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# Clinical and economic impact of medication non-adherence in drug-susceptible tuberculosis: a systematic review

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## SUMMARY

**BACKGROUND:** Despite considerable efforts to globally eradicate TB, and the availability of effective antibiotics, TB elimination goals are falling behind. While non-adherence to TB drug regimens may compromise effective treatment, its full impact is still unknown.

**OBJECTIVE:** To determine the clinical and economic impact of non-adherence to TB medication on treatment outcomes in drug-susceptible TB patients (DS-TB).

**METHODS:** A systematic review was performed using PubMed and Embase for studies published between 2009 and 2019 reporting associations between adherence and WHO-defined TB treatment outcomes and economic outcomes in DS-TB patients.

**RESULTS:** A total of 14 studies were included. Eight focused on the association between non-adherence and

death, 2 on treatment failure, 1 study on successful treatment outcome, 1 study on both successful and unsuccessful treatment outcomes and 2 on cost outcomes. Most studies (71.4%) were retrospective cohort or case-control studies. The results showed that non-adherence to TB drug regimens was associated with death, treatment failure and lower cure rates.

**CONCLUSION:** Non-adherence to TB drugs has a profound impact on both clinical and economic TB outcomes. To reach WHO TB elimination goals, preventing non-adherence and the implementation of cost-effective intervention programmes should receive the highest priority.

**KEY WORDS:** medication adherence; outcomes; failure; cure; tuberculosis

DESPITE THE EXISTENCE of effective TB medications, TB continued to be the primary cause of death of almost 1.3 million people worldwide in 2017.<sup>1</sup> Besides increasing access to TB medicines, monitoring of treatment, including adherence and outcomes, is crucial to achieve global TB control. A treatment success rate of  $\geq 85\%$  was defined as the target for global TB control.<sup>1</sup>

One of the main barriers to achieving favourable treatment outcomes is drug non-adherence.<sup>2,3</sup> Adherence is defined as ‘the extent to which a person’s behaviour to take medicines, to follow a diet, and/or to execute lifestyle changes corresponds with agreed recommendations from a healthcare provider’.<sup>4</sup>

Non-adherent patients cannot gain optimal benefits of their medication. According to recent studies in

non-communicable chronic diseases, non-adherence is associated with worsening conditions, mortality, poorer quality of life and reduction in work productivity.<sup>5,6</sup> To achieve the goal of eradicating TB worldwide, it is crucial to improve adherence to treatment among patients. In order to enhance adherence, the importance of providing directly observed therapy (DOT) has been emphasised by the WHO. Two recent systematic reviews, however, showed contrasting effects of DOT, where one found that DOT did not have any significant effect on treatment outcomes compared to self-administered treatment (SAT) and the other did.<sup>7,8</sup> This may partly explain the low implementation rates for DOT; however, poor awareness on the impact of non-adherence may also play a role. In order to accelerate

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the implementation of adherence-enhancing interventions and public health actions, there is a need for systematic and comprehensive evidence on the full societal impact of non-adherence on both clinical and economic parameters. In this systematic review, we aimed to focus on the full clinical and economic impact of non-adherence to TB drug regimens in drug-susceptible TB (DS-TB) patients.

## METHODS

### *Study design*

This systematic review was reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.<sup>9</sup> The protocol of this study was prospectively registered in the PROSPERO database (<https://www.crd.york.ac.uk/prospéro>) under registration number: CRD42018112142. As this systematic review involved data from published studies, ethics clearance and written informed consent were not required.

### *Data sources and search strategy*

A systematic search of the PubMed and Embase databases was conducted using a combination of TB disease, adherence, medication, outcome and study design terms for articles published between January 2009 and September 2019 (for details, see Supplementary Data Section 1). The focus of this systematic review was the clinical impact of non-adherence. As economic studies are not always registered in medical databases, a separate, secondary targeted search was performed to investigate the economic consequences of non-adherence to TB medication (Supplementary Data Section 2).

