# Caregivers' knowledge and perceptions are associated with children's TB preventive treatment completion

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**SETTING:** Forty-six health centers in south Lima, Peru. **OBJECTIVE:** To assess the association between caregivers' knowledge and perceptions around isoniazid preventive therapy (IPT) and whether their children complete IPT.

**DESIGN:** We conducted a retrospective medical record review of children who initiated IPT during 2017–2018. We administered structured surveys to caregivers of the children about their knowledge about and perceptions of IPT. We used a modified Poisson regression to determine factors associated with IPT completion.

**RESULTS:** We included 550 children, of whom 31% did not complete IPT. Independent factors associated with not completing IPT were low caregiver knowledge about TB and IPT (adjusted risk ratio [aRR] 1.41, 95% CI 1.06– 1.78), low caregiver perception of the importance of IPT (aRR 1.76, 95% CI 1.30–2.39), low caregiver satisfaction with the health services (aRR 1.57, 95% CI 1.14–2.16), experience of adverse events (aRR 2.08, 95% CI 1.51– 2.87), and living in a household with moderate or severe family dysfunction (aRR 1.53, 95% CI 1.07–2.19).

**CONCLUSION:** IPT completion among children was associated with the knowledge and perceptions of their caregivers, as well as the experience of adverse events. To improve IPT completion among children, health care providers should prioritize education and counseling for caregivers, promote positive interpersonal relationships with them, and monitor adverse events.

Children in close contact with adults who have TB are at high risk of being infected themselves, and if TB disease develops, they can develop fatal disseminated forms such as miliary TB and TB meningitis.<sup>1,2</sup> The WHO recommends that household contacts of TB patients receive preventive therapy.<sup>3</sup> The most common regimen used for preventive therapy in low- and middle-income countries is 6 months of daily isoniazid (isoniazid preventive therapy, IPT). It is estimated that only 33% of young children (age <5 years) worldwide who were household contacts of TB patients received preventive therapy in 2019; the number who completed this treatment was not reported to the WHO.<sup>4</sup>

Studies identifying factors associated with preventive therapy completion under programmatic conditions have been published from diverse settings. In South Africa, more children completed preventive therapy when treatment was supervised by health care workers or community treatment supporters, and when a shorter treatment regimen was used.<sup>5</sup> In India, IPT completion was better in rural clinics than in urban clinics.<sup>6</sup> In Brazil, IPT non-completion was associated with the human development index of the patient's residence, having contact with a TB patient who had not completed treatment,<sup>7</sup> and low socioeconomic status.<sup>8</sup> In Peru, IPT completion has been associated with receiving a tuberculin skin test, TB treatment completion of the index patient, and health facility characteristics.<sup>9</sup>

Many of these studies have identified associations between IPT completion and demographic or clinical characteristics of the child or the index patient. However, to inform programmatic improvement, it is important to also assess factors that health care providers can modify while a person is in care. For example, providers can potentially affect patients' perceptions of the importance of treatment through education or counseling. For children, IPT is likely to depend on the caregiver, but relatively few studies have focused on caregivers' perceptions or knowledge of IPT.10,11 Moreover, the association between caregivers' perceptions and knowledge and whether their children complete IPT is unclear. One mixed methods study found no quantitative association between IPT completion and caregiver knowledge and perceptions, and yet found these to be important facilitators of adherence in qualitative analysis.12 This qualitative evidence that caregiver perceptions affect IPT completion is corroborated by other research,13 but quantitative evidence of an association is lacking. To address this knowledge gap, we conducted a study in Lima, Peru, to assess the association between caregivers' knowledge and perceptions of IPT and whether their children completed IPT.

#### **METHODS**

#### Study design

We conducted a cross-sectional study to measure the association between the knowledge and perceptions of caregivers and whether their children completed IPT. To adjust for other factors that could affect IPT completion, we used the WHO conceptual framework for medication adherence.<sup>14</sup>

#### Study population

The Directorate of the Integrated Health Networks of South Lima (*Dirección de Redes Integradas de Salud* [DI-RIS] Lima Sur) manages 136 health facilities in 13 districts in the south of Lima, comprising a catchment population of 1.86 million. For this study, we enrolled

