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Title: Early ART initiation improves HIV status disclosure and social support in people living with HIV, linked to care within a universal test and treat program in rural South Africa (ANRS 12249 TasP trial)

Running head: Effect of early ART initiation on HIV status disclosure and social support

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1 Abstract

2 We investigated the effect of early antiretroviral treatment (ART) initiation on HIV status disclosure
3 and social support in a cluster-randomized, treatment-as-prevention (TasP) trial in rural South Africa.
4
5 Individuals identified HIV-positive after home-based testing were referred to trial clinics where they
6
7 were invited to initiate ART immediately irrespective of CD4 count (intervention arm) or following
8
9 national guidelines (control arm). We used Poisson mixed effects models to assess the independent
10
11 effects of a) time since baseline clinical visit, b) trial arm, and c) ART initiation on HIV disclosure
12
13 (n=182) and social support (n=152) among participants with a CD4 count >500 cells/mm³ at baseline.
14
15 Disclosure and social support significantly improved over follow-up in both arms. Disclosure was
16
17 higher (incidence rate ratio [95% confidence interval]: 1.24 [1.04;1.48]), and social support increased
18
19 faster (1.22 [1.02;1.46]) in the intervention arm than in the control arm. ART initiation improved both
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21 disclosure and social support (1.50 [1.28;1.75] and 1.34 [1.12;1.61], respectively), a stronger effect
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23 being seen in the intervention arm for social support (1.50 [1.12;2.01]).
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25 Besides clinical benefits, early ART initiation may also improve psychosocial outcomes. This should
26
27 further encourage countries to implement universal test-and-treat strategies.
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41 **Keywords:** HIV, early antiretroviral treatment, test and treat, HIV status disclosure, social support,
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43 South Africa.
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19 **INTRODUCTION**

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3 20 Early initiation of antiretroviral therapy (ART) in people living with HIV (PLHIV) (i.e., ART initiation
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5 21 when CD4 count is high and before symptom onset) preserves immune function, reduces morbidity
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7 22 and increases life expectancy (1,2). It also increases viral suppression at 12 months (3), which reduces
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10 23 the risk of HIV transmission to sexual partners (4,5).

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13 24 Over the last 10 years, evidence for the clinical benefits of early ART initiation has led the World
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15 25 Health Organization (WHO) to update its treatment initiation recommendations: from a CD4 count of
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17 26 ≤ 350 cells/mm³ in 2010 (6) to ≤ 500 cells/mm³ in 2013 (7), to initiation irrespective of CD4 count in
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20 27 2015 (8).

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23 28 In addition, as suggested by modelling and observational studies (9–11), early ART may have the
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25 29 potential to decrease HIV incidence at the population level. In this context, several large-scale trials
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28 30 in HIV hyper-endemic areas, including the ANRS 12249 TasP trial in South Africa (12), have been
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30 31 implemented to assess whether adopting a universal test-and-treat (UTT) strategy (i.e., regular and
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32 32 wide-ranging universal testing campaigns with HIV treatment offered immediately after HIV
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35 33 diagnosis, irrespective of CD4 count) might led to reduced HIV incidence in the general population
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37 34 (13–15). While recent results from these trials all showed an increase in the proportions of PLHIV
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40 35 with viral suppression, only two trials saw a reduction in HIV incidence at the population level
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42 36 (13,16,17). Apart from reducing HIV incidence, the implementation of a UTT strategy also raises
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45 37 questions about the psychosocial implications of early ART initiation.

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48 38 Data in the literature on the psychosocial effects of early ART initiation is scarce, both at the
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50 39 individual and community levels. Two psychosocial outcomes are of particular importance in this
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52 40 context: HIV disclosure and social support The latter can be defined as supportive acts by a partner(s)
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54 41 and loved ones which are either emotional (showing understanding, love and care), or instrumental
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57 42 (providing advice or material/financial help) (18,19). HIV disclosure to loved ones is itself associated
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43 with greater social support (18). Both outcomes are predictors of higher ART adherence, improved
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2 44 clinical outcomes (18,20) and quality of life (18,21), as well as reduced stigma (22).
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5 45 As ART initiation facilitates HIV status disclosure to partners (23,24), which in turn is associated with
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7 46 disclosure to other loved ones (25), it is therefore possible that early ART initiation may accelerate
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9 47 disclosure and possibly social support (18). However, because of the very limited time available
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11 48 before initiating treatment, it may also put greater pressure on PLHIV to promptly disclose their
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13 49 seropositivity, something which could possibly lead to stigma, conflict and domestic violence (3). In
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15 50 addition, early ART initiation in PLHIV with high CD4 counts might enable them to remain
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17 51 asymptomatic, reducing their perceived need to disclose their HIV infection (26), especially in those
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19 52 at risk of experiencing stigma, conflict or domestic violence after disclosure. Evidence for these
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21 53 possible effects of early ART on psychosocial outcomes is still uncertain and they are under-
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23 54 documented (27).
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29 55 Accordingly, this study aimed to explore the effects of early ART initiation on two critical psychosocial
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31 56 outcomes in PLHIV linked to care in a UTT setting with high HIV prevalence. More specifically, it
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33 57 investigated the effect of early ART initiation on HIV disclosure and on social support among
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35 58 asymptomatic PLHIV with CD4 counts >500 cells/mm³ who were linked to HIV care in a trial clinic
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37 59 after home-based HIV testing as part of the UTT ANRS 12249 TasP trial.
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45 61 **MATERIALS AND METHODS**

48 62 **TasP trial design**

51 63 ANRS 12249 TasP is a phase 4, open-label, cluster-randomized trial conducted between March 2012
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53 64 and June 2016 in communities of the Hlabisa subdistrict in rural KwaZulu-Natal, in South Africa,
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55 65 where adult HIV prevalence was estimated at approximately 30% (28). The Hlabisa sub-district covers
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57 66 approximately 1400 km² (29) and had a population of 71,925 as of 2011 (30). The main objective of
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67 the trial was to investigate whether universal HIV testing of all the adult population, followed by
68 referral to dedicated trial clinics for immediate ART initiation (irrespective of immunological status or
69 clinical stage) of all those identified HIV-positive, would reduce HIV incidence in the area. The trial
70 was implemented in 22 geographic clusters (11 control and 11 intervention clusters, randomly
71 allocated), each comprising approximately 1000 adult residents.

72 In all clusters, home-based rapid HIV testing and counselling were offered every six months to all
73 members of eligible households (i.e., residents aged ≥ 16 years). People identified HIV-positive (i.e.,
74 newly diagnosed or reporting a prior HIV-positive test result) were referred (or newly referred for
75 those with a prior HIV-positive test result but not currently linked to HIV care) to the dedicated trial
76 clinic for their cluster, usually located less than 5 km or a 45-minute walk from their home.

77 The trial clinics in the intervention clusters offered ART immediately to all HIV-positive participants,
78 irrespective of CD4 cell count and clinical stage. Instead, in the control cluster clinics, HIV-positive
79 participants were offered ART according to the eligibility criteria set out in the 2013 South African
80 guidelines: (i) CD4 cell count ≤ 350 cells/mm³; (ii) pregnancy; (iii) WHO stage 3 or 4 (31). On 1 January
81 2015, these criteria were revised to include CD4 cell count ≤ 500 cells/mm³, hepatitis B coinfection
82 and having an HIV-negative partner (32). In all the trial clinics, participants on ART (for both the
83 control and intervention arms) had monthly clinical follow-up visits, whereas pre-ART non-eligible
84 participants in the control clusters were provided quarterly clinical follow-up. HIV care (including
85 ART) was also provided by government (i.e., not trial-specific) clinics located in the trial area
86 according to national guidelines. At their request, participants could transfer out from trial clinics to a
87 government clinic, inside or outside the trial area.