### *Study selection*

Randomised controlled trials (RCTs) and observational studies (cohort, case-control and cross-sectional) reporting both adherence and treatment outcomes as defined by WHO guidelines<sup>10</sup> (Supplementary Table S1) in patients treated for DS-TB were included. DS-TB patients were classified as confirmed DS-TB patients, who were susceptible to all first-line anti-TB drug based on the drug susceptibility testing (DST), and presumed cases, who were treated with first-line anti-TB drugs without DST results.<sup>10</sup> There was no restriction on language or geographical area. Papers without a clear definition of the allowed treatment gap to consider someone non-adherent were excluded. Review articles, commentaries, conference abstracts, editorials and animal studies were also excluded. Of note, treatment interruption was defined as incomplete treatment due to side effects and/or non-adherence;<sup>11</sup> in this systematic review, we focused only on non-adherence. A similar process was followed in the

selection of papers reporting on the association of non-adherence with economic outcomes.

All titles, abstracts and finally full texts were retrieved and reviewed independently by RAC and FG. Any discrepancies were resolved by discussion; in case no consensus was reached, a third reviewer was consulted (ISP). Potentially relevant references of the included studies were hand searched and assessed by the first reviewer (RAC), and rechecked by the second reviewer (FG). All of these screening steps were conducted using Rayyan QCRI, a web application for systematic reviews (<https://www.rayyan.qcri.org>).<sup>12</sup>

### *Data extraction*

Using a pre-defined template, one researcher (RAC) first extracted data on study characteristics, population characteristics, duration of follow-up, treatment regimens, definition and measurement of treatment adherence, and relationship between treatment non-adherence and treatment outcomes; this was then checked by the second reviewer (FG).

### *Quality assessment*

The quality of the included studies was assessed using the Newcastle–Ottawa Scale (NOS) for observational studies<sup>13</sup> in terms of selection, compatibility between cases and controls, and outcomes or exposures by two reviewers (RAC and FG). Inter-reviewer differences were discussed and resolved by consensus: in case no consensus could be reached, a third reviewer was consulted (ISP). (Supplementary Table S2).

## RESULTS

### *Study selection*

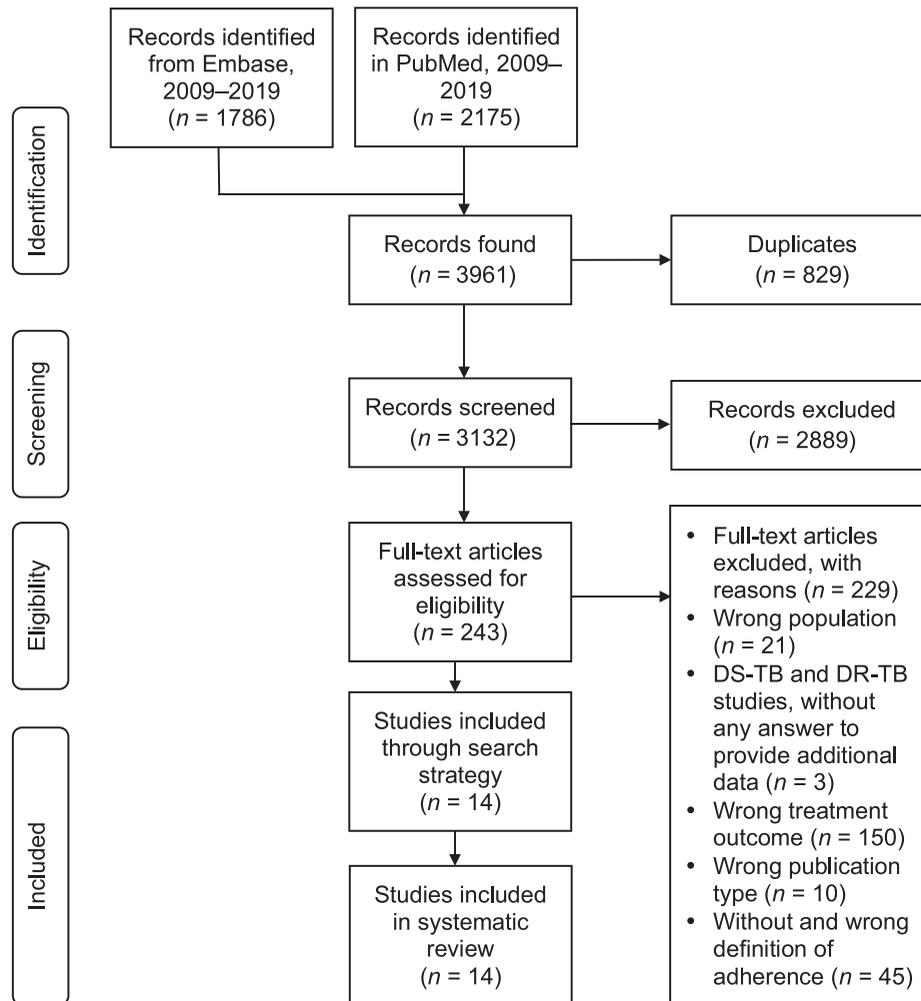
The PubMed and Embase searches for clinical studies yielded a total of 3000 articles. After the examination of 211 full-text manuscripts, 12 articles on adherence and clinical outcomes were included. Reference checking of the included studies provided no additional articles. The search for studies evaluating economic impact yielded two additional articles, resulting in a total of 14 articles (Figure 1).

