Initiation and completion rates of isoniazid preventive therapy among people living with HIV in Far-Western Region of Nepal: a retrospective cohort study

Govinda Prasad Dhungana, Pruthu Thekkur, Palanivel Chinnakali, Usha Bhatta, Basudev Pandey, Wei-Hong Zhang

ABSTRACT

Objectives Isoniazid preventive therapy (IPT), for people living with HIV (PLHIV) is the proven and recommended intervention to avert tuberculosis (TB). In 2015, Nepal implemented 6 months of IPT for all PLHIV registered for HIV care in antiretroviral therapy (ART) centres. After programmatic implementation, there has been no systematic assessment of IPT initiation and completion rates among PLHIV. We aimed to assess IPT initiation and completion rates in the Far-Western Region (FWR) of Nepal.

Design We conducted a retrospective cohort study using secondary data extracted from registers maintained at ART centres.

Setting All 11 ART centres in the FWR of Nepal.

Participants All PLHIV registered for care between January 2016 and December 2017 in 11 ART centres.

Primary outcome measures IPT initiation and completion rates were summarised as percentages with 95% CI. Independent association between patient characteristics and non-initiation of IPT was assessed using cluster-adjusted generalised linear model (log binomial regression) and adjusted relative risk (RR) with 95% CI was calculated.

Result Of the 492 PLHIV included, 477 (97.0%) did not have active TB at registration. Among 477 without active TB, 141 (29.8%, 95% CI 25.7% to 34.1%) had been initiated on IPT and 85 (17.8%) were initiated within 3 months of registration. Of 141 initiated on IPT, 133 (94.3%, 95% CI 89.1% to 97.5%) had completed 6 months of IPT. Being more than 60 years of age (RR-1.3, 95% CI 1.1 to 1.7), migrant worker (RR-1.3, 95% CI 1.1 to 1.4) and not being initiated on ART (RR-1.4, 95% CI 1.1 to 1.8) were significantly associated with IPT initiation.

Conclusions In FWR of Nepal, three out of 10 eligible PLHIV had received IPT. Among those who have received IPT, the completion rate was good. The HIV care programme needs to explore the potential reasons for this low coverage and take context specific corrective action to fix this gap.

INTRODUCTION

Tuberculosis (TB) is the leading cause of mortality among people living with HIV (PLHIV). Globally, around 400,000 TB-related deaths occurred among PLHIV in 2017, accounting for about one-third of all-cause mortality. Prevention, early diagnosis and treatment of TB can therefore help avert significant number of deaths among PLHIV.

In 2008, to decrease the TB burden among PLHIV, the WHO recommended ‘Three I’s’ strategy consisting of three interventions: (i) intensified TB case finding and linkage to high-quality anti-TB treatment (ii) TB prevention using isoniazid preventive therapy (IPT) and early antiretroviral therapy (ART), irrespective of CD4 count and clinical staging and (iii) infection control in HIV care facilities and other congregate settings.

Early initiation of ART is a standalone intervention to reduce TB incidence among PLHIV and TB burden in countries with high prevalence of HIV. Since most countries have adopted ‘test and treat’ strategy for PLHIV, ART coverage has improved with around 21.7 million PLHIV on ART in 2017.
Though ART reduces the risk of TB among PLHIV, ART alone may not be enough to bring down the risk of developing TB among PLHIV to that of HIV negative individuals. Hence, there is a evidence based need for interventions like IPT to complement the effect of ART.

IPT for 6 or 36 months has proven to be beneficial in reducing the risk of TB in both adults and children. Studies have reported that IPT and ART have a synergistic effect in reducing the burden of TB and mortality among PLHIV. Although the WHO recommended IPT for PLHIV in 2004, majority of the countries did not implement IPT in their HIV care programme. Globally, only about 42% of all the newly diagnosed PLHIV were started on IPT in 2016. Also, studies have reported varied IPT completion rates ranging from 64% to 96%.