88 Clinical data were collected by care providers at baseline (i.e., first trial clinic visit) and then at each
89 follow-up visit using case report forms. In addition, socioeconomic and psychosocial information on
90 HIV disclosure, social support, quality of life and relationship status (having a regular partner,
91 relationship duration, break-ups) was obtained from face-to-face questionnaires administered to

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2 92 participants during their baseline clinic visit and every 6 months thereafter. Further details on the
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4
5 93 trial protocol are available elsewhere (27,33).

6
7 94 The Biomedical Research Ethics Committee (BREC) of the University of KwaZulu-Natal (BFC 104/11)
8
9 95 and the South African Medicines Control Council approved the trial. All participants provided written
10 96 informed consent.

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14 15 16 98 **Study population**

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19 99 For the present study, we first selected participants meeting the following criteria at their baseline
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21 100 clinic visit: not ART-treated, WHO stage 1 or 2, CD4 count >500 cells/mm³, and not pregnant. We
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23 101 chose a fixed CD4 threshold (>500 cells/mm³) irrespective of the date of the baseline clinic visit, in
24
25 102 order to include participants with similar characteristics. Accordingly, no participant was eligible for
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27 103 ART initiation according to South Africa's 2013 and 2015 national guidelines. In the intervention arm,
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29 104 all participants were invited to immediately initiate ART: those who accepted therefore benefitted
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31 105 from early ART. Conversely, in the control arm, ART initiation was offered later in the follow-up, if
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33 106 and when a participant became eligible according to South Africa's 2013 or 2015 guidelines: those
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35 107 who initiated treatment therefore benefitted from delayed ART. Then, for each analysis for the
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37 108 study's two outcomes (HIV disclosure and social support), from the selected trial participants, we
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39 109 excluded those having fewer than two available measures for the study outcome during the 24-
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41 110 month follow-up period. This choice was justified by the fact that we aimed to assess the effect of
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43 111 early ART initiation on the evolution of psychosocial outcomes. Accordingly, two study populations
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45 112 were obtained, one for the HIV disclosure outcome, and one for the social support outcome.

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49 50 114 **Study outcomes**

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115 The two study outcomes were HIV disclosure and social support scores. They were assessed using
116 two questions asked at the baseline clinic visit and every 6 months thereafter in psychosocial
117 questionnaires. The two questions were: “Have you disclosed to anyone that you are HIV-positive?”
118 and “Does anyone provide you with social support to help you cope with your HIV infection?”. The
119 HIV disclosure score (range: 0-5) was computed by attributing one point when HIV status was
120 disclosed to each one of the following categories: (i) regular partner; (ii) family (male relatives,
121 female relatives, children); (iii) friends; (iv) neighbors; (v) other people (employer, traditional healer,
122 educational institution, anyone else). Similarly, the social support score (range: 0-4) was computed
123 by attributing one point when the participant reported receiving social support from each one of the
124 following categories: (i) regular partner; (ii) household members (other than the regular partner, if
125 any); (iii) other family members; (iv) friends and neighbors. Scores were expected to increase over
126 follow-up but to taper off as they reached their highest values.

128 **Explanatory variables**

129 We assessed the effect of three key variables on psychosocial outcomes: i) the trial arm (intervention
130 *versus* control); ii) time since the baseline clinic visit (in years), iii) a time-varying variable entitled
131 ‘having initiated ART’, taking the value 0 as long as the participant had not started ART in a trial clinic,
132 and 1 from the moment (i.e., the follow-up visit) when the participant initiated ART. This variable
133 took into account the exact timing of ART initiation, as a minority of patients did not initiate ART
134 immediately when offered for a variety of reasons, both in the intervention and control arms.

135 Other explanatory variables included the following clinical, socioeconomic and psychosocial data,
136 assessed at the baseline clinic visit and used as fixed variables in the analysis: sex, age, educational
137 level, employment status, newly HIV diagnosed at referral (i.e., not reporting any prior HIV-positive
138 diagnosis during the home-based testing, not registered as a HIV patient in a government clinic, and
139 not currently or previously linked to HIV care in a government clinic), time to linkage to a trial clinic

140 after referral (<1 month, 1 to 6 months, >6 months), and CD4 cell count. In addition, we used another
141 time-varying variable entitled ‘having a regular partner’, to take into account potential changes in
142 relationships over the follow-up period. We also used HIV prevalence in the geographical cluster of
143 residence (<30% or ≥30%) to account for potential effects related to the high prevalence setting.

145 **Statistical analysis**

146 The two study populations’ baseline characteristics were described using numbers (percentages) for
147 categorical variables and the median [interquartile range, IQR] for continuous variables. They were
148 then compared between the two trial arms using the Chi-square and Wilcoxon rank-sum tests for
149 categorical and continuous variables, respectively. Using the same tests, we also compared the
150 characteristics of the two study populations with those of the participants excluded because they
151 had fewer than two measures for the corresponding study outcome.

152 All available values of the two outcomes, measured at baseline and every six months thereafter
153 during the 24-month follow-up period, were included in the analyses. To describe the evolution of
154 the outcomes over follow-up, we compared the medians of each of the two outcome scores between
155 the two trial arms in cross-sectional analyses (i.e. at each 6-month time point during the follow-up
156 period) using the Wilcoxon rank-sum test.

157 Finally, we performed a longitudinal analysis using Poisson mixed-effects models which took into
158 account the correlation between repeated measures, in order to estimate the effect of early ART on
159 HIV disclosure and social support, after adjustment for other explanatory variables. To do this, we
160 built four different models for each outcome: i) in model 1, we introduced the two variables ‘time
161 since baseline clinic visit’ and ‘trial arm’ to investigate, respectively, the evolution of outcomes over
162 time and whether the intervention arm was associated with higher outcome scores; ii) in model 2,
163 we added an interaction between the variables ‘trial arm’ and ‘time since baseline’ to test whether
164 the outcome scores increased faster in the intervention arm than in the control arm; iii) in model 3,

165 we introduced the variable 'having initiated ART' (in addition to the 'trial arm' and 'time since
166 baseline clinic visit') to assess the effect of treatment initiation on the outcomes; iv) in model 4, we
167 added an interaction between the 'trial arm' and 'having initiated ART' variables to investigate the
168 effect of treatment initiation according to the trial arm (early ART in the intervention arm *versus*
169 delayed ART in the control arm). Each model was also adjusted for any explanatory variables
170 significantly associated with the two outcomes.

171 All statistical analyses were conducted using Stata statistical software (version 14.2, StataCorp,
172 College Station, Texas 77845 USA).

173

174 RESULTS

175 *Profiles of two study populations*

176 Among all the HIV-positive participants referred to the trial clinics over the trial period, 3014 visited a
177 trial clinic at least once (Figure 1). Of the latter, 1592 (52%) were not on ART at their baseline clinic
178 visit, including 495 (271 and 224 in the control and intervention arms, respectively) who met the
179 present study's criteria (i.e., CD4 counts >500 cells/mm³, WHO stage 1 or 2, and not pregnant). Of
180 these pre-selected participants, we excluded 23 as their psychosocial questionnaires at baseline clinic
181 visit were either unavailable or incomplete, leaving 472 potential participants. For the analysis on HIV
182 disclosure, 290 of this group were secondarily excluded as they did not have two available measures
183 for the HIV disclosure score. For the social support analysis, 320 of the 472 were secondarily
184 excluded as they did not have two measures for the social support score. The two study populations
185 therefore included 182 trial participants in the HIV disclosure analysis and 152 in the social support
186 analysis. All those in the latter analysis were also included in the HIV disclosure analysis.