### *Study characteristics*

Characteristics of the 12 eligible clinical impact articles are given in Table 1. Most of the studies were retrospective.<sup>11,14–21</sup> Population sizes ranged from 83 to 2416 patients, with mean age varying between 32.7 and 61.2 years.<sup>18,22,23</sup> The number of males was higher than females in all but two studies.<sup>14,19</sup> Patients were mostly treated using a daily dosage of isoniazid, rifampicin, pyrazinamide and ethambutol.<sup>15–17,23</sup>

### *Treatment adherence*

Definitions of treatment non-adherence varied across studies, but non-adherence was mostly defined as missing <90% of the prescribed doses<sup>16,17,21</sup> or



**Figure 1** Selection process of the clinical and economic studies included in the review. DS-TB = drug-susceptible tuberculosis; DR-TB = drug-resistant tuberculosis.

<80% of the prescribed doses.<sup>18,23</sup> Measurements of adherence also varied, from reviewing treatment charts or pill counts<sup>14–17,23,24</sup> to self-reports.<sup>23</sup> In one study, non-adherence mostly occurred in the first months of the treatment, probably due to the improvement in clinical symptoms at the beginning of the treatment.<sup>22</sup> In contrast, in Chirwa et al.'s study,<sup>24</sup> non-adherence in the continuation phase was more common compared to the intensive phase (22.9% vs. 20.4%).

#### Treatment outcomes

Most of the studies ( $n = 12$ ) reported unsuccessful treatment (death and treatment failure) as clinical outcomes.<sup>11,14,23,15–22</sup> Of these, 8 studies reported death,<sup>11,14,16–21</sup> 2 reported treatment failure,<sup>15,23</sup> and 2 articles focused on the association of non-adherence with successful treatment outcome<sup>22,24</sup> (Figure 2 and Supplementary Table S4).

#### Treatment non-adherence and death

Of the nine studies evaluating the impact of non-adherence on death, seven showed a significantly

increased risk of death in non-adherent patients. To note, two studies were carried out in TB-HIV co-infected patients.<sup>19,21</sup> Essomba et al. considered non-adherence as a significant risk factor for death in TB-HIV co-infected patients, where the probability of death in non-adherent patients was 22.8 times higher than in adherent patients.<sup>19</sup> Similarly, Zheng et al. reported a 4.5 times higher risk of death in TB-HIV co-infected patients with unsatisfactory adherence than in those with satisfactory adherence.<sup>21</sup>

Among TB patients without HIV coinfection, a study by Finlay et al. reported a higher proportion of death in the non-adherent group than in the adherent group (23% vs. 16%),<sup>20</sup> and in Kayigamba et al.'s study,<sup>16</sup> more patients died in the non-adherent group than in the adherent group (23% vs. 11%). Similarly, a study among hospitalised patients showed that non-adherent patients had a 13.42 times higher risk of death than adherent patients.<sup>17</sup> A study of TB patients with or without diabetes mellitus reported that poorly adherent patients were 2.11 times more likely to die than adherent patients.<sup>18</sup> In another