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#### KEY WORDS

tuberculosis; preventive therapy; isoniazid; children; adolescents

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PHA 2021; 11(2): 85–90 e-ISSN 2220-8372 caregivers whose children had received IPT in 46 of the health centers that reported the highest TB caseloads in 2017, representing 80% of the total TB cases in the DIRIS Lima Sur. In Peru, contacts of patients with pulmonary TB should receive IPT after ruling out TB disease if they are 1) aged <5 years or 2) 5–19 years and have a TST inducation of  $\geq 10 \text{ mm.}^{15}$  All people living with HIV should also receive IPT, but because of the low HIV prevalence in the general population (0.3% among adults aged 15–49 years), contacts are not routinely tested for HIV.<sup>16</sup>

We reviewed medical records to identify children aged <19 years who initiated IPT during 2017–2018. We excluded children who had moved outside the jurisdiction of the our health facility, who had been diagnosed with TB during IPT, or for whom IPT had been suspended by the managing physician. We recruited the caregivers of eligible children during May–August 2019. Caregivers were eligible for inclusion if they were ≥18 years old and were the family member who had been in charge of managing the child's IPT.

#### **Data collection**

Data were collected using a structured survey administered to caregivers in their homes. The outcome of the analysis was whether the child completed 24 weeks of IPT. Study staff knew the IPT outcome recorded on the contact's medical record at the time of the survey. They were trained to ask standardized questions to all caregivers about whether their child had completed IPT and how many months the child had been on treatment. If the caregiver said that the child had completed IPT but the medical record did not, the caregiver was asked for the approximate completion date and health facility (in case the child had been transferred during treatment). This information was then verified in the isoniazid dispensing records. If the medical records said that the child had completed IPT but the caregiver said that they had not, then the caregiver's account was believed.

We evaluated factors affecting IPT completion based on the WHO framework for medication adherence.<sup>14</sup> Our principal predictors of interest were in the domain of knowledge, attitudes, and perceptions. Specifically, we assessed caregivers' knowledge about TB and IPT and their perception of the importance of IPT. In the domain of health system-related factors, we assessed caregivers' satisfaction with the health care staff who managed IPT. In the domain of social and economic factors, we considered the age and sex of the child; the age, sex, education level, and occupation of the caregiver; and family function, as measured by the Family APGAR (adaptation, partnership, growth, affection, and resolve) Questionnaire.<sup>17</sup> In the domain of factors related to treatment, we considered whether the child had any adverse event during IPT, as reported by the caregiver and verified in the medical records.

We defined a low level of knowledge as correctly answering <6 of the 8 true-false questions about TB and IPT based on information in the Peru national TB guidelines.<sup>15</sup> To assess caregivers' perception of the importance of IPT and their satisfaction with health care staff, we treated survey responses as a Likert scale and calculated the average response over the two questions in each category. Low perceived importance of IPT was defined as an average score of <2 out of a possible 3, and low satisfaction with health services was defined as an average score of <3 out of a possible 4. We defined moderate or severe dysfunction as corresponding to scores indicating low or moderate satisfaction with family function on the Family APGAR Questionnaire.<sup>17</sup> The questionnaire was validated by TB experts and pilot tested with 15 participants.

#### Statistical analysis

To assess factors associated with IPT completion, we calculated risk ratios (RRs) with 95% confidence intervals (CIs) using modified Poisson regression with generalized estimating equations to account for correlation among children in the same household. In multivariable analysis, we included a priori caregiver knowledge and caregiver perception of IPT importance. We included other variables with a *P* value of  $\leq 0.15$  in bivariate analysis. We limited multivariable analysis to children with complete data. Statistical analysis was performed using SAS v9.4 (SAS Institute, Cary, NC, USA).

#### **Ethics**

This study was approved by the ethics committees of the Hospital Nacional Dos de Mayo and the DIRIS Lima Sur, Lima, Peru. Written informed consent was provided by caregivers.

#### RESULTS

We identified 592 children who initiated IPT during 2017–2018, and we enrolled caregivers of 550 (93%) of these children. We excluded 39 children whose families had moved outside the jurisdiction of the health facility, 1 child who developed TB disease, and 2 children for whom IPT was suspended. The 550 children included lived in 367 households; 35% of households had more than one child. We administered surveys to 367 caregivers (Table 1).

In total, 380 (69%) of the children completed IPT. These included 45 (8%) children whose medical records indicated that they did not complete IPT; caregiver's accounts of IPT completion were verified from isoniazid dispensing records and at health facilities to which children had been transferred. Adverse events (AEs) were reported by caregivers and verified in medical records for 34 (6%) children (Table 2).