187 Comparison of the two study populations' characteristics with those of trial participants who were
188 excluded because they did not have two available measures for the study outcomes, suggested they
189 had similar socioeconomic profiles (Appendix 1 and 2). However, a higher proportion of excluded

190 participants were newly HIV diagnosed (19% *versus* 8%, $p=0.001$ for the study population on HIV
1 disclosure; 18% *versus* 9%, $p=0.018$ for the study population on social support) and had only been
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5 192 linked to care more than six months after referral (33% *versus* 13%, $p<0.001$ for the study population
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7 193 on HIV disclosure; 31% *versus* 13%, $p<0.001$ for the study population on social support), while a
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9 194 lower proportion had previously received HIV care in government clinics (35% *versus* 52%, $p=0.001$
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11 195 for the study population on HIV disclosure; 39% *versus* 49%, $p=0.048$ for the study population on
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13 196 social support). HIV disclosure and social support scores were not significantly different at baseline
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15 197 between the two study populations and excluded participants.
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19 198 Characteristics of the 182 trial participants in the HIV disclosure analysis are presented in Table 1,
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22 199 overall and by arm. Most were women (84%), and median age was 32 [interquartile range (IQR): 25-
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24 200 48] years. At baseline, most (79%) reported having a regular partner, and 82% resided in a
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26 201 geographical cluster where HIV prevalence was $>30\%$. Overall, socioeconomic status was low, with
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28 202 80% of participants being unemployed and almost half (46%) having primary school education or
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30 203 less. Approximately half (52%) were currently receiving or had already received HIV care in
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32 204 government clinics, and only 8% were newly HIV diagnosed. Almost two-thirds (61%) of the
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34 205 participants were linked to HIV care in a trial clinic within one month of referral. No significant
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36 206 difference was observed at baseline between both trial arms, except for the proportion of
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38 207 participants residing in a geographical cluster where HIV prevalence was $\geq 30\%$ (90% in the
39
40 208 intervention arm *versus* 75% in the control arm, $p=0.010$). Median [IQR] time since baseline visit in a
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42 209 trial clinic was 13.2 [7.0-18.5] months. The proportions of participants having initiated ART at various
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44 210 time points over follow-up were as follows: one month after the baseline clinic visit, 8% had initiated
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46 211 ART in the control arm *versus* 48% in the intervention arm; these figures were 15% *versus* 92% after 3
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48 212 months, 22% *versus* 97% after 6 months, and 29% *versus* 98% after 12 months, respectively.
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55 213 Characteristics of the 152 study participants included in the social support analysis were similar to
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57 214 those for the HIV disclosure analysis (Appendix 3).
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Evolution of study outcomes (HIV disclosure and social support) over time

At baseline, the median [IQR] HIV disclosure score in the control and intervention arms was 1 [1-2] and 2 [1-2] ($p=0.72$), respectively, while the median social support score was 2 [1-3] and 1 [1-2] ($p=0.12$), respectively (Figure 2). Both outcomes improved over time: 24 months after baseline, the median [IQR] HIV disclosure score was 4 [3-4] and 4 [3-5], respectively, while the median [IQR] social support score was 2 [1-3] and 3 [2-4] ($p=0.47$), respectively ($p=0.25$).

In addition, Figure 3, which illustrates the distribution of both outcome scores (according to visit and trial arm), shows that the proportions of participants with an HIV disclosure score ≥ 3 increased in both arms over follow-up and were systematically higher in the intervention arm at all time points (i.e., M0 to M24). The largest differences between trial arms were observed 6 and 12 months after baseline, while differences tended to decrease after 18 months of follow-up. The proportions of participants with a social support score ≥ 3 also increased in both arms over follow-up but tended to increase faster in the intervention arm. More specifically, although a slightly higher proportion of participants had a score ≥ 3 in the control arm than in the intervention arm between baseline and 12 months, the proportions of participants with a score ≥ 3 were similar in both arms at 18 months, and after 24 months, they were slightly higher in the intervention arm.

The effects of time since baseline, trial arm and having initiated ART on both study outcomes

Results of the Poisson mixed effects models are presented in Table 2. Model 1 indicates a significant increase over time for both HIV disclosure and social support scores (adjusted incidence rate ratio (IRR), 95% confidence interval (CI): 1.46 [1.35; 1.58], $p<0.001$, and 1.33 [1.21; 1.46], $p<0.001$, for each year of follow-up, respectively). In addition, model 1 shows that participants in the intervention arm disclosed to more categories of people than participants in the control arm (adjusted IRR [95% CI]: 1.26 [1.12; 1.41], $p<0.001$). No difference was observed between arms for the social support score

240 (1.03 [0.90; 1.17], $p=0.690$). In model 2, the evolution over time of the HIV disclosure score was
241 similar in both trial arms (1.02 [0.87; 1.19] for the interaction term between time since baseline and
242 arm, $p=0.839$). Conversely, a faster increase over time was observed for the social support score in
243 the intervention arm (1.22 [1.02; 1.46] for the interaction term between time since baseline (in
244 years) and arm, $p=0.032$). In model 3, having initiated ART was associated with higher scores (1.50
245 [1.28; 1.75], $p<0.001$, for HIV disclosure, and 1.34 [1.12; 1.61], $p=0.002$, for social support). The
246 principal effect of the intervention arm on the HIV disclosure score was no longer significant (1.05
247 [0.92; 1.20], $p=0.467$) after adjustment for ART initiation. Model 4 showed that having initiated ART
248 had a similar effect on the HIV disclosure score in both arms (1.15 [0.89; 1.48] for the interaction
249 term between ART initiation and trial arm, $p=0.288$). However, it had a stronger effect on the social
250 support score in the intervention arm (1.50 [1.12; 2.01] for the interaction term between ART
251 initiation and arm, $p=0.006$).

252 DISCUSSION

253 Our study highlighted two key findings. First, HIV disclosure and social support increased over time in
254 both trial arms, independently of ART initiation. This may be explained by the fact that PLHIV are
255 willing to disclose to more people over time as they come to accept their status and overcome
256 feelings of shame (34). Wider disclosure translates into more opportunities to receive HIV-related
257 social support, and so the latter increases over time. Second, early ART initiation had no detrimental
258 effect on the two study outcomes. On the contrary, it was associated with accelerated HIV disclosure
259 and increased social support. More specifically, HIV disclosure was significantly higher in the
260 intervention arm and was strongly correlated with ART initiation, as demonstrated by the significant
261 effect of the 'having initiated ART' variable. In addition, when controlling for the latter, the effect of
262 the trial arm variable was no longer significant, suggesting that early ART initiation offered in the
263 intervention arm did not affect disclosure per se, but modified its timing: the sooner ART was
264 initiated, the faster HIV disclosure occurred. With regard to social support, we observed that it

265 increased significantly faster over time in the intervention arm. This may be explained by a 'catch-up'
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2 266 phenomenon, as the level of social support reported by participants tended to be lower at baseline in
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4 267 the intervention arm than in the control arm. However, given the relatively short follow-up period
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7 268 (median time since baseline was approximately one year), we were unable to observe whether social
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9 269 support would continue to increase in the intervention arm while remaining stable in the control
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11 270 arm. In addition, PLHIV who initiated ART benefited from greater social support, but only in the
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13
14 271 intervention arm, as indicated by the interaction term between 'having initiated ART' and trial arm,
15
16 272 which was significantly associated with social support, while the main effect of 'having initiated ART'
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18 273 was no longer significant. This suggests that in a UTT setting, early ART initiation could result in
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21 274 greater social support than delayed ART.

24 275 The beneficial indirect (i.e., non-clinical) effects of ART initiation on psychosocial outcomes observed
25
26 276 in our study are consistent with the literature (23,35,36). As suggested by previous research, there
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28
29 277 are several possible reasons to explain why ART initiation encourages PLHIV to disclose their HIV-
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31 278 positive status, such as the desire to be open about taking daily medication or going to the clinic
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33
34 279 (37,38) or a greater need for adherence support (23). Counselling alongside ART initiation may be
35
36 280 another reason for increased disclosure after ART initiation. Furthermore, information about the role
37
38 281 of ART in maintaining good health and eliminating transmission risk may encourage PLHIV to disclose
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40
41 282 their status to their partner, which is a first step towards wider disclosure. Finally, reassurance
42
43 283 provided by caregivers during counselling sessions alongside ART initiation could also reduce
44
45 284 internalized stigma and fear of negative disclosure-related reactions, making patients more
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47
48 285 comfortable about disclosing their status with their partners. Our findings therefore suggest that
49
50 286 delayed treatment initiation in turn delays the possibility of indirect beneficial effects of ART
51
52 287 initiation on HIV disclosure.