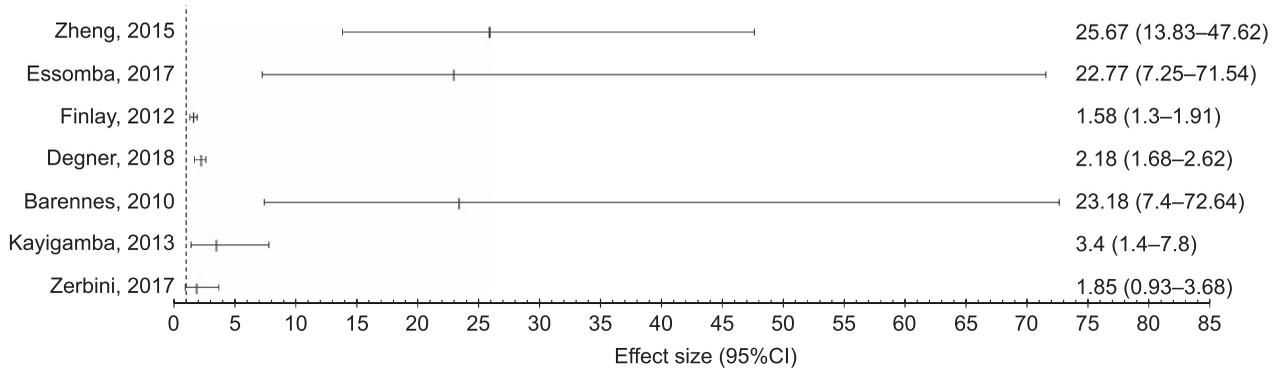
**Table 1** Characteristics of studies reporting clinical and economic outcomes associated with adherence to TB treatment

Author country, year	Study design (follow-up)	Population	Medication*	Definition	Method of the measurement	Reported outcome associated with adherence						
						Adherence	Cure	Completed	Success	Failed	Death	Cost
Zerbini, Argentina, 2017 <sup>14</sup>	Retrospective case control	(n = 438) Mean age: 58 years (range: 19–94) Male: 56.7% Majority age: <32 years Males: 61.3%	Not specified	Patients who took recommended doses were considered adherent	Treatment cards				X			7
Namukwaya, Uganda, 2011 <sup>15</sup>	Retrospective case control	(n = 150) Majority age: <32 years Males: 61.3%	2RHZE/6EH	Interruption >2 consecutive weeks or missing the scheduled appointment within a week on two or more occasions Taking ≥90% of doses	Meticulous history taking and interviewing patients, cross-checked using treatment cards			X				7
Kayigamba, Rwanda, 2013 <sup>16</sup>	Retrospective cohort	(n = 581) Median age: 31 (IQR: 25–41) Males: 61.8% (n = 172) Mean age: 46.9 years (SD 16.9) Males: 65.7% (n = 2416) Mean age: 61.2 years (SD 20.0) Males: 68.3%	2RHZE/4RH	Taken at least 90% of the prescribed number of tablets days	Treatment charts			X				8
Barenes, Lao PDR, 2010 <sup>17</sup>	Retrospective cohort (8 months)	(n = 172) Mean age: 46.9 years (SD 16.9) Males: 65.7% (n = 2416) Mean age: 61.2 years (SD 20.0) Males: 68.3%	2RHZE/6HE, 2SRHZ/6HE and others	Completed >80% of a 6-month TB treatment regimen within 9 months of TB treatment initiation or completing >80% of TB treatment until death	Pill counts and cross-checked with monthly visit data of district hospital Not specified			X				4
Degner, Taiwan, 2018 <sup>18</sup>	Retrospective cohort	(n = 1164) Median age: 30–39 years, depending on treatment group (mean not reported) Males: 57.65% (n = 96) Mean age: 32.7 years Males: 52%	1–8 weeks HRZE/18 weeks HR 2–8 weeks HRZE/18 weeks H <sub>3</sub> R <sub>3</sub> 3–8 weeks H <sub>3</sub> R <sub>3</sub> E <sub>3</sub> /18 weeks H <sub>3</sub> R <sub>3</sub> 4–7 days/week for 14 doses, then twice weekly HRZE/18 weeks H <sub>2</sub> R <sub>2</sub> FDC: New cases: 6 months HRZE Retreated cases: 8 months HRZES	Interruption ≥ 2 consecutive months	Interview with structured questionnaire			X				3
Finlay, South Africa, 2012 <sup>20</sup>	Retrospective case control	(n = 394) Mean age: 39 years (SD 10) Males: 45.9%	2RHZE/6HE	Five categories: fully adherent, missed <20% of doses, missed about one half of the doses, missed most doses, and not adherent at all	Chart review (monthly home visit), monthly pill count and self-reporting			X				6
Kirenga, Uganda, 2014 <sup>23</sup>	Prospective cohort (2 years)	(n = 96) Mean age: 32.7 years Males: 52%	2RHZE/6HE	1) Missed >1 dose during last week before the PSA encounter or missed ≥1 week during last month before the start of encounter, 2) Ratio between the number of prescriptions dispensed and the theoretical number of orders expected <0.95	Questionnaire			X				7
Essomba, Cameroon, 2017 <sup>19</sup>	Retrospective (6 months from treatment initiation)	(n = 394) Mean age: 39 years (SD 10) Males: 45.9%	Not specified	Interruption in the prescribed regimen of any duration that resulted in <3 anti-TB drugs during the intensive phase or <2 anti-TB medications in the continuation phase	Medical records			X				8
Nahid, USA, 2011 <sup>11</sup>	Retrospective cohort (18 months)	(n = 565) Mean age: 40.98 years Males: 80%	1–8 weeks HRZE/18 weeks HR 2–8 weeks HRZE/18 weeks H <sub>3</sub> R <sub>3</sub> 3–8 weeks H <sub>3</sub> R <sub>3</sub> E <sub>3</sub> /18 weeks H <sub>3</sub> R <sub>3</sub> 4–7 days/week for 14 doses, then twice weekly HRZE/18 weeks H <sub>2</sub> R <sub>2</sub>	Interruption in the prescribed regimen of any duration that resulted in <3 anti-TB drugs during the intensive phase or <2 anti-TB medications in the continuation phase	Medical records			X				8