TABLE 1	Social and demographic characteristics of caregivers and
contacts	

Characteristics	п	%
Caregivers ( $n = 367$ )		
Age, years		
18–30	164	45
31–45	129	35
≥46	74	20
Sex		
Male	69	19
Female	298	81
Is the caregiver the TB patient?		
Yes	173	47
No	194	53
Highest level of education attained		
Primary or lower	39	11
Secondary	241	66
Post-secondary	87	24
Contacts ( $n = 550$ )		
Age, years		
0-4	358	65
5–9	117	22
10–15	62	11
16–18	13	2
Sex		
Male	311	57
Female	239	43

# **TABLE 2** AEs reported by caregivers among children during IPT $(n = 550)^*$

Adverse event	п	%
No AEs reported	516	94
Stomach pain	16	3
Nausea	13	2
Loss of appetite	10	2
Vomiting	9	2
Rash	1	<1
Other	3	1

\*Caregivers were asked specifically about five AEs. Other events reported were insomnia, constipation, and diarrhea.

AE = adverse event; IPT = isoniazid preventive therapy.

#### **TABLE 3** Caregiver knowledge about TB and IPT (n = 367)

# TB and IPT knowledge among caregivers

Over 90% of caregivers knew that TB is transmitted through the air (97%), and that transmission can be prevented by good ventilation (95%) and avoiding being close to a person with TB who is coughing (91%) (Table 3). However, less than half of caregivers knew that TB cannot be transmitted by sharing utensils (42%), and that having TB patients use separate dishes and utensils is not an appropriate TB preventive measure (38%). The median number of knowledge questions answered correctly by caregivers was 6 (interquartile range [IQR] 5–7) out of 8.

# Perceptions of IPT importance and IPT services

Only 195 (53%) caregivers believed that it was very important for their child to complete IPT (Table 4). In addition, 169 (46%) caregiv-

	Caregivers who responded correctly		
Questions		%	
Knowledge about TB transmission			
Can TB be transmitted through the air when a person coughs or sneezes?	354	97	
Can TB can be transmitted by sharing utensils?	152	42	
Can TB can be transmitted by touching a person with TB?	297	81	
Knowledge about TB preventive measures			
Can family members avoid getting TB by maintaining well-ventilated rooms?	352	96	
Can family members avoid getting TB by maintaining physical distance from the person who has TB?	252	69	
Can family members avoid getting TB by not being close to the person with TB when they cough or sneeze?	332	91	
Can family members avoid getting TB by keeping separate plates and utensils for the person with TB?	137	38	
Knowledge about IPT			
What could happen if a child does not take IPT?*	321	88	

\*Responses mentioning that the child could fall sick with TB were considered correct.

#### **TABLE 4** Caregiver responses to questions about importance of IPT and satisfaction with health services (n = 367)

	Caregiver responses		
Questions	n	%	
Perceptions about importance of IPT			
How important did you feel it was for your child to complete IPT?			
Not important or not very important	23	6	
Somewhat important	148	40	
Very important	195	53	
No response	1	<1	
Before starting treatment, how likely did you think it was that your child would develop TB?			
Not likely or not very likely	67	18	
Somewhat likely	129	35	
Very likely	169	46	
No response	2	1	
Satisfaction with health services			
How would you rate your satisfaction with the attention you received from the health facility staff?			
Very unsatisfied	10	3	
Unsatisfied	23	6	
Satisfied	196	53	
Very satisfied	136	37	
No response	1	<1	
How would you rate the friendliness and courtesy of the person who gave you the isoniazid?			
Very poor	5	1	
Poor	11	3	
Good	169	46	
Very good	179	49	
No response	3	1	

IPT = isoniazid preventive therapy.