56 288 According to the literature, the positive effect of ART initiation on social support may be partly due to
57
58 289 the observed increase in disclosure following ART initiation, the former being at least partially

290 dependent on the latter. Furthermore, the numerous constraints associated with lifelong ART
1
2 291 treatment (e.g. transportation for check-ups, treatment reminders, etc.) provide PLHIV's family
3
4 292 members the opportunity to offer greater material, financial and moral support to their loved one
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6
7 293 once he/she has initiated treatment (20,38). In our study, the indirect beneficial effect of ART
8
9 294 initiation on social support was observed only in the intervention arm. In Western settings, previous
10
11 295 research suggested that HIV disease progression had negative effects on social networks and
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13 296 support, possibly because of changes in affect and cognition, or psychiatric disorders inducing social
14
15 297 withdrawal or social selectivity (39,40). Although all the PLHIV in our study had high CD4 counts at
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18 298 baseline, our results may suggest that family members and friends may be more likely to provide
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21 299 social support to PLHIV who initiate ART early than when treatment is delayed. This may be
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23 300 explained by the more positive perception of early ART initiation in communities strongly affected by
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26 301 HIV (41).

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29 302 Our findings showing the psychosocial benefits of early ART initiation are consistent with the results
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31 303 of another early ART initiation clinical trial in West Africa which highlighted that early ART had no
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33 304 adverse social consequences on either conjugal relationships or HIV-related discrimination (42).
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36 305 Similarly, in another study conducted within the ANRS 12249 TasP trial, the authors found no
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38 306 increase in sexual behavior risks (43). The beneficial effects of early ART on the two study outcomes
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41 307 we explored (HIV disclosure and social support) may also have positive synergies with other
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43 308 outcomes which are key factors for the treatment success. This is especially the case with ART
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45 309 adherence, as suggested by another study conducted using data from the ANRS 12234 TasP trial,
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48 310 which showed that higher CD4 counts at ART initiation were not associated with sub-optimal ART
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50 311 adherence in the first 12 months (44). Besides individual benefits, earlier HIV disclosure and greater
51
52 312 social support may also have potential benefits at the community level. Disclosure to partners could
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55 313 help to reduce HIV transmission through decreased risky sexual behaviors, increased condom
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57 314 negotiation and use (45–49), higher partner HIV testing (24), and better ART adherence (50). As part
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60 315 of a UTT strategy, the potential benefits of HIV disclosure following early ART initiation may also

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316 contribute to better control HIV epidemics nationwide. Moreover, in the context of South Africa,
317 where HIV is highly endemic in the general population, and not limited to excluded minorities, we
318 found that social support increased as HIV disclosure increased. This suggests a positive social impact
319 of HIV disclosure, which is consistent with previously published studies in South Africa describing
320 greater social support from relatives following HIV disclosure (49,51,52).

321 **Strengths and limitations of the study**

322 Our study brings added evidence for the positive effects of earlier ART initiation on two critical
323 psychosocial outcomes in a UTT setting: HIV disclosure and social support. To provide a better
324 understanding of these effects, we disentangled the respective effects of time, trial arm and ART
325 initiation. The two-arm cluster-randomized design of the ANRS 12249 TasP allowed us to examine
326 the causal effect of early ART on these outcomes.

327 Our study has limitations. Firstly, we excluded a large number of trial participants because they had
328 fewer than two measures for each of the study outcomes (i.e., 290/495 and 320/495 for the HIV
329 disclosure and social support analyses, respectively). Most of these excluded participants were
330 included in the last year of the trial (in 2016) which explains why they did not have two measures for
331 each outcome. Their characteristics were overall similar to those of the two study populations,
332 except they were more likely to be newly HIV diagnosed and to have experienced a longer delay
333 before linkage to care. Furthermore, their HIV disclosure and psychosocial support scores were not
334 significantly different from those of the two study populations at baseline. Although we cannot
335 completely exclude the risk of selection bias, these data suggest that if the trial's follow-up period
336 had been longer - enabling us to include those individuals - our present results would probably have
337 been similar.

338 Secondly, the methodology used to measure disclosure and social support had several drawbacks.
339 For a start, the maximum possible scores for disclosure and social support were automatically lower
340 for participants with no regular partner, as one point was awarded for those disclosing to their

341 regular partners. As the relatively small size of both study populations prevented us from performing
1
2 342 a stratified analysis to distinguish those with from those without a regular partner, we addressed this
3
4 343 limitation by adjusting all models for the variable ‘having a regular partner’ which was assessed at
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6
7 344 each time point. Moreover, the HIV disclosure score did not measure involuntary HIV disclosure by a
8
9 345 third person, despite the fact that this is associated with more frequent adverse social consequences
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11 346 (53). However, the parallel increase in both HIV disclosure and social support scores following ART
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13 347 initiation suggested that negative social implications of HIV disclosure were limited. In addition, we
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15 348 did not ask PLHIV why they disclosed their HIV status. Neither did we ask them in what specific ways
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17 349 they received social support to help them cope with the disease. Such information might have helped
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19 350 us to understand in greater detail the mechanisms underlying the effects of early ART initiation
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21 351 observed in this study.

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26 352 Thirdly, given the limited study population size, we were not able to conduct a stratified analysis
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28 353 according to gender. Such an analysis would have been valuable, given that current evidence -
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30 354 despite being mixed – tends to suggest that patterns of HIV disclosure and seeking social support
31
32 355 may be gender dependent (45).

36 356 **Conclusion**

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40 357 The implementation of a universal test and treat strategy raises questions about the psychosocial
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42 358 implications of early ART initiation. Our findings, together with those from other recent studies, are
43
44 359 reassuring as they suggest that early ART does not have detrimental effects on HIV disclosure or on
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46 360 social support. On the contrary, it tends to improve these two key outcomes. They also suggest that
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48 361 more time may be needed to see the beneficial effects of early ART on social support than on
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50 362 disclosure. This is to be expected, since social support is at least partially dependent on disclosure.
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52 363 Our findings should further encourage countries to implement UTT strategies.
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364	Figure 1- Flowchart of the study population
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2	Figure 2 – Box plots of HIV disclosure and social support outcome scores per visit and per trial arm,
3	ANRS 12249 TasP trial
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5	Figure 2a: Box plots of the HIV disclosure score per visit and per trial arm
6	
7	Figure 2b – Box plots of the social support score per visit and per trial arm
8	
9	Figure 3- Distribution (per visit and trial arm) of the HIV disclosure and social support outcome
10	scores, ANRS 12249 TasP trial
11	
12	Figure 3a- Distribution of the HIV disclosure score per visit and per trial arm
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14	Figure 3b- Distribution of the social support score per visit and per trial arm
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8