Table 1 (continued)

Author country, year	Study design (follow-up)	Population	Medication*	Definition	Method of the measurement	Reported outcome associated with adherence					
						Cure	Completed	Success	Failed	Death	Cost
Viegas, Brazil, 2017 <sup>22</sup>	Prospective cohort	(n = 83); Mean age: 42.19 years Males: 59.0%	FDC of RHZE/RH	High adherence: Morisky scale score: 8 Average adherence: 6–8 Low adherence: <6	Morisky scale (in three interviews: 1, end of Month 1; 2, end of Month 2; 3, end of Month 6)	X			X		4
Chirwa, Malawi, 2013 <sup>24</sup>	Descriptive	(n = 524); Mean age: 36 years (SD 12.4) Males: 57.6%	FDC: New cases: 2HRZE/4HR Retreatment cases: 2HRZE/4HR + S	Actual number of days of missed treatment (for any duration)	Treatment cards (hospitalised records for 2 initial weeks of treatment and community DOT or hospital DOT for the rest of the treatment) Clinical records	X					6
Zheng, China, 2015 <sup>21</sup>	Retrospective (1 year)	(n = 519); Median age: 46 years; Males: 84.39%	2H <sub>3</sub> R <sub>3</sub> Z <sub>3</sub> E <sub>3</sub> /4H <sub>3</sub> R <sub>3</sub> 2HRZE/4HR 2H <sub>3</sub> R <sub>3</sub> Z <sub>3</sub> E <sub>3</sub> S <sub>3</sub> /6H <sub>3</sub> R <sub>3</sub> E <sub>3</sub> and other regimens (not specified) Daily fixed-dose 2HRZE/4RH Daily dose 2RHZ/4RH	Completing >90% of prescribed doses is defined as adherence	Clinical records				X		7
Budgeell, South Africa, 2018 <sup>25</sup>	Retrospective cohort study (median: 6.4 months)	(n = 88); Median age: 4 years; Males: 55.7%	Daily fixed-dose 2HRZE/4RH Daily dose 2RHZ/4RH	Interruption >2 consecutive months	TB clinic cards					X	6
Lei, China, 2016 <sup>26</sup>	Prospective cohort study (6 months)	(n = 481); Median age: 39 years; Males: 67.8%	2H <sub>3</sub> R <sub>3</sub> Z <sub>3</sub> E <sub>3</sub> /4H <sub>3</sub> R <sub>3</sub>	Missed ≥1 dose of drugs or follow-up appointment	Self-design questionnaires cross-checked by patients' treatment cards					X	9

\* Numbers before the letters indicate the duration in months of the phase of treatment; numbers in subscript indicate the number of times the drug is taken each week. TB = tuberculosis; NOS = Newcastle-Ottawa Scale; R = rifampicin; H = isoniazid; E = ethambutol; Z = pyrazinamide; IQR = interquartile range; SD = standard deviation; S = streptomycin; FDC = fixed-dose combination; PSA = psychosocial agents; DOT = directly observed treatment.



