 0.48 / 1000 PY  
191 (95%CI: 0.07-3.37) among patients younger than 25 years to 8.35 / 1000 PY (95%CI: 5.11-  
192 14.32) in those 50 years and above. The incidence rate also increased with an increase in  
193 BMI from a rate of 0 /1000 PY in patients with a BMI of < 18 kg/m<sup>2</sup> to a rate of 5.84 / 1000  
194 PY (95%CI: 3.24-10.55) in those who had a BMI of at least 30 kg/ m<sup>2</sup>. Hypertensive  
195 participants had a higher incidence rate than those without hypertension. We did not see any

196 trend in the incidence of T2DM over the years associated with the change in national ART  
197 guidelines. Table 1 highlights the incidence of T2DM for various patient categories. In  
198 univariable analysis, patients who had used protease inhibitors were more likely to develop  
199 T2DM than those who had not (RR=1.80, 95%CI: 1.04-3.09). Table 2 shows the results of  
200 the univariable and multivariable analyses that identified risk factors of diabetes.

201 In the multivariable analysis, men were more likely to develop T2DM than women  
202 (aHR=2.13). Patients >40 years old had a higher risk of developing T2DM (aHR=2.16) than  
203 patients <40 years old. Obesity (BMI >30 kg/m<sup>2</sup>) was an independent risk factor for T2DM  
204 (aHR=2.26). HIV-related characteristics (baseline WHO stage and baseline CD4 count) were  
205 not associated with risk of developing diabetes. There was no evidence of proportional  
206 hazard assumptions violation (p=0.19).

207

## 208 **Discussion**

209 Overall incidence of T2DM in this cohort of HIV-infected people was 2.8 per 1000 PY of  
210 follow-up. The incident rate increased with increases in age and BMI. We identified the  
211 following independent risk factors for developing T2DM: Age > 40 years, male gender, and  
212 obesity. HIV-related factors (baseline CD4 cell count and baseline WHO clinical stage) were  
213 not independent risk factors for the development of T2DM. We did not include use of PIs in  
214 the multivariable model because PI use is in the causal pathway for pathogenesis of T2DM  
215 and hence cannot be controlled for, however, use of PIs was a significant risk factor in the  
216 univariable analysis.

217 We found a much lower T2DM incidence rate than has been reported in other studies. A  
218 study from Thailand showed an incidence rate of 5.0 per 1000 PY among patients living with  
219 HIV [17]. The Data collection on Adverse events of Anti-HIV Drugs (D.A.D) study showed an  
220 incidence rate of 5.7 per 1000 PY [18] and in the Swiss HIV Cohort study the incidence rate  
221 was 4.4 per 1000 PY [4]. In a study done in South Africa, Karamchand *et al* found a crude

222 incidence rate of 13.2 per 1000 PY among HIV infected adults on first-line ART [19]. To the  
223 best of our knowledge, there are no studies that have looked at the incidence of T2DM in  
224 either HIV positive or negative people in Zimbabwe hence we are not able to compare our  
225 findings with national statistics. Several factors might explain the discrepancy between our  
226 study results and other studies. The median BMI of 22.3 kg/m<sup>2</sup> among our participants was  
227 much lower than, for example, in the Swiss HIV Cohort. We used routinely collected clinic  
228 data where patients were screened for T2DM during regular clinic visits and under-reporting  
229 is possible. Routine haemoglobin A1C measurements would have better estimated the  
230 incidence of T2DM in our cohort, but the incidence of T2DM we found in patients over 40  
231 years of age was still comparable to the findings of both Swiss HIV cohort study and the  
232 D.A.D study [4], [18].

233 This analysis identified key risk factors for the development of T2DM among patients living  
234 with HIV. These risk factors are similar to those identified among the general population and  
235 are also consistent with findings from other cohort studies [4], [18]. Not surprisingly, the  
236 incidence rate increased with age and was highest in the patients above 50 years of age,  
237 highlighting the increased burden of health problems among individuals who are ageing with  
238 HIV. Our findings of an increased risk of T2DM with increasing age and BMI are consistent  
239 with findings from studies that have looked at risk factors of T2DM among both HIV positive  
240 and HIV negative individuals [20]. As in people not infected with HIV, age is an important risk  
241 factor for both T2DM and cardiovascular diseases. Since aging cannot be avoided, it is  
242 important to regularly screen the elderly for diseases such as diabetes. While studies have  
243 demonstrated a lower BMI in HIV-infected patients with diabetes compared to non-infected  
244 matched cohorts [21], the association between T2DM and obesity persists in HIV infected  
245 patients. For example, Galli *et al.* found that the prevalence of T2DM in those with normal  
246 BMI was 3.2% in HIV patients and 1.1% in HIV uninfected. However, in the overweight and  
247 obese categories, T2DM prevalence rose to 3.9% and 12.7% among HIV infected patients  
248 compared with 3.1% and 7.8% respectively in HIV-uninfected patients [22]. HIV treatment