9 403 **References**

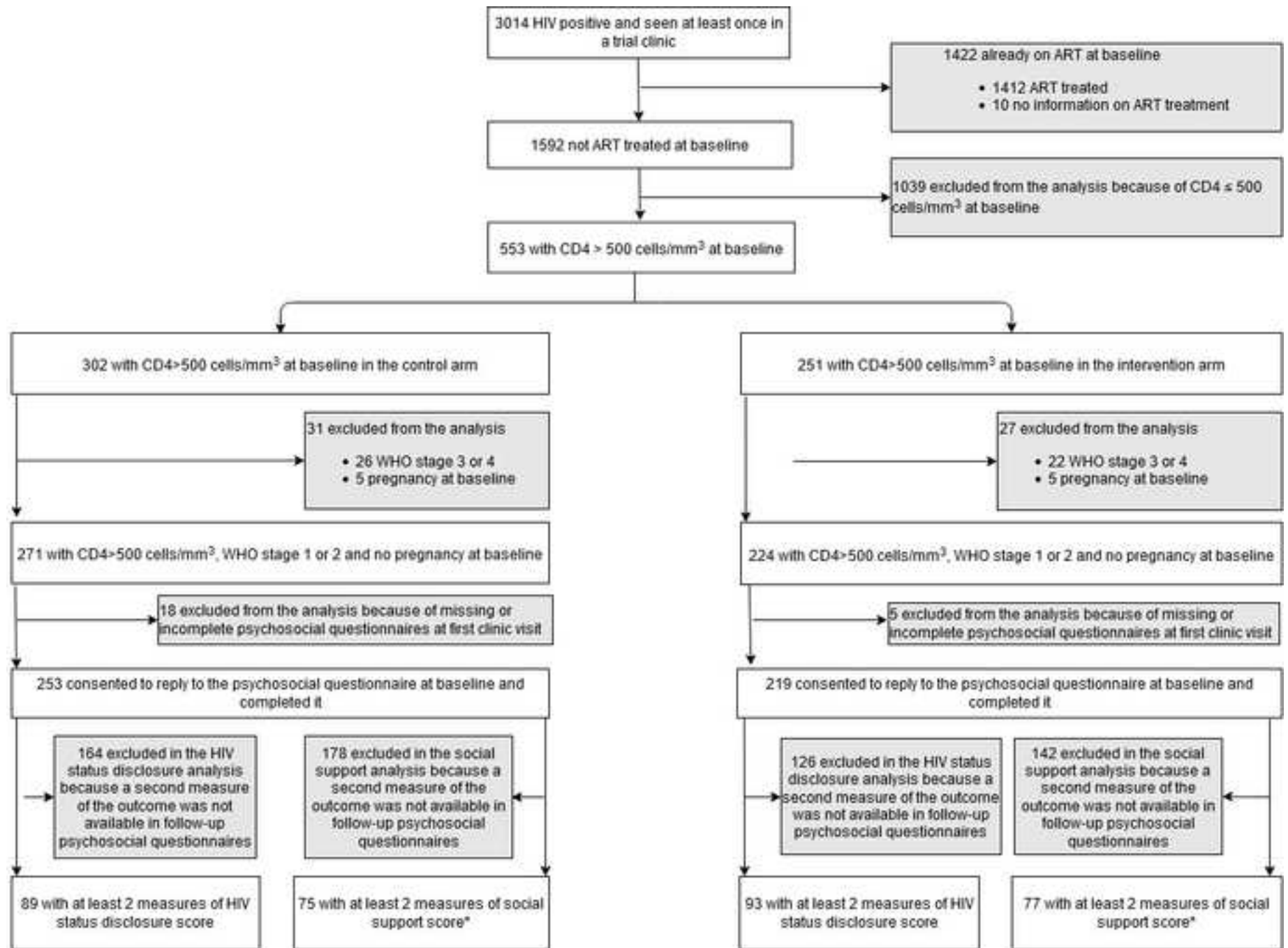
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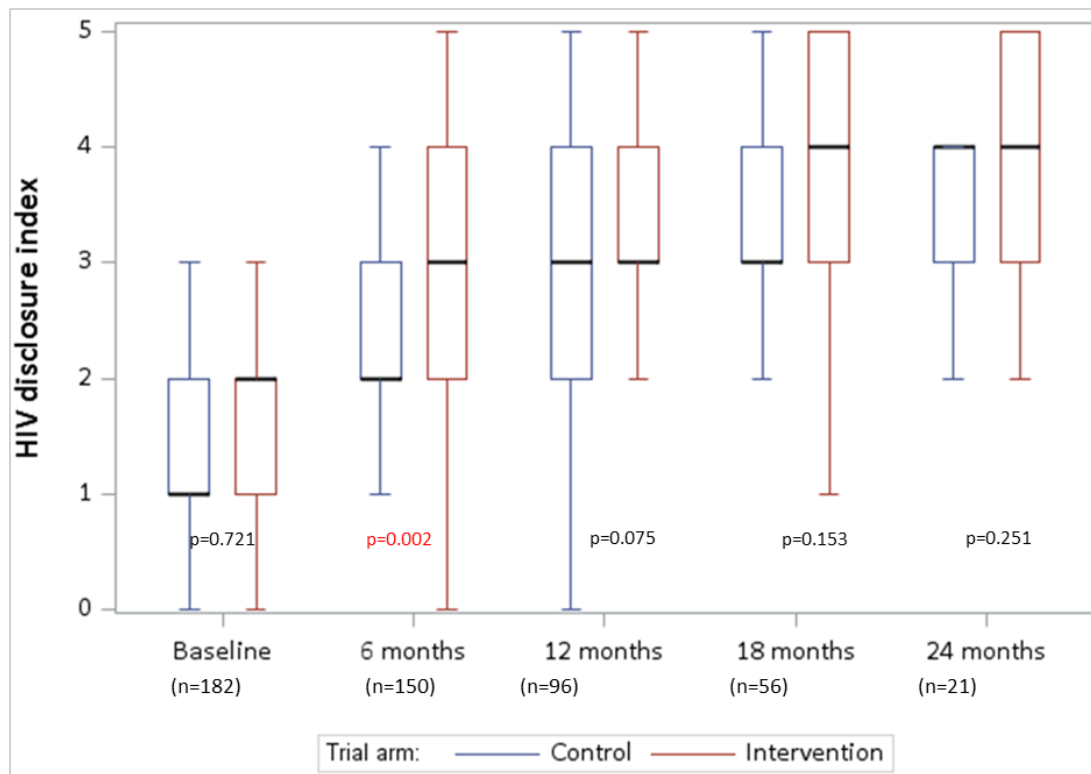
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*. All participants included in the social support score analysis (ie. 75 in the control arm and 77 in the intervention arm) were among those included in the HIV status disclosure score analysis.

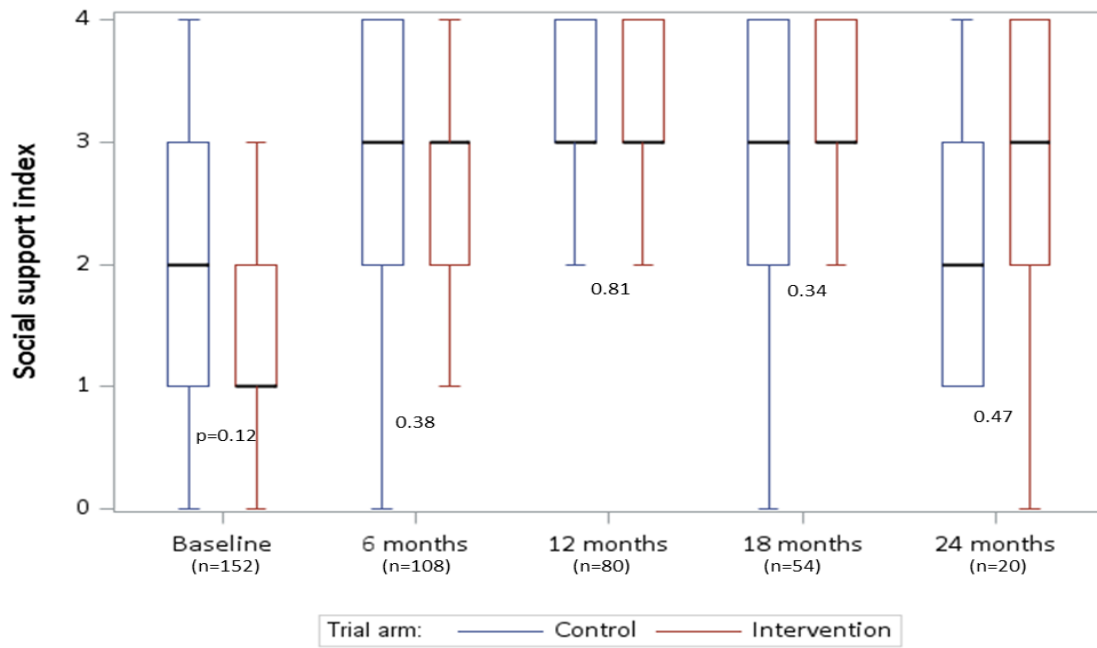
Figure 1 – Box plots of HIV disclosure and social support outcome scores per visit and per trial arm, ANRS 12249 TasP trial