Nepal, a landlocked country in South Asia, is experiencing a concentrated HIV epidemic with an overall estimated prevalence of 0.3%. Nepal has substantial TB burden with estimated 45,000 new TB patients (incidence rate of 152 per 100,000 population) and 6900 deaths due to TB in 2017. In Nepal, TB is ranked as the sixth leading cause of death and is thus considered as a major public health problem. In 2012, sentinel surveillance estimated high prevalence (11%) of TB among PLHIV. In the wake of this, the National Centre for AIDS and Sexually Transmitted Disease Control (NCASC) and National TB Centre (NTC) jointly implemented IPT as a pilot programme in five ART centres located in tertiary care hospitals in December 2012. Operational research conducted during this pilot phase reported low IPT initiation rate (32%) but high completion rate (87%). In December 2015, IPT for PLHIV was scaled up to all ART centres in the country. However, there has been no evaluation of IPT coverage and completion rates after programmatic implementation of IPT in Nepal.

Far-Western Region (FWR, also known as Province seven) of Nepal is an underdeveloped region with highest prevalence of job-related outward migration. The region has low literacy and high poverty levels. There is anecdotal evidence that TB/HIV care provision is complicated in the region due to poor healthcare facilities and outward migration leading to attrition from care.

Though IPT has been implemented in the ART centres of the FWR of Nepal since January 2016, no concurrent evaluations have been conducted to assess the coverage and completion rates of IPT. There is no evidence of poor IPT coverage in the region. Systematic assessment of IPT coverage and completion rates will help the programme managers to revisit the strategies adopted and take corrective actions. Therefore, this study was planned to assess the IPT coverage and completion rate, and to identify key sociodemographic and baseline clinical characteristics associated with non-initiation of IPT.

**METHODOLOGY**

**Study design**

A cohort study was conducted using secondary data collected routinely by the National HIV programme.

**Study setting**

**General setting**

This study was carried out in the ART centres of FWR of Nepal. The FWR is one of the five developmental regions of the Nepal: Eastern, Central, Western, Mid-Western and Far-Western Region. The region has nine districts and a population of around 2.5 million. The region has poor health indicators, high prevalence of poverty (40%) and low literacy rate (50%). Due to lack of job opportunities and poverty in the region, there is job-related migration to cities of Nepal and India. With concentrated epidemic among the outward migrants, the region has relatively higher estimated HIV prevalence (0.4%) compared with the national estimate (0.3%).

**Specific setting**

There are 11 ART centres in the FWR Region which are colocated with district hospital or tertiary care centres. At least one ART centre is present in each of the nine districts of the region. The NCASC under Ministry of Health and Population provides HIV treatment and care services through these ART centres. All services in these ART centres are provided free of cost.

**HIV testing and linking to HIV care in the region**

HIV testing services are provided through ‘Voluntary Counselling and Testing centres’ (VCTC) located in the secondary level public health facilities. All ART centres also have VCTC facilities. In VCTC, those individuals detected to be seropositive for HIV are counselled and referred to the nearby ART centres for care and treatment. All the laboratory and clinical examination details during registration and follow-up are documented in the ART register maintained at ART centres.

Patients successfully referred to ART centre are registered in the ‘ART register’ of ART centre with a unique ‘ART ID number’. As per ‘test and treat’ policy, all registered PLHIV are initiated on appropriate ART by the ART medical officer after clinical and laboratory evaluation. After providing adherence counselling, once-daily fixed-dose combination (FDC) drugs are dispensed for 15 days. If the individual is found to be adherent, the drugs are dispensed for a period 1 month.

**Isoniazid preventive therapy for PLHIV**

Since 2016, HIV/TB comprehensive package was implemented in the ART centres of the region. All newly registered PLHIV are screened for active TB using the WHO symptom screen and national TB guidelines (cough, excessive night sweat, fever for ≥2 weeks and weight loss of ≥3 kg with in 4 weeks) during their first visit. Individuals with any of the four symptoms are evaluated for TB using sputum smear microscopy and chest radiography. After evaluation, those PLHIV without TB and without known conditions are initiated on isoniazid preventive therapy (IPT) for 6 months.
liver disease, active alcohol use, prior isoniazid resistance, peripheral neuropathy and unexplained illness are considered eligible to receive IPT and IPT should be dispensed to them by the ART medical officer.