**Figure 2** Death associated with adherence to tuberculosis treatment. CI = confidence interval.

study, Nahid et al. investigated the causes of death in pulmonary DS-TB patients.<sup>11</sup> They found that non-adherent patients (56.8%) had a significantly increased rate of death compared to adherent patients (20.8%) during the intensive phase of treatment (hazard ratio, 3.2). They did not find a statistically significant association in the continuation phase, although the number of deaths in non-adherent patients during the continuation phase was numerically higher (30.3% vs. 20.7%).

In contrast, a small study by Viegas et al. reported no significant association between non-adherence and death. In their study, most of the patients adhered to treatment, and 2.4% of patients died because of the non-TB-related causes.<sup>22</sup> A study among pulmonary and extrapulmonary TB patients with or without HIV coinfection reported a non-significant association between death and treatment non-adherence.<sup>14</sup>

#### Non-adherence and treatment failure

Two studies evaluated the association between non-adherence and treatment failure (for definitions, see Supplementary Table S1). Namukwaya et al. showed that poorly adherent patients had a 14.7 times higher risk of treatment failure than adherent patients.<sup>15</sup>

Likewise, in hospitalised TB and TB-HIV co-infected patients, more non-adherent patients failed treatment than adherent patients (25% vs. 21%).<sup>23</sup>

#### Non-adherence and treatment success

Two articles describing the association between adherence and treatment success were identified. Chirwa et al. showed that the proportion of non-adherent patients who achieved cure during the intensive phase of treatment was 9.6 times lower than those who fully adhered to treatment.<sup>24</sup> However, the number of missing doses during the continuation phase had no significant influence on the cure.<sup>24</sup> Viegas et al. reported a lower cure rate in Brazilian TB patients with low adherence (4.8%) and average adherence (10.8%) than in patients with high adherence (61.5%).<sup>22</sup>

#### Adherence and cost consequences

Two studies reporting the association between adherence and costs were identified (Tables 1 and 2). Budgell et al. showed that among children and adolescents the average treatment costs for one non-adherent patient was US\$33.81 lower than adherent patients (US\$108.86 vs. US\$142.67).<sup>25</sup> In this study, the costs of medication, laboratory tests, outpatient

**Table 2** Economic outcomes associated with adherence to tuberculosis treatment

Study	Non-adherent Cost (Patients, n)	Adherent Cost (Patients, n)	Relative outcomes	Significance P value	Additional information
Budgell <sup>25</sup>	US\$15.93 (1)	US\$27.65 (79)	NR	NR	Medication cost
	US\$0.00 (1)	US\$8.62 (79)	NR	NR	Laboratory monitoring tests
	US\$38.21 (1)	US\$43.74 (79)	NR	NR	
	US\$54.73 (1)	US\$62.66 (79)	NR	NR	Outpatient visits
	US\$108.86 (1)	US\$142.67 (79)	NR	NR	Fixed cost
Lei <sup>26</sup>	≤RMB 450 (74)	≤RMB 450 (172)	aOR: 2.08 (1.35–3.19)	<0.001	Average treatment cost
	>RMB 450 (99)	>RMB 450 (136)			Monthly treatment (median cost: RMB 450, including self-paid TB drugs, liver protecting drugs, cough remission drugs, travelling, accommodation and nourishment)

NR = not reported; aOR = adjusted odd ratio; RMB = renminbi.

visits and fixed costs (rental cost of the health care centre, the facilities and staff salaries) were respectively US\$11.72, US\$8.62, US\$5.53 and US\$7.93 higher in adherent patients. In contrast, in another study, patients with higher total treatment costs were more likely to be non-adherent. Treatment costs was defined as direct costs of self-paid TB drugs, liver protecting and cough remission drugs, travelling and accommodation.<sup>26</sup>