Figure 2a: Box plots of the HIV disclosure score per visit and per trial arm



p-value: Wilcoxon rank-sum test

Figure 2b – Box plots of the social support score per visit and per trial arm



p-value: Wilcoxon rank-sum test

Figure 3- Distribution (per visit and trial arm) of the HIV disclosure and social support outcome scores, ANRS 12249 TasP trial

Figure 3a- Distribution of the HIV disclosure score per visit and per trial arm

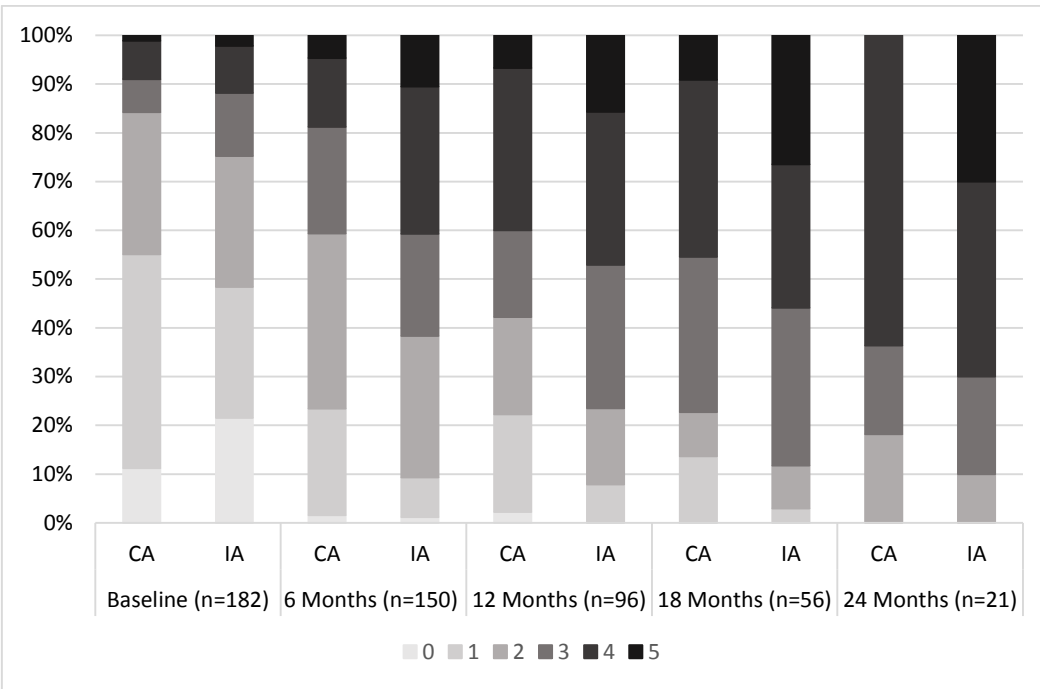
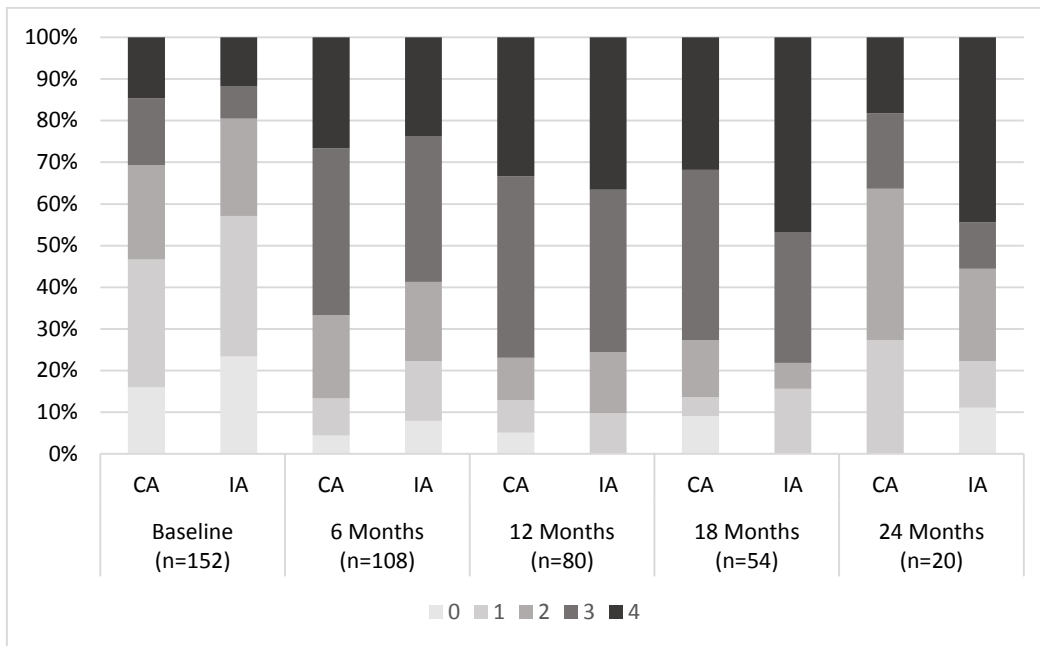


Figure 3b- Distribution of the social support score per visit and per trial arm



Abbreviations: CA: Control arm ; IA: Intervention arm.

Table 1 - Characteristics of the study population with regard to the HIV disclosure outcome (n=182), ANRS 12249 TasP trial

	Control arm (n=89)	Intervention arm (n=93)	Total (n=182)	P- value ^a
<i>Sociodemographic and economic characteristics at baseline (i.e. first clinic visit)</i>				
Female gender, n (%)	76 (85%)	76 (82%)	152(84%)	0.504
Age (in years), median [IQR]	34 [25-49]	32 [26-46]	32 [25-48]	0.279
Having a regular partner, n (%)				
Yes	67 (75%)	77 (83%)	144 (79%)	0.212
HIV prevalence in the geographical cluster of residence, n (%)				
≥30%	80 (90%)	70 (75%)	150 (82%)	0.010
Educational level, n (%)				
Primary or less	44 (49%)	40 (43%)	84 (46%)	0.263
Some secondary	30 (34%)	28 (30%)	58 (32%)	
At least completed secondary	15 (17%)	25 (27%)	40 (22%)	
Employment status[§], n (%)				
Employed	10 (11%)	11 (12%)	21 (12%)	0.591
Student	5 (6%)	9 (10%)	14 (8%)	
Inactive	73 (83%)	73 (78%)	146 (80%)	
<i>Clinical characteristics</i>				
Having received HIV care in government clinics (currently or previously), n (%)				
Yes	51 (57%)	43 (46%)	94 (52%)	0.135
Newly diagnosed at referral, n (%)				
Yes	7 (8%)	7 (8%)	14 (8%)	0.932
CD4 cell count/mm³ at baseline, median [IQR]	674 [581-840]	658 [551-784]	660 [568-816]	0.347
Time to linkage to a trial clinic after referral, n (%)				
0 - 1 month	53 (60%)	58 (62%)	111 (61%)	0.513
1 month – 6 months	26 (29%)	21 (23%)	47 (26%)	
More than 6 months	10 (11%)	14 (15%)	24 (13%)	
Time since baseline (in years), median [IQR]	13.2 [7.6 –19.2]	13.7 [6.7 – 19.4]	13.3 [7.0 – 19.4]	0.725
Followed for at least 6 months, n (%)	89 (100%)	93 (100%)	182 (100%)	
Followed for at least 12 months, n (%)	55 (62%)	54 (58%)	109 (60%)	0.607
Followed for at least 18 months, n (%)	27 (30%)	34 (37%)	61 (34%)	0.374
Followed for at least 24 months, n (%)	11 (12%)	10 (11%)	21 (12%)	0.734
Having initiated ART in a trial clinic, n (%)				
At the 6 month-visit	14 (22%)	83 (97%)	97 (65%)	0.000
At the 12 month-visit	13 (29%)	50 (98%)	63 (66%)	0.000
At the 18 month-visit	13 (59%)	33 (97%)	46 (82%)	0.000
At the 24 month-visit	9 (82%)	10 (100%)	19 (90%)	0.476

Abbreviations: IQR=interquartile range; ART=Antiretroviral treatment.