PLHIV who are eligible for IPT receive isoniazid (300 mg for adults and 200 mg for children) and pyridoxine (25 mg) for 6 months. The IPT drugs are dispensed along with ART drugs during monthly visit to ART centre. IPT is stopped in case PLHIV develops active TB or severe adverse drug events. The details of the drugs dispensed, adverse drug reaction and completion of the IPT are recorded in ‘IPT register’ maintained at ART centres.

Study population
PLHIV registered in ART centres of FWR, Nepal during January 2016 to December 2017 were eligible for the study. The minimum sample size was calculated to be 204, assuming percentage of IPT initiation to be 32%,

Data variables, sources of data and data collection
Data variables like ART ID number, age, gender, marital status, education, occupation, mode of HIV transmission, tobacco use, alcohol use, date of registration at ART centre, date of HIV testing, WHO clinical staging at baseline, CD4 count, ART start date, ART regimen, TB disease during registration, liver disease at registration, severe illness at registration and date of IPT initiation were extracted from the ‘ART register’. The outcome variables like IPT status, IPT completion, date of IPT completion and reasons for non-completion were extracted from the ‘IPT register’. Self-designed data collection proforma was used to extract details from the registers.

Six trained ‘data collectors’ extracted data during June–August 2018. The principal investigator visited each ART centre at least once during the data collection period and verified at least 10% of the proformas filled by each ‘data collector’ for quality and completeness.

Operational definition
IPT eligible: PLHIV without active TB or not diagnosed with TB within 3 months of ART registration in whom there is no documented evidence of liver disease, active alcohol use, jaundice, prior isoniazid resistance, peripheral neuropathy and unexplained illness in the ‘ART register’ during initial assessment.

IPT initiation: IPT is said to be initiated when the eligible PLHIV receives IPT after eligibility assessment.

IPT completion: The IPT is said to be completed if the individual started on IPT receives it during six consecutive visits to ART centre and is indicated as ‘IPT completed’ in ‘IPT register’.

Data entry and analysis
Data were double entered and validated using EpiData V.3.1 entry software. Data were analysed using Stata V.12.0 software. Categorical variables like IPT eligibility, IPT initiation, IPT initiation within 3 months and IPT completion were summarised as percentages with 95% CI.

The association between sociodemographic and baseline clinical characteristics with not initiating of IPT was assessed using bivariate log binomial regression. Unadjusted relative risk (RR) with 95% CI was calculated as measure of association. To assess the independent association, a cluster (ART centre) adjusted generalised linear model (Poisson regression) with variables having p value <0.25 in the univariate log binomial regression was developed. Adjusted RR with 95% CI was calculated. Quantitative variables like age and CD4 level were classified into appropriate class intervals prior to calculating adjusted RR with 95% CI.

Sensitivity analysis
In the current study, except for details of TB symptom screening and diagnosis of TB, none of the other details on IPT eligibility criteria (liver disease, active alcohol use, jaundice, prior isoniazid resistance, peripheral neuropathy and unexplained illness) were documented in the ‘ART registers’. Hence, only those with active TB could be considered as not eligible for IPT. Sensitivity analysis was conducted to accommodate for potential deficiency in documentation of IPT eligibility examination results.

Patient and public involvement
Principal investigator and the data collectors did not interact directly with the PLHIV registered for care in the ART centres during this retrospective record review. The investigators interacted with the ART centre in-charge, counsellors and peer educators of all the ART centres included in the study. Findings from this study will help the national TB programme and NCASC programme of Nepal to identify the gaps in IPT implementation and eventually improve the care and treatment of PLHIV.

RESULTS
Between January 2016 and December 2017, a total of 492 PLHIV had been registered at ART centres of FWR, Nepal. Of 492 PLHIV, 267 (54%) were male and the mean (SD) age was 36 (14) years. Sociodemographic and clinical characteristics are described in Table 1. Of total, 8% were children (0–14 years) and 3% were elderly (60 years). At the time of registration, 44% were in WHO clinical staging III or IV. Of total, 98% were initiated on ART and majority of them (86%) were on tenofovir, lamivudine, efavirenz regimen in FDC. The details on education and occupation status were missing for more than 50% of the study participants.

