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Catastrophic cost among multi-drug resistant tuberculosis patients in Japan: first national survey

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Abstract

Background

Multi-drug resistant tuberculosis (MDR-TB) remains a major global health concern, often contributing substantially to financial hardship among patients and their households. World Health Organization (WHO) defines catastrophic TB cost as a total cost of TB diagnosis and treatment above 20% of household's annual income. This study aimed to quantify direct and indirect costs associated with MDR-TB treatment and determine the proportion of affected households experiencing catastrophic expenditures for the first time in Japan.

Methods

This was a cross-sectional study following the WHO protocol for TB cost survey. Eligible patients were recruited via medical facilities, and were interviewed face-to-face, using the modified WHO questionnaire. Direct and indirect costs were calculated for pre-diagnosis phase, standard treatment phase and MDR-TB treatment phase, and the proportions of those facing catastrophic cost were estimated. Participants were also asked about effect on employment/study and coping strategies.

Results

A total of 27 participants were enrolled across seven facilities. The mean age was 45.2 years (± 20.4; range 20–83), and 48.1% were male. Among the 23 participants for whom cost estimation was possible, the mean total cost was 1,164,856 JPY (7,766 USD). Indirect costs accounted for 53.4% of total costs (mean 622,174 JPY). MDR-TB treatment medical costs constituted the largest direct cost component (27.1%, mean 315,766 JPY). Mean pre-TB annual household income was 3,421,565 JPY (22,811 USD). Twelve of 23 participants experienced catastrophic costs. Prior to diagnosis, 16 were employed, among whom five became unemployed. Participants also reported multiple coping strategies, including reducing non-food expenditure and food expenditure. Five participants received financial support or loans from family or acquaintances. Borrowed amounts ranged from 320,000 to 2,000,000 JPY (2,100–13,300 USD).

Conclusions

Catastrophic costs affected more than half of households despite universal health insurance and a TB-specific public subsidy framework in Japan. The burden was driven by direct medical costs for MDR-TB treatment and by income loss during prolonged treatment. Targeted reforms are needed, including extension of the TB-specific subsidy to encompass all core MDR-TB drugs, accelerated adoption of shorter regimens, and strengthened income protection for economically vulnerable patients.

Background

Multi-drug resistant tuberculosis (MDR-TB) remains a major global health concern, with an estimated 390,000 new cases in 2024 (1). MDR-TB requires prolonged, toxic, and costly treatment, contributing substantially to morbidity, mortality, and financial hardship (2). World Health Organization (WHO) defines catastrophic TB cost as a total cost (direct and indirect) of TB diagnosis and treatment above 20% of patient's household annual income (3). Between 2015 and 2025, cost surveys using WHO's protocol have been conducted and reported from 40 countries, though exclusively in high- and middle-TB-burden countries, and these studies have shown that a pooled 47% and 81% of affected households experience catastrophic costs related to treatment expenses for drug-susceptible (DS) TB and MDR-TB, respectively (1).

In high-income countries with universal health coverage and social protection schemes, however, the extent to which these systems prevent catastrophic costs remains unclear. Japan is a low-TB burden country – in 2024, 10,051 people were newly notified with active TB, of whom 45 were diagnosed as culture-confirmed MDR-TB (4). It has universal health insurance (5) and a TB-specific public subsidy provided under the Infectious Diseases Control Law (6). Hence, cost related to pre-diagnosis care seeking is covered under the national insurance, with patients typically paying 10 to 30% of medical costs, and once diagnosed, TB-specific subsidy covers 100% of TB-related medical costs during hospitalization, and 95% during outpatient care, with the remaining 5% covered by the national health insurance. Some local governments, such as Tokyo, further provide additional MDR-TB subsidies (7), and Japan's high-cost medical expense benefit system caps monthly out-of-pocket expenditures at income-tiered thresholds (8).