^a Chi-square test for categorical variables, and Wilcoxon rank-sum test for continuous variables.

[§]One missing value (n=181).

Table 1. Factors associated with HIV status disclosure and social support, Poisson mixed effects models, univariable and multivariable analyses, ANRS 12249 TasP trial

	HIV disclosure score (n=182)					Social support score (n=152)				
	Univariable analysis IRR (P-value) [95% CI]	Multivariable analyses adjusted IRR (P-value) [95% CI]				Univariable analysis IRR (P-value) [95% CI]	Multivariable analyses adjusted IRR (P-value) [95% CI]			
		Model 1	Model 2	Model 3	Model 4		Model 1	Model 2	Model 3	Model 4
Time since baseline clinic visit (in years)	1.46 (<0.001) [1.35 ; 1.58]	1.46 (<0.001) [1.35 ; 1.58]	1.45 (<0.001) [1.29 ; 1.62]	1.24 (<0.001) [1.12 ; 1.38]	1.24 (<0.001) [1.12 ; 1.37]	1.33 (<0.001) [1.21 ; 1.45]	1.33 (<0.001) [1.21 ; 1.46]	1.21 (0.004) [1.06 ; 1.37]	1.17 (0.011) [1.03 ; 1.32]	1.16 (0.019) [1.02 ; 1.31]
Trial arm										
Control ^a	1	1	1	1	1	1	1	1	1	1
Intervention	1.20 (0.006) [1.05 ; 1.36]	1.26 (<0.001) [1.12 ; 1.41]	1.24 (0.015) [1.04 ; 1.48]	1.05 (0.467) [0.92 ; 1.20]	0.98 (0.798) [0.80 ; 1.18]	0.98 (0.708) [0.86 ; 1.11]	1.03 (0.690) [0.90 ; 1.17]	0.87 (0.176) [0.72 ; 1.06]	0.91 (0.198) [0.78 ; 1.05]	0.73 (0.005)** [0.58 ; 0.91]
Interaction: Trial arm x Time since baseline (in years)			1.02 (0.839) [0.87 ; 1.19]					1.22 (0.032) [1.02 ; 1.46]		
Initiated ART										
No ^a	1			1	1	1		1	1	
Yes	1.80 (<0.001) [1.61 ; 2.02]			1.50 (<0.001) [1.28 ; 1.75]	1.40 (0.001) [1.14 ; 1.71]	1.45 (<0.001) [1.28 ; 1.65]		1.34 (0.002) [1.12 ; 1.61]	1.11 (0.396) [0.88 ; 1.40]	
Interaction: Trial arm x having initiated ART in a trial clinic					1.15 (0.288) [0.89 ; 1.48]					1.50 (0.006) [1.12 ; 2.01]
Gender										
Male ^a	1					1				
Female	1.08 (0.400) [0.90 ; 1.30]					1.19 (0.078) [0.98 ; 1.43]				
Age (in years)										
<30 ^a	1					1				
[30-45[1.10 (0.246) [0.94 ; 1.28]					1.00 (0.963) [0.86 ; 1.17]				
[45 and over)	1.05 (0.536) [0.90 ; 1.23]					0.95 (0.505) [0.82 ; 1.11]				
Having a regular partner										
No ^a	1	1	1	1	1	1	1	1	1	1
Yes	1.41 (<0.001) [1.20 ; 1.65]	1.38 (<0.001) [1.18 ; 1.60]	1.38 (<0.001) [1.18 ; 1.60]	1.36 (<0.001) [1.17 ; 1.58]	1.36 (<0.001) [1.17 ; 1.58]	1.52 (<0.001) [1.28 ; 1.82]	1.51 (<0.001) [1.27 ; 1.80]	1.52 (<0.001) [1.28 ; 1.82]	1.49 (<0.001) [1.25 ; 1.78]	1.51 (<0.001) [1.27 ; 1.80]
HIV prevalence in the cluster of residence										
<30% ^a	1	1	1	1	1	1	1	1	1	1
≥30%	1.06 (0.457) [0.90 ; 1.25]	1.27 (0.001) [1.10 ; 1.46]	1.27 (0.001) [1.10 ; 1.46]	1.27 (0.001) [1.10 ; 1.46]	1.27 (0.001) [1.10 ; 1.46]	1.17 (0.061) [0.99 ; 1.37]	1.30 (0.002) [1.10 ; 1.53]	1.30 (0.002) [1.10 ; 1.53]	1.30 (0.002) [1.10 ; 1.53]	1.29 (0.002) [1.10 ; 1.52]

Table 2 continued

	HIV status disclosure score (n=182)					Social support score (n=152)				
	Univariable analysis IRR (P-value) [95% CI]	Multivariable analyses adjusted IRR (P-value) [95% CI]				Univariable analysis IRR (P-value) [95% CI]	Multivariable analyses adjusted IRR (P-value) [95% CI]			
		Model 1	Model 2	Model 3	Model 4		Model 1	Model 2	Model 3	Model 4
Educational level										
Primary or less ^a	1					1				
Some secondary	0.94 (0.375) [0.81 ; 1.08]					0.97 (0.638) [0.83 ; 1.12]				
At least completed secondary	0.96 (0.657) [0.82 ; 1.14]					0.96 (0.650) [0.81 ; 1.14]				
Employment status[#]										
Inactive ^a	1					1				
Employed	0.92 (0.425) [0.75 ; 1.13]					0.86 (0.183) [0.69 ; 1.07]				
Student	0.89 (0.361) [0.70 ; 1.14]					0.93 (0.543) [0.74 ; 1.17]				
Having ever received HIV care in government clinics										
No ^a	1	1	1	1	1	1	1	1	1	1
Yes	1.29 (<0.001) [1.13 ; 1.46]	1.26 (<0.001) [1.12 ; 1.41]	1.26 (<0.001) [1.12 ; 1.41]	1.24 (<0.001) [1.11 ; 1.39]	1.25 (<0.001) [1.11 ; 1.40]	1.23 (0.001) [1.09 ; 1.40]	1.20 (0.004) [1.06 ; 1.37]	1.20 (0.005) [1.06 ; 1.37]	1.19 (0.007) [1.05 ; 1.36]	1.20 (0.005) [1.06 ; 1.37]
Newly diagnosed at referral										
No ^a	1					1				
Yes	0.66 (0.004) [0.49 ; 0.88]					0.64 (0.002) [0.48 ; 0.85]				
Time to link to a trial clinic after referral										
0 – 1 month ^a	1					1				
1 months - 6 months	1.01 (0.907) [0.87 ; 1.17]					0.96 (0.635) [0.83 ; 1.12]				
More than 6 months	0.96 (0.674) [0.79 ; 1.17]					0.96 (0.719) [0.79 ; 1.17]				

Abbreviations: IRR: Incidence Rate Ratio; CI: Confidence Interval; ART: Antiretroviral treatment.