Of the total 492 PLHIV, 15 (3.0%) had been diagnosed with active TB; 11 had TB at the time of registration and four were diagnosed within 3 months. In total, 477 (97.0%, 95% CI 95.0% to 98.3%) PLHIV were eligible for IPT. Of 477 PLHIV, 85 (17.8%, 95% CI 14.5% to 21.6%) were initiated on IPT within 3 months of registration and 56 (11.7%) were initiated later. Median (IQR) duration
between registration and initiation of IPT was 41 (0–198) days. Of 141 initiated on IPT, 133 (94%, 95% CI 89.1% to 97.5%) completed 6 months of therapy. Eight patients (6%) did not complete IPT; five were lost to follow-up and three discontinued due to adverse drug effects. Eligibility for IPT, IPT initiation and completion rates are described in figure 1. The IPT initiation rate ranged from 0% to 57% across 11 ART centres (figure 1 and online supplementary table 1).

Sociodemographic and clinical characteristics associated with non-initiation of IPT are described in table 2 and table 3. Non-initiation was higher among children (78%) and elderly (83%) compared with PLHIV aged 45–59 years (64%). Non-initiation rate was higher among migrant workers (82%). All PLHIV who were not on ART (n=11) had not been initiated on IPT. In adjusted analysis, age more than 60 years (RR-1.3, 95% CI 1.1 to 1.7), migrant worker (RR-1.3, 95% CI 1.1 to 1.4) and non-initiation of ART (RR-1.4, 95% CI 1.1 to 1.8) were independently associated with higher rates of non-initiation of IPT.

Sensitivity analysis
Considering about 10% of those without active TB at registration would have been found to be ineligible for IPT, about 431 (87.3%) would have been eligible for IPT initiation. Considering 141 individuals were started on IPT among those eligible based on sensitivity analysis, the IPT initiation rate would be 32.7% (141 out of 431).
To our knowledge, this is the first study from Nepal assessing the IPT eligibility, initiation and completion rate among PLHIV in the programmatic setting after universalisation of IPT in 2015. Though majority of PLHIV were eligible for IPT, only three out of 10 were initiated on IPT. Among those initiated on IPT, almost all (95%) completed 6 months of IPT.

In the current study, proportion of PLHIV eligible for IPT (97%) was found to be higher than those reported by previous studies. The study conducted in Kathmandu, Nepal during pilot phase of IPT implementation had reported about 87% of PLHIV to be eligible for IPT. This Kathmandu study also had considered all those without active TB as eligible for IPT, similar to the current study. Contrary to our study where a cohort of newly registered patients was included, the previous study was a cross-sectional study and had included PLHIV on care since several years. As risk of TB increases over time and ART initiation rate was low, there might have been relatively higher proportion of active TB patients (13%) in previous study compared with this study (3%).

Similar to our study, a study conducted in Malawi among newly registered PLHIV reported that about 2% were ineligible for IPT as they had been diagnosed with active TB at registration. The Malawi study also reported that 9% were not eligible due to failure to for IPT due to at least one contraindication for initiating IPT. In the current study, except for details of TB symptom screening and diagnosis of TB, none of the other details on IPT eligibility were documented in the ‘ART registers’. This might be either due to poor compliance to IPT eligibility testing itself or deficiency in documentation of these examination details.

In the current study, we found the IPT coverage rate (30%) to be relatively poor compared with other studies. The current study had poor IPT coverage even after adjusting for overestimation of IPT eligibility (33%). Low IPT coverage may be due to several structural and provider level deficiencies in the FWR of Nepal. The poor infrastructure in health facilities for assessing eligibility, limited manpower, untrained health workforce, poor adherence to guidelines, interrupted drug supply and drug stock-outs, and lack of monitoring on IPT eligibility, initiation and completion rates might have led to low coverage of IPT in FWR of Nepal. The IPT initiation rates varied across the ART centres (0%–56%) within FWR indicating that IPT coverage rates are by large dependent on ART centres and therefore, indirectly related to infrastructural and provider capacity of the centre. Also, patient groups like old age, migrant worker and those not initiated on ART had very low coverage of IPT.