249 programs should educate patients on the dangers of obesity so as to minimise the risk of  
250 developing T2DM. Furthermore, elderly PLHIV should be educated on the association of  
251 ageing and the risk of developing T2DM. In the univariable analysis, our results showed that  
252 patients who had used PIs (ritonavir boosted atazanavir and / or lopinavir) were 1.8 times  
253 more likely to develop new-onset T2DM. These findings are consistent with other studies  
254 that have demonstrated the association between PI use and metabolic complications such  
255 as T2DM [20], [23]. Use of ART medicines has increasingly become important as a potential  
256 risk factor for T2DM. In a review article on diabetes and HIV, Murphy and Gerard report that  
257 PLHIV following treatment with some first generation ART drug classes (protease inhibitors)  
258 had higher rates of diabetes incidence compared to HIV negative participants [24]. In South  
259 Africa, it was recently reported that treatment with efavirenz, as well as stavudine and  
260 zidovudine, increased the risk of incident diabetes [25]. In this cohort, we could not assess  
261 the association between efavirenz or nevirapine with T2DM because efavirenz became  
262 available only a year ago and before that all patients received nevirapine as part of their first  
263 line ART regimen. We could also not assess the associations of different PIs because  
264 Patients have received both Lopinavir and Atazanavir at different times depending on which  
265 drug was available and the recording of different PIs was not very accurate.

266 We identified hypertension as being associated with developing T2DM, however, this  
267 association was not significant in the multivariable analysis. We did not assess the possible  
268 effects of the antihypertensive medicines on the risk of developing T2DM. The high burden  
269 of hypertension in this cohort illustrates the increasing burden of non-communicable  
270 diseases (NCDs) among HIV infected adults. NCDs collectively contribute to the decreased  
271 life expectancy of HIV-infected patients on treatment. Furthermore, treatment of co-  
272 morbidities among PLHIV increases the pill burden and this may in turn affect adherence to  
273 medicines [26]. Men were more likely to develop T2DM in this cohort. This finding is  
274 inconsistent with global estimates that indicate that sex has little effect on diabetes. Sex  
275 distribution among diabetic patients varies widely in sub-Saharan Africa, with no discernable

276 trend [27]. Our study did not show any association between baseline CD4 cell count and  
277 WHO clinical stage with the risk of developing T2DM. However, other studies have found an  
278 increased risk of T2DM with lower CD4 cell count and longer duration of HIV infection.  
279 Furthermore, studies have found associations between high HIV viral load and diabetes [22],  
280 [28].

281 The major strength of our study was that patient characteristics are typical for many clinics  
282 in sub-Saharan Africa [29], so our results are likely to accurately reflect routine clinical care  
283 in the region. Our LTFU rate was lower than in other clinics [30], [31], hence our results were  
284 less affected by patient dropouts. Because the clinic uses an electronic record system with a  
285 rigorous data quality control system, our data was complete for all variables except baseline  
286 BMI; results were similar with and without imputing missing BMI.

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288 Our study had several limitations, chiefly because we used routine clinic data. Limitations  
289 included a lack of population based samples, absence of HIV negative, HIV positive and  
290 ART naïve comparison groups and incomplete measurement of key T2DM risk factors such  
291 as nutrition and physical exercise. The number of new-onset T2DM in our cohort was very  
292 low and this in turn limited the power of our study. In our analysis, we could not control for  
293 possible time dependent confounding because of unavailability of complete follow up data.  
294 Since all participants were enrolled at a single urban site, this may reduce the  
295 generalizability of our findings to the population of Zimbabwe and beyond.

## 296 **Conclusion**

297 Even though the incidence of T2DM in this HIV cohort was lower than has been observed in  
298 other cohorts, our results show that T2DM is a problem as the population of HIV-infected  
299 patients continues to age. HIV-infected patients in sub-Saharan Africa need more than ART;  
300 they need a comprehensive approach to care that includes better health services for  
301 prevention, early detection and treatment of chronic diseases.

302 **Competing Interest**

303 The authors have no competing interests to declare.

304 **Acknowledgements**

305 The authors acknowledge Kali Tal and Ruedi Luethy for their editorial and clinical comments.  
306 Research reported in this publication was supported by National Institute Of Allergy And  
307 Infectious Diseases of the National Institutes of Health under Award Number U01AI069924  
308 (PI: Egger and Davies). The content is solely the responsibility of the authors and does not  
309 necessarily represent the official views of the National Institutes of Health. O Keiser was  
310 supported by a professorship grant from the Swiss National Science Foundation (grant#  
311 163878).