		Bivariate analysis		Multivariable analysis			
Characteristic		RR	95% CI	P value	aRR	95% CI	P value
Caregiver TB knowledge	High	Reference					
5 5	Low	1.71	1.22-2.61	0.003	1.41	1.06–1.78	0.017
Caregiver perception of IPT	High	Reference					
importance	Low	2.11	1.57–2.84	< 0.001	1.76	1.30-2.39	< 0.001
Caregiver satisfaction with	High	Reference					
health services	Low	2.00	1.46-2.74	< 0.001	1.57	1.14–2.16	0.005
Caregiver sex	Female	Reference					
-	Male	1.25	0.89–1.74	0.197			
Caregiver age, years	18–30	Reference					
	31–45	1.07	0.75-1.55	0.682			
	≥46	0.87	0.62-1.22	0.409			
Caregiver is the TB patient	No	Reference					
5 .	Yes	1.41	1.05-1.91	0.025	1.22	0.92-1.61	0.166
Caregiver highest education	More than secondary	Reference					
level	Secondary or below	1.25	0.86–1.82	0.233			
Caregiver works	No	Reference					
-	Yes	1.32	0.98–1.80	0.067	1.23	0.93-1.64	0.149
Caregiver perception of family	Functional	Reference					
function	Moderate or severe						
	dysfunction	1.78	1.22–2.61	0.003	1.53	1.07–2.19	0.018
Child contact sex	Female	Reference					
	Male	1.11	0.96–1.28	0.154			
Child contact age, years	0–4	Reference					
	5–9	0.88	0.75–1.04	0.136	0.93	0.82-1.06	0.282
	10–18	0.97	0.82-1.14	0.720	0.99	0.83-1.18	0.881
Child experienced adverse	No	Reference					
event	Yes	2.36	1.75-3.17	< 0.001	2.08	1.51-2.87	< 0.001

TABLE 5 Bivariate and multivariable associations between caregiver characteristics and IPT completion in child contacts

IPT = isoniazid preventive therapy; RR = risk ratio, CI = confidence interval, aRR = adjusted RR.

ers said that before initiating IPT, they had felt that it was very likely that their child would develop TB, compared to 67 (18%) who had felt it was unlikely (Table 4). The median score for perceived importance of IPT was 2.5 (IQR 2–3) out of 3 points. With respect to their experiences with the health services, 332 (90%) caregivers felt satisfied or very satisfied with the attention received, and 348 (95%) felt the staff were friendly and courteous. The median score for health system satisfaction was 3.5 (IQR 3–4) out of 4 points.

### **Risk factors for not completing IPT**

In bivariate analysis, non-completion of IPT was associated with low caregiver knowledge, low caregiver perception of IPT importance, and low caregiver satisfaction with health services, the caregiver not being the index patient and moderate or severe family dysfunction (Table 5). We included 520 children with complete data in the multivariable analysis. Low caregiver knowledge about TB and IPT (adjusted risk ratio [aRR] 1.41, 95% CI 1.06–1.78), low caregiver perception of IPT importance (aRR 1.76, 95% CI 1.30–2.39), and low caregiver satisfaction with health services (aRR 1.57, 95% CI 1.14–2.16) remained independently associated with IPT non-completion. In addition, children who experienced AEs were twice as likely not to complete IPT (aRR 2.08, 95% CI 1.51–2.87). Moderate or severe family dysfunction also remained independently associated with IPT non-completion (aRR 1.53, 95% CI 1.07–2.19).

# **DISCUSSION**

In this study, IPT completion in child contacts of TB patients was associated with their caregivers' knowledge about TB and perceptions of the importance of IPT. IPT completion was also associated with the occurrence of AEs, caregivers' satisfaction with health services, and family environment. Our findings contrast with previous studies that did not find significant associations between caregivers' knowledge and their children's IPT completion.<sup>12,18</sup> However, our results are consistent with studies of adult patients, which have found that adults are less likely to complete IPT if they lack knowledge about its purpose<sup>19</sup> or do not believe that they are at risk for TB.<sup>20</sup> It is possible that the relationship between caregivers' knowledge and perceptions and their willingness or ability to support children's treatment completion may vary across settings. Nevertheless, our findings highlight the importance of efforts on the part of the health system to educate, counsel, and build positive relationships with caregivers of children receiving IPT.

We found that the majority of caregivers were satisfied with the services they received from the health system; however, dissatisfied caregivers were more likely to report that their children did not complete IPT. Because the survey was administered after children had already stopped IPT, we cannot tell whether dissatisfaction was a cause of IPT non-completion, or whether dissatisfaction resulted from a situation that contributed to IPT non-completion (e.g., AEs that went unattended by the health system). However, previous studies have reported that positive support from health care providers is a facilitator of IPT adherence<sup>12</sup> and that negative relationships between caregivers and health care providers can impede adherence.<sup>21</sup> Together, this evidence suggests that fostering trusting relationships between caregivers and health care providers could promote IPT adherence. Few children in our study experienced AEs, consistent with observations from international clinical trials<sup>22</sup> and routine practice in Peru.<sup>23</sup> However, caregiver-reported AEs was a risk factor for not completing IPT. This finding is consistent with other studies that have used interviews to identify AEs,<sup>24,25</sup> but not with some studies based on treatment registers.<sup>7,26</sup> Studies based on recall may be subject to bias if patients who struggled to complete treatment are more likely to recall experiencing AEs; on the other hand, studies based on treatment registers may be subject to the opposite bias if patients who remain in care are more likely to have their AEs recorded by the health system. Notwithstanding these limitations, the results of our study and other interview-based studies suggests that concern over AEs may present a challenge to IPT completion, and therefore, active monitoring of AEs is important for supporting adherence.