However, several structural features of MDR-TB care in Japan may limit the effectiveness of these protections. Firstly, MDR-TB treatment is centralized in designated specialist hospitals, often requiring patients to be referred across multiple institutions during their diagnostic and treatment course, and consequently, long-distance travel (9). Secondly, while Xpert MTB/RIF assay is reimbursed under the national health insurance and has been adopted at some designated hospitals, culture-based drug susceptibility testing remains the diagnostic standard, meaning patients frequently begin standard treatment before switching to MDR-TB regimens. Thirdly, MDR-TB treatment continues to rely primarily on individualized, longer regimens, generally extending to at least 18 months after culture conversion. Although recent Japanese recommendations acknowledge WHO-endorsed shorter all-oral regimens, their implementation remains limited (10). Several core drugs used internationally, such as clofazimine and linezolid, are not registered as anti-TB drugs in Japan and are therefore excluded from the TB-specific subsidy, leaving patients subject to the standard national health insurance co-payments of 10 to 30% rather than the nominal 5% patient share. Pretomanid is unavailable, and bedaquiline and delamanid, although subsidized, are priced substantially higher than internationally procured equivalents (11) - for example, the direct daily drug cost of delamanid for an adult MDR-TB patient in Japan is approximately 160 USD per day (based on the National Health Insurance listed price of Japanese Yen (JPY) 5,999.2 per 50 mg tablet, at a standard dose of 100 mg twice daily) (12), meaning MDR-TB

patients in Japan may face drug costs for delamanid up to approximately 20 times higher than those available through the Stop TB Partnership's Global Drug Facility (GDF) international procurement mechanism.

These structural characteristics raise concerns about whether Japan's financial protection mechanisms adequately prevent catastrophic costs among MDR-TB patients, and particularly, among the socioeconomically vulnerable groups. To date, no systematic assessment has evaluated catastrophic costs among MDR-TB patients in Japan. This study therefore aimed to quantify direct and indirect costs associated with MDR-TB treatment and determine the proportion of affected households experiencing catastrophic expenditures.

Methods

Study design and participants

This was a cross-sectional study following the WHO protocol for TB cost survey published in 2017 (13). Participants were recruited through medical facilities participating in the Tuberculosis Research Committee, a long-standing multicenter clinical research network in Japan composed of medical institutions involved in national anti-TB drug resistance surveys (14). For this study, 7 medical facilities, located in Fukuoka, Nagoya, Osaka (two facilities), and Tokyo (three facilities), were invited to collaborate and refer eligible patients. As the designated hospitals in Tokyo also receive MDR-TB referrals from northern Japan, these facilities collectively managed approximately half of all MDR-TB patients nationally, providing reasonable geographic coverage.

Individuals were eligible if they were aged ≥ 18 years, had received MDR-TB treatment for at least two weeks at the time of interview, and provided written informed consent. Eligible participants were identified and referred by attending physicians. Because Japan's national TB programme mandates a two-year post-treatment follow-up, patients who had completed MDR-TB treatment but remained under follow-up were also eligible to maximize enrolment. Recruitment took place between 1 March 2024 and 30 June 2026.

Data collection

The questionnaire based on the WHO protocol for TB patient cost survey (13) was adapted to Japan's MDR-TB context and translated into Japanese (see supplementary file). LK, KU and KS conducted face-to-face structured interviews using paper-based questionnaires, with professional medical interpreters arranged for foreign-born participants when needed, at the hospital where patients were receiving treatment or follow-up care. Participants were asked to bring medical receipts and any documentation of direct or indirect costs to the interview. Because MDR-TB treatment is prolonged, participants interviewed early in treatment phase were invited to participate in a second interview to reduce recall

bias and capture any changes in socioeconomic circumstances. When a second interview was conducted, cost data from the first interview were updated if substantial changes were reported.

Given the small number of MDR-TB cases in Japan, no formal sample size calculation was performed. We aimed to recruit 30 participants, representing approximately 70% of newly registered MDR-TB cases annually. No imputation was performed for missing data; the extent and nature of missing data are reported descriptively.

Estimating cost and income

Three cost categories were assessed: direct medical, direct non-medical, and indirect costs. Detailed definitions can be found in the WHO's protocol (13), however, briefly;

Direct medical costs included out-of-pocket payments for consultations, diagnostic tests, bed charges and private room fees, additional visits due to side-effects, and medications not reimbursed by universal health insurance or TB-specific subsidies (national or local).

Direct non-medical costs included transportation, food, and other care-seeking expenses, including costs incurred by accompanying persons.

Participants reported costs incurred up to the time of their interview. Unless otherwise indicated by attending physicians, it was assumed that patients would continue the same MDR-TB regimen and visit frequency until treatment completion; costs were extrapolated accordingly.

Indirect costs were estimated using the self-reported household income loss approach, comparing pre-TB income with income during the MDR-TB episode. For students relying solely on family remittances, the remittance amount was considered their income. Participants were also asked about coping strategies, including selling