312 **Authors' Contributions**

313 CC wrote the first draft of the study protocol. All authors contributed to the final version of the  
314 protocol. CC and TS did the statistical analyses, with interpretation of results by CC and OK.  
315 CC wrote the first draft of the report which was revised by OK, CM, BK, ME and BB. All authors  
316 revised and approved the final version for submission.

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327 **Table 1: Participant baseline and clinical characteristics**

	Variable	Patients (N)	Person years at risk	Diabetes cases	Incidence Rate/1000 pyrs (95% CI)
<b>Sex</b>	<b>Female</b>	2,761	14,178	30	2.12 (1.48-3.03)
	<b>Male</b>	1,349	6,326	27	4.27 (2.93-6.22)
<b>Age (years)</b>	<b>&lt;25</b>	491	2,105	1	0.48 (0.07-3.37)
	<b>≥25-&lt;40</b>	2,149	11,068	21	1.81 (1.17-2.80)
	<b>≥40-&lt;50</b>	954	5,111	19	3.72 (2.37-5.83)
	<b>≥50</b>	402	1,916	16	8.35 (5.11-14.32)
<b>*BMI (kg/m<sup>2</sup>)</b>	<b>&lt;18</b>	429	2,006	0	
	<b>≥18-&lt;24</b>	1,962	10,037	22	2.19 (1.44-3.33)
	<b>&gt;24-&lt;30</b>	998	5,486	22	4.01 (2.64-6.09)
	<b>≥30</b>	364	1,882	11	5.84 (3.24-10.55)
<b>WHO STAGE</b>	<b>1/2</b>	2,193	10,462	31	2.96 (2.08-4.21)
	<b>3/4</b>	1,917	10,041	26	2.59 (1.76-3.80)
<b>CD4 Count (cell/μl)</b>	<b>&lt;200</b>	2,083	10,571	31	2.93 (2.06-4.17)
	<b>≥200</b>	2,027	9,933	26	2.62 (1.78-3.84)
<b>Hypertension</b>	<b>Yes</b>	638	4170	24	5.75 (3.86-5.89)
	<b>No</b>	3,472	16,333	33	2.02 (1.44-2.84)
<b>PI Use</b>	<b>Yes</b>	734	4,750	20	4.22 (2.72-6.53)
	<b>No</b>	3,376	15,759	37	2.35 (1.70-2.24)
<b>NVP Use</b>	<b>Yes</b>	2,934	16,443	49	2.98 (2.25-3.94)
	<b>No</b>	1,176	4,067	8	1.97 (0.99-3.94)
<b>EFV Use</b>	<b>Yes</b>	846	2,037	3	1.47 (0.47-4.57)
	<b>No</b>	3,264	18,466	54	2.92 (2.24-3.82)

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329 BMI=Body Mass Index; T2DM= diabetes mellitus; CI= confidence intervals,PI = Protease

330 Inhibitor; NVP=Nevirapine; EFV=Efavirenz; WHO= World Health Organisation

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336 **Table 2: Factors associated with new-onset T2DM among HIV infected patients**

Characteristics	Univariable Analysis		Multivariable Analysis (based on multiple imputation)		Multivariable Analysis (complete case analysis; n=3 753)	
	HR (95% CI)	P	aHR (95 CI)	P	aHR (95 CI)	P
<b>Male gender</b>	2.01 (1.20-3.40)	0.040	2.13 (1.22- 3.72)	0.01	2.31 (1.30- 4.13)	0.004
<b>Age &gt; 40yrs</b>	3.08 (1.80-5.28)	0.001	2.16 (1.22-3.83)	0.01	2.32 (1.29-4.16)	0.005
<b>WHO stage 3/4</b>	0.84 (0.52-1.47)	0.611	0.76 (0.44-1.31)	0.32	0.76 (0.44-1.33)	0.34
<b>BMI &gt; 30 kg/m2</b>	2.33 (1.20-4.50)	0.010	2.26 (1.17-4.36)	0.01	3.10 (1.51-6.36)	0.002
<b>CD4&lt;200 cells/μl</b>	0.89 (0.53-1.50)	0.220	0.67 (0.38-1.18)	0.17	0.73 (0.41-1.30)	0.28
<b>Hypertension</b>	3.94 (2.34-6.65)	0.000	1.79 (1.02-3.12)	0.04	1.60 (0.91-2.84)	0.11
<b>PI use</b>	1.80 (1.04-3.09)	0.032	-	-	-	-

337 Hypertension= Receiving antihypertensive medication or documented diagnosis of hypertension; BMI=Body Mass  
 338 Index; aHR = adjusted Hazard ratios, PI=Protease Inhibitor, PI use excluded from multivariable analysis because  
 339 it is the causal pathway for T2DM

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