The HIV care programme recommends initiating IPT among eligible PLHIV at the time of registration. Even if IPT is not initiated during registration, it needs to be initiated within the next few visits to ART centre. However, only 18% of the PLHIV were initiated on IPT within 3 months of being eligible at the time of registration. Initiation of IPT after 3 months might not reflect the health system response for IPT eligibility assessment done at the time of registration. Majority of the previous studies were cross-sectional studies and had considered ‘ever initiated on IPT’ to
define IPT coverage. The IPT initiation rate within 3 months of eligibility provides a better monitoring indicator which covers both IPT coverage and timeliness of initiation of IPT. Consistent with the other studies, the IPT completion rates were high (94%) in the current study. Hence, it can be reasoned that the hurdle for prevention of TB among PLHIV is low rate of IPT initiation.

Along with IPT coverage and completeness, some more programmatically relevant aspects were noted during this study. The ‘ART register’ was incomplete with details on education and occupation missing for more than half of the registered PLHIV. The CD4 count at registration, which is used to assess the immunological improvement and decide on the course of ART was not available in about one-third of the registered PLHIV. In contrast to incompleteness of documentation and low IPT coverage, the study setting had a high ART initiation rate (98%), which was appreciable. This high ART initiation rate may be due to adoption of ‘test and treat’ strategy, improved efforts of the NCASC in procurement and supply of ART drugs, frequent training of all the NCASC and health staff regarding ART and use of ART initiation rate as an indicator to monitor the performance of ART centre. Lessons learnt in improving the ART coverage can be considered to improve the IPT coverage in study setting.

This study has a few strengths. First, this is the first study assessing the IPT coverage in the programme setting of resource limited Far-Western Region of Nepal. Second, there was no selection bias as all the PLHIV registered for care in the 11 ART centres of Far-Western Region were included.

### Table 2  Sociodemographic factors associated with non-initiation of IPT among PLHIV registered between January 2016 and December 2017 in the Far-Western Region of Nepal, n=477