## DISCUSSION

### *Main findings*

The vast majority of reviewed studies showed significantly higher risks of death, treatment failure and decreased cure rates among drug non-adherent than adherent DS-TB patients. Although the findings of two studies were non-significant due to limited power and small sample sizes,<sup>14,22</sup> these agreed with the other studies. Measurement of drug adherence was most commonly conducted by assessment of treatment charts during hospital or home visits. Although this is a simple and cheap method, especially in large populations, the reliability of these data depend on the quality of registration at the health centre.<sup>27</sup> For example, in one study,<sup>11</sup> 135 of 700 patients were excluded due to incomplete medical records, and this could result in an underestimation of the outcomes.

According to most studies, there was a significant association between the degree of adherence and outcomes. However, in some cases, incomplete information on HIV status, multidrug-resistant TB and severity of TB<sup>14–18,24</sup> may have confounded this association. It is therefore difficult to rule out the effects of these variables on the outcomes, and this may have led to an overestimation of the impact of non-adherence on treatment outcomes.

Of note, our results indicate an association between the timing of non-adherence and treatment outcomes. In Nahid et al.,<sup>11</sup> non-adherence during the intensive phase of treatment was significantly related to death but this was not the case in the continuation phase. These findings are in line with another study,<sup>24</sup> in which patients non-adherent in the intensive phase were less likely to be cured than those non-adherent in the continuation phase of the treatment. These findings could be explained by the higher importance of the bactericidal mechanism during the intensive phase than in the continuation phase, as the rate of bactericidal activity is higher immediately after the start of the treatment.<sup>28</sup>

Regarding the association between adherence and economic outcomes, the evidence was mixed. In one small study ( $n = 80$ ), treatment costs were lower in non-adherent patients; however, only one patient was non-adherent, making equal comparisons between groups difficult.<sup>25</sup> Since adherence to medi-

cation in this study increased the medication cost, outpatients visit and laboratory costs, study findings highlighted the importance of financial support in increasing treatment adherence, and subsequently achieving better treatment outcomes. In a larger prospective study, the total (pharmaceutical and non-pharmaceutical) treatment costs were higher in non-adherent patients.<sup>26</sup> Given the lack of details on the specifics of the treatment costs (e.g., severity of TB, hospitalisations and additional medications), it is difficult to quantify the exact economic impact of non-adherence. More studies on the economic impact of non-adherence to TB treatment are therefore required.

### *Limitations*

Following a rigorous and systematic approach, this review is the first to provide insights into the full clinical and economic impact of non-adherence to TB medication in DS-TB patients. Nevertheless, our review had some limitations that need to be discussed. First, due to the scarcity of studies in this particular field, we did not limit our study selection to specific high-quality study designs, methodologies or adherence definitions. Therefore, the data obtained were extremely heterogeneous, which made it difficult to synthesise quantitative results and perform a meta-analysis. Only a descriptive data synthesis based on preliminary searches and expert opinion of the authors could be performed. Of note, efforts are currently being made to standardise the adherence taxonomy in respiratory medicine, but this is not accepted by all researchers in the field of TB.<sup>29</sup> Second, in order to focus on the impact of non-adherence in terms of recent TB drug regimens and treatment outcomes as defined by WHO, we limited the studies to the last decade, and this may have excluded relevant historical studies. Finally, the low number of articles reporting on the association between non-adherence and costs made it difficult to draw firm conclusions; however, we have added the economic consequences of non-adherence to this systematic review to emphasise the important role played by financial support in increasing adherence and in encouraging further investigation into the economic aspects of non-adherence.

### *Implications for future research, policy and practice*

Given that non-adherence to TB treatment has been strongly associated with worse outcomes, it is of utmost importance to identify factors that lead to non-adherence and provide effective and cost-effective adherence-enhancing interventions. It should be noted that interventions to enhance adherence to TB treatment include directly observed therapy (DOT), digital health technologies such as video-observed therapy (VOT), educational strate-

gies and financial incentives.<sup>30,31</sup> Specific vulnerable groups of patients to be targeted include older patients, HIV-TB co-infected patients, TB patients with comorbidities and low-income patients.<sup>32</sup> Furthermore, as most unsuccessful treatment outcomes are associated with non-adherence during the intensive phase,<sup>11,24</sup> it is especially important to focus efforts on this phase.

Looking ahead, more evidence on the temporal association between the duration of non-adherence to TB treatment and the occurrence of outcomes is required.<sup>33</sup> Such studies may help to set a standard definition for clinically relevant non-adherence, which will lead to the harmonisation of future studies and more precise results. Also, we recommend that prospective studies in larger populations of TB patients be conducted, as this design is less prone to missing data and selection bias.

In conclusion, there is a clear association between non-adherence to TB treatment and both clinical and economic outcomes in patients with DS-TB. Non-adherence to TB medication requires increased attention from healthcare providers and policy makers alike.

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Conflicts of interest: none declared.

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**R É S U M É**

**CONTEXTE :** En dépit d'efforts considérables d'éradication de la TB, et de la disponibilité d'antibiotiques efficaces, les objectifs d'élimination de la TB ont pris du retard. Si la non adhérence aux protocoles de médicaments de la TB est susceptible de compromettre l'efficacité du traitement, son impact d'ensemble reste inconnu.

**OBJECTIF :** Déterminer l'impact clinique et économique de la non observance des médicaments de la TB sur les résultats du traitement parmi les patients TB pharmacosensibles (DS-TB).

**MÉTHODE :** Une revue systématique a été réalisée sur PubMed et Embase à la recherche d'études, publiées entre 2009 et 2019, rapportant des associations entre adhérence et résultats du traitement définis par l'OMS et des résultats économiques chez des patients DS-TB.

**RÉSULTATS :** Au total, 14 études ont été incluses. Huit

étaient focalisées sur l'association entre non adhérence et décès ; deux, sur l'échec du traitement ; une étude sur les bons résultats du traitement ; une étude à la fois sur les bons et mauvais résultats du traitement et enfin deux sur les résultats en termes de coût. La majorité des études (71,4%) ont été des cohortes rétrospectives ou des études cas témoins. Les résultats ont montré que la non adhérence aux protocoles de traitement de la TB avait été associée au décès, à l'échec du traitement et à des taux de guérison plus faibles.

**CONCLUSION :** La non adhérence aux médicaments de la TB a un impact profond à la fois sur les résultats cliniques et économiques de la TB. Si l'on veut atteindre les objectifs OMS d'élimination de la TB, la prévention de la non adhérence et la mise en œuvre de programmes d'intervention rentables devraient bénéficier de la plus haute priorité.

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**RESUMEN**

**MARCO DE REFERENCIA:** Pese a los esfuerzos notables para erradicar la TB en el mundo y la disponibilidad de antibióticos eficaces, las metas de eliminación de la TB están retrasadas. El incumplimiento de las pautas terapéuticas de la TB pone en peligro la eficacia del tratamiento, pero se desconoce su repercusión total.

**OBJETIVO:** Determinar las repercusiones clínicas y económicas del incumplimiento del tratamiento contra la TB sobre los desenlaces terapéuticos en pacientes con TB farmacosenible (DS-TB).

**MÉTODO:** Se realizó una revisión sistemática en PubMed y Embase de los estudios publicados del 2009 al 2019, que comunicaban la asociación entre el cumplimiento terapéutico y los desenlaces del tratamiento de la TB como los define la OMS y los resultados económicos en pacientes con DS-TB.

**RESULTADOS:** Se incluyeron 14 estudios. Ocho se centraban en la asociación entre el incumplimiento

terapéutico y la muerte, dos en el fracaso del tratamiento, un estudio en el éxito del tratamiento, un estudio en los resultados favorables y desfavorables del tratamiento y dos estudios en los resultados de costos. La mayoría (71,4%) eran estudios de cohortes retrospectivos o estudios de casos y testigos. Los resultados demostraron que el incumplimiento de las pautas de tratamiento de la TB se asociaba con la muerte, el fracaso terapéutico y tasas de curación más bajas.

**CONCLUSIÓN:** El incumplimiento del tratamiento de la TB tiene consecuencias mayores tanto en los resultados clínicos como en los económicos. Con el objeto de cumplir las metas de la OMS de eliminación de la TB es necesario atribuir la más alta prioridad a la prevención del incumplimiento y la ejecución de programas costoeficaces.

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