^a: Reference category

[#]: One missing value (n=181).

Appendix 1 – Baseline characteristics regarding HIV disclosure for the study population on (n=182) and for participants excluded because only one measure of this outcome was available for the whole study period (n=290), ANRS 12249 TasP trial

Covariates	Study population (n=182)	Excluded participants (n=290)	Total (n=472)	P-value ^a
<i>Sociodemographic and economic characteristics</i>				
Female gender, n (%)	152(84%)	240 (83%)	392 (83%)	0.831
Age (in years), median [IQR]*	32 [25-48]	30 [24-44]	31 [25-45]	0.155
Having a regular partner, n (%)				
Yes	144 (79%)	235 (81%)	379 (80%)	0.611
HIV prevalence in the geographical cluster of residence, n (%)				
≥30%	150 (82%)	211 (73%)	361 (77%)	0.016
Educational level [#] , n (%)				
Primary or less	84 (46%)	117 (41%)	201 (43%)	0.162
Some secondary	58 (32%)	116 (41%)	174 (37%)	
At least completed secondary	40 (22%)	53 (19%)	93 (20%)	
Employment status [§] , n (%)				
Employed	21 (12%)	38 (13%)	59 (13%)	0.788
Student	14 (8%)	19 (7%)	33 (7%)	
Inactive	146 (81%)	224 (80%)	370 (80%)	
<i>Clinical characteristics</i>				
Having received HIV care in government clinics (currently or previously), n (%)				
Yes	94 (52%)	105 (35%)	199 (42%)	0.001
Newly diagnosed, n (%)				
Yes	14 (8%)	56 (19%)	70 (15%)	0.001
CD4 cell count/mm ³ , median [IQR]	660 [568-816]	665 [569-801]	662 [569-807]	0.566
Time to linkage to a trial clinic after referral, n (%)				0.000
0 - 1 month	111 (61%)	143 (49%)	254 (54%)	
1 month – 6 months	47 (26%)	51 (18%)	98 (21%)	
More than 6 months	24 (13%)	96 (33%)	120 (25%)	
HIV disclosure score, median [IQR]	1 [1-2]	2 [1-2]	1 [1-2]	0.915

Abbreviations: IQR=interquartile range; ART=Antiretroviral treatment.

^a Chi-square test for categorical variables, and Wilcoxon rank-sum test for continuous variables.

*Three missing values (n=469). [#]Four missing values (n=468). [§]Ten missing values (n=462).

Appendix 2 – Baseline characteristics regarding social support for the study population (n=152) and of for participants excluded because only one measure for this outcome was available for the whole study period (n=320), ANRS 12249 TasP trial

	Study population (n=152)	Excluded participants (n=320)	Total (n=472)	P-value ^a
<i>Sociodemographic and economic characteristics</i>				
Female gender, n (%)	128 (84%)	264 (83%)	392 (83%)	0.643
Age (in years), median [IQR]*	32 [25-48]	30 [24-44]	31 [25-45]	0.340
Having a regular partner, n (%)				
Yes	120 (79%)	259 (81%)	379 (80%)	0.612
HIV prevalence in the geographical cluster of residence, n (%)				
≥30%	124 (82%)	237 (74%)	362 (77%)	0.072
Educational level[#], n (%)				
Primary or less	70 (46%)	131 (41%)	201 (43%)	0.211
Some secondary	48 (32%)	126 (40%)	174 (37%)	
At least completed secondary	34 (22%)	59 (19%)	93 (20%)	
Employment status[§], n (%)				
Employed	15 (10%)	44 (14%)	59 (13%)	0.343
Student	13 (9%)	20 (6%)	33 (7%)	
Inactive	123 (81%)	247 (80%)	371 (80%)	
<i>Clinical characteristics</i>				
Having received HIV care in government clinics (currently or previously), n (%)				
Yes	74 (49%)	125 (39%)	199 (42%)	0.048
Newly diagnosed at referral, n (%)				
Yes	14 (9%)	56 (18%)	70 (15%)	0.018
CD4 cell count/mm³, median [IQR]	661 [572-824]	663 [569-796]	662 [569-807]	0.938
Time to linkage to a trial clinic after referral, n (%)				0.000
0 - 1 month	94 (62%)	160 (50%)	254 (54%)	
1 month – 6 months	38 (25%)	60 (19%)	98 (21%)	
More than 6 months	20 (13%)	100 (31%)	120 (25%)	
Social support score, median [IQR]	1 [1-2.5]	1 [0-2]	1 [1-2]	0.265

Abbreviations: IQR=interquartile range; ART=Antiretroviral treatment.

^a Chi-square test for categorical variables, and Wilcoxon rank-sum test for continuous variables.

*Three missing values (n=469). [#]Four missing values (n=468). [§]Ten missing values (n=462).

Appendix 3 -Characteristics of the study population regarding the outcome social support (n=152), ANRS 12249 TasP trial

	Control (n=75)	Intervention (n=77)	Total (n=152)	P-value ^a
<i>Sociodemographic and economic characteristics at baseline (i.e. first clinic visit)</i>				
Female gender, n (%)	63 (84%)	65 (84%)	128 (84%)	0.944
Age (in years), median [IQR]	32 [24-48]	32 [25-47]	32 [25-48]	0.535
Having a regular partner, n (%)				
Yes	56 (75%)	64 (83%)	120 (79%)	0.201
HIV prevalence in the geographical cluster of residence, n (%)				
≥30%	68 (91%)	56 (73%)	124 (82%)	0.004
Educational level, n (%)				
Primary or less	36 (48%)	34 (44%)	70 (46%)	0.556
Some secondary	25 (33%)	23 (30%)	48 (32%)	
At least completed secondary	14 (19%)	20 (26%)	34 (22%)	
Employment status ⁵ , n (%)				
Employed	8 (11%)	7 (9%)	15 (10%)	0.379
Student	4 (5%)	9 (12%)	13 (9%)	
Inactive	62 (84%)	61 (79%)	123 (81%)	
<i>Clinical characteristics</i>				
Having received HIV care in government clinics (currently or previously), n (%)				
Yes	41 (55%)	33 (43%)	74 (49%)	0.145
Newly diagnosed at referral, n(%)				
Yes	7 (9%)	7 (9%)	14 (9%)	0.959
CD4 cell count/mm ³ at baseline, median [IQR]	687 [581-840]	655 [551-815]	661 [572-824]	0.490
Time to linkage to a trial clinic after referral, n (%)				0.851
0 - 1 month	46 (61%)	48 (62%)	94 (62%)	
1 month – 6 months	20 (27%)	18 (23%)	38 (25%)	
More than 6 months	9 (12%)	11 (14%)	20 (13%)	
Time since baseline (in years), median [IQR]	13.9 [7.3 – 19.8]	15.1 [8.3 – 19.8]	14.1 [7.8 – 19.8]	0.804
Followed for at least 6 months, n(%)	75 (100%)	77 (100%)	152 (100%)	
Followed for at least 12 months, n(%)	49 (65%)	50 (65%)	99 (65%)	0.959
Followed for at least 18 months, n(%)	27 (36%)	32 (42%)	59 (39%)	0.482
Followed for at least 24 months, n(%)	11 (15%)	9 (12%)	20 (13%)	0.587
Having initiated ART in a trial clinic after baseline, n (%)				
At the 6 month-visit	9 (20%)	62 (98%)	71 (66%)	0.000

At the 12 month-visit	12 (31%)	40 (98%)	52 (65%)	0.000
At the 18 month-visit	13 (59%)	31 (97%)	44 (81%)	0.001
At the 24 month-visit	9 (82%)	9 (100%)	18 (90%)	0.479

Abbreviations: IQR=interquartile range; ART=Antiretroviral treatment.

^a Chi-square test for categorical variables, and Wilcoxon rank-sum test for continuous variables.

[§]One missing value (n=151).