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total, N (%)*</th>
<th>Not initiated on IPT, N (%)†</th>
<th>Unadjusted RR (95% CI)</th>
<th>Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>477 (100)</td>
<td>336 (70.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age groups (years)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>&lt;15</td>
<td>40 (8.4)</td>
<td>31 (77.5)</td>
<td>1.2 (1.0 to 1.5)</td>
<td>1.3 (0.7 to 2.4)</td>
</tr>
<tr>
<td>15–29</td>
<td>89 (18.6)</td>
<td>63 (70.8)</td>
<td>1.1 (0.9 to 1.3)</td>
<td>1.1 (0.9 to 1.4)</td>
</tr>
<tr>
<td>30–44</td>
<td>221 (46.3)</td>
<td>155 (70.1)</td>
<td>1.1 (0.9 to 1.3)</td>
<td>1.1 (0.9 to 1.3)</td>
</tr>
<tr>
<td>45–59</td>
<td>98 (20.5)</td>
<td>63 (64.3)</td>
<td>1.1 (0.9 to 1.3)</td>
<td>1.1 (0.9 to 1.3)</td>
</tr>
<tr>
<td>≥60</td>
<td>29 (6.07)</td>
<td>24 (82.8)</td>
<td>1.3 (1.0 to 1.6)</td>
<td>1.3 (1.1 to 1.7)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>253 (53.0)</td>
<td>182 (72.0)</td>
<td>1.0 (0.9 to 1.2)</td>
<td>1.0 (0.8 to 1.1)</td>
</tr>
<tr>
<td>Female and others</td>
<td>224 (46.9)</td>
<td>154 (68.8)</td>
<td>1.1 (0.9 to 1.3)</td>
<td>1.1 (0.9 to 1.3)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illiterate</td>
<td>78 (16.3)</td>
<td>65 (83.3)</td>
<td>1.2 (0.9 to 1.5)</td>
<td>1.2 (0.9 to 1.5)</td>
</tr>
<tr>
<td>Just literate§</td>
<td>70 (14.7)</td>
<td>54 (77.1)</td>
<td>1.1 (0.9 to 1.4)</td>
<td>1.0 (0.9 to 1.2)</td>
</tr>
<tr>
<td>Had formal education</td>
<td>38 (8.0)</td>
<td>27 (71.1)</td>
<td>1.1 (0.9 to 1.3)</td>
<td>1.1 (0.9 to 1.3)</td>
</tr>
<tr>
<td>Not recorded</td>
<td>291 (61.0)</td>
<td>190 (65.3)</td>
<td>0.9 (0.7 to 1.1)</td>
<td>0.9 (0.7 to 1.2)</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Unemployed</td>
<td>20 (4.2)</td>
<td>16 (80.0)</td>
<td>1.1 (0.7 to 1.8)</td>
<td>1.0 (0.8 to 1.4)</td>
</tr>
<tr>
<td>Farmer</td>
<td>10 (2.1)</td>
<td>7 (70.0)</td>
<td>1.1 (0.7 to 1.8)</td>
<td>1.0 (0.8 to 1.4)</td>
</tr>
<tr>
<td>Housewife</td>
<td>87 (18.2)</td>
<td>66 (75.9)</td>
<td>1.1 (0.7 to 1.7)</td>
<td>1.2 (1.0 to 1.4)</td>
</tr>
<tr>
<td>Migrant worker</td>
<td>77 (16.1)</td>
<td>63 (81.8)</td>
<td>1.2 (0.8 to 1.8)</td>
<td>1.3 (1.1 to 1.4)</td>
</tr>
<tr>
<td>Others</td>
<td>22 (4.6)</td>
<td>15 (68.2)</td>
<td>1.0 (0.6 to 1.6)</td>
<td>0.9 (0.6 to 1.5)</td>
</tr>
<tr>
<td>Not recorded</td>
<td>261 (54.7)</td>
<td>169 (64.8)</td>
<td>0.9 (0.6 to 1.4)</td>
<td>1.1 (0.9 to 1.4)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>367 (76.9)</td>
<td>266 (72.5)</td>
<td>1.4 (1.1 to 1.7)</td>
<td>1.2 (1.0 to 1.5)</td>
</tr>
<tr>
<td>Unmarried</td>
<td>52 (10.9)</td>
<td>39 (75.0)</td>
<td>1.4 (1.1 to 1.9)</td>
<td>1.3 (0.8 to 2.0)</td>
</tr>
<tr>
<td>Widow/separated</td>
<td>58 (12.2)</td>
<td>31 (53.5)</td>
<td>1.1 (0.9 to 1.4)</td>
<td>1.1 (0.9 to 1.4)</td>
</tr>
</tbody>
</table>

*Column percentage.
†Row percentage.
‡Cluster adjusted (ART centres) generalised linear (Poisson) model; those categories (except ‘not recorded’ and ‘others’) with lowest proportion of IPT non-initiation were considered as reference categories in the model.
§Able to read and write but no formal education.
ART, antiretroviral therapy; IPT, isoniazid preventive therapy; PLHIV, people living with HIV; RR, relative risk.
Third, about 10% data extraction forms were rechecked by the principal investigator for data quality. Fourth, data quality was assured as data was double entered and validated using EpiData software. Fifth, the Strengthening the Reporting of Observational Studies in Epidemiology checklist has been used for reporting this study.

This study has a few limitations. First, secondary data were used which had missing information on few sociodemographic details. Also, recording errors and incompleteness of documentation cannot be ruled out. Second, the proportion eligible for IPT might have been overestimated, as only all those PLHIV without active TB could be considered as eligible for IPT. However, we have conducted sensitivity analysis to derive the eligibility and initiation rate estimates adjusting for this overestimation. Third, the study was not powered to find association between baseline characteristics of PLHIV and initiation of IPT. Also, the model developed for assessing the independent effect of patient level characteristics on IPT initiation might be deficient as few important confounders like socioeconomic status, migration and adherence to ART could not be included in it. Fourth, completeness of IPT was assessed based on the receipt of IPT drugs during six consecutive visits and did not take into consideration the adherence to drugs.