Our observation that family function was associated with IPT completion is consistent with studies from other disease areas, which have found that the family function is associated with adherence to chronic disease treatment in children.<sup>27</sup> Family support has also been shown to be associated with adherence to treatment for TB disease in adults.<sup>28</sup> While the mechanisms may be similar, it is unknown how exactly the family environment affects IPT completion in child contacts, and future studies could help increase understanding in this area.

In Peru, health care providers train caregivers to supervise IPT for all contacts; however, in practice, caregivers may play a more limited role in supervising IPT for adolescents compared to younger children. Given their greater independence, adolescents may have distinct needs for treatment support.<sup>29</sup> Older adolescents have been shown to be at higher risk for incomplete treatment for TB disease than younger children.<sup>30,31</sup> There is little literature on the needs of adolescent contacts receiving preventive therapy. Thus, it is a limitation of our study that we only assessed the knowledge and perceptions of caregivers. Future research should also assess how knowledge and perceptions among adolescent contacts affect preventive therapy completion.

Our study is subject to several limitations. Caregiver responses could have been affected by incomplete recall or recall bias. However, we were able to verify some information, such as IPT completion and the occurrence of AEs, from medical records. Also, because of the timing of the survey, the knowledge and perceptions reported during the survey may not reflect the situation while the children were taking IPT, and it is difficult to speculate on possible causal mechanisms. Social desirability bias could have made caregivers reluctant to express negative opinions about the importance of IPT or satisfaction with health services. We attempted to mitigate this risk by administering the surveys in participants' homes, ensuring confidentiality, and training the survey administrators to ask questions in a standardized manner.

# **CONCLUSION**

Our findings suggest that health systems should prioritize education and counseling among caregivers of child contacts receiving IPT. Education and counseling could help caregivers better understand the importance of IPT in preventing TB disease and promote positive relationships between families affected by TB and the health system. Increased understanding and positive relationships could in turn support IPT adherence and the monitoring of AEs. Ultimately, increasing the effective use of IPT will help reduce TB morbidity and mortality among children.

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**CONTEXTE** : Quarante-six centres de santé au Sud de Lima, Pérou. **OBJECTIF** : Evaluer l'association entre les connaissances et les perceptions relatives au traitement préventif par l'isoniazide (TPI) des responsables des enfants et le fait que leurs enfants aient achevé le TPI.

SCHÉMA : Nous avons réalisé une revue rétrospective des dossiers médicaux des enfants qui ont démarré le TPI entre 2017 et 2018. Nous avons administré aux responsables des enfants des questionnaires structurés relatifs à leurs connaissances et perceptions du TPI. Nous avons utilisé une régression de Poisson modifiée afin de déterminer les facteurs associés à l'achèvement du TPI.

**RÉSULTATS** : Nous avons inclus 500 enfants dont 31% n'ont pas achevé le TPI. Les facteurs indépendants associés au non achèvement 31 Snow K, et al. Tuberculosis in adolescents and young adults: epidemiology and treatment outcomes in the Western Cape. Int J Tuberc Lung Dis 2017; 21(6): 651-657.

étaient faibles connaissances relatives à la TB et au TPI (risque relatif ajusté [RRa] 1,41 ; IC 95% 1,06-1,78), faibles perception par les responsables de l'importance du TPI (RRa 1,76 ; IC 95% 1,30-2,39), faible taux de satisfaction des responsables par rapport aux services de santé (RRa 1,57 ; IC 95% 1,14-2,16), survenue d'effets secondaires (RR 2,08 ; IC 95% 1,51-2,87) et dysfonction familiale modérée ou grave (RRa 1,53; IC 95% 1,07-2,19).

CONCLUSION : L'achèvement du TPI chez les enfants a été associé aux connaissances et perceptions de leurs responsables, ainsi qu'à la survenue d'effets secondaires. Pour améliorer l'achèvement du TPI chez les enfants, les prestataires de soins de santé devraient accorder la priorité à l'éducation des responsables, promouvoir des relations inter personnelles positives avec eux et surveiller les effets secondaires.

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