Few recommendations can be put forth based on the findings of this study. First, there is need for carrying out clinical and laboratory examinations to assess the eligibility for IPT and document the details of the same in ‘ART register’. The ‘ART register’ needs to be restructured with inclusion of appropriate columns (fields?) to document the details of assessment of IPT eligibility, which is currently not available. Second, the programme monitoring and supervision needs to be strengthened and special emphasis needs to be given on completeness of records. Third, the programme managers need to explore the possible reasons for low initiation rates of IPT using qualitative research methods and take corrective actions based on those findings. Fourth, cohort-based IPT initiation rate can be added as an indicator in the quarterly reporting formats of ART centre and also used for monitoring the programme implementation.

CONCLUSION
In FWR of Nepal, about three out of 10 eligible PLHIV are receiving IPT. Among those who have received IPT, the completion rate was good. The HIV care programme needs to explore the potential reasons for this low coverage and take context-specific corrective action to fix this gap.

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### Table 3: Clinical factors associated with non-initiation of IPT among PLHIV registered between January 2016 and December 2017 in the Far-Western Region of Nepal, n=477

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total, N (%)*</th>
<th>Not initiated on IPT, N (%)†</th>
<th>Unadjusted RR (95% CI)</th>
<th>Adjusted RR (95% CI)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>477 (100)</td>
<td>336 (70.4)</td>
<td>1.0 (0.9 to 1.3)</td>
<td>1.1 (0.9 to 1.3)</td>
</tr>
<tr>
<td>CD4 count</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 200</td>
<td>124 (26.0)</td>
<td>92 (74.2)</td>
<td>1.0 (0.9 to 1.3)</td>
<td>1.1 (0.9 to 1.3)</td>
</tr>
<tr>
<td>200–350</td>
<td>73 (15.3)</td>
<td>44 (60.3)</td>
<td>0.8 (0.7 to 1.1)</td>
<td>0.9 (0.7 to 1.1)</td>
</tr>
<tr>
<td>350–500</td>
<td>74 (15.5)</td>
<td>40 (54.1)</td>
<td>0.8 (0.6 to 1.0)</td>
<td>0.8 (0.7 to 0.9)</td>
</tr>
<tr>
<td>More than 500</td>
<td>69 (14.7)</td>
<td>49 (71.0)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Not recorded</td>
<td>137 (28.7)</td>
<td>111 (81.0)</td>
<td>1.1 (1.0 to 1.4)</td>
<td>1.2 (0.9 to 1.6)</td>
</tr>
<tr>
<td>WHO clinical staging</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I or II</td>
<td>274 (57.4)</td>
<td>195 (71.2)</td>
<td>1.0 (0.9 to 1.2)</td>
<td></td>
</tr>
<tr>
<td>III or IV</td>
<td>172 (36.1)</td>
<td>119 (69.2)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Not recorded</td>
<td>31 (6.5)</td>
<td>22 (71.0)</td>
<td>1.0 (0.8 to 1.3)</td>
<td></td>
</tr>
<tr>
<td>ART status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On ART</td>
<td>466 (97.7)</td>
<td>325 (69.7)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Not initiated on ART</td>
<td>11 (2.3)</td>
<td>11 (100)</td>
<td>1.5 (1.4 to 1.6)</td>
<td>1.4 (1.1 to 1.8)</td>
</tr>
</tbody>
</table>

*Column percentage. †Row percentage. ‡Cluster adjusted (ART centres) generalised linear (Poisson) model; those categories (except ‘not recorded’ and ‘others’) with lowest proportion of IPT non-initiation were considered as reference categories in the model.

ART, antiretroviral therapy; IPT, isoniazid preventive therapy; PLHIV, people living with HIV; RR, relative risk.
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Contributors GPD was the principal investigator; PT and PC were the SORT IT course mentors; BP and WHZ are the senior authors. GPD and UB were involved in data collection; GPD, PT and PC analysed the data and prepared the first draft of paper. All authors were involved in conception, design, inference of results, providing critical review to the manuscript and approval of the manuscript from this protocol.

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Competing interests None declared.

Patient consent for publication Not required.

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Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Technical appendix, statistical code, and dataset available from the https://www.dropbox.com/sh/uxndiz29f1g77qr/AAAJ3jTi_hXUb0rsD1v6zgbb?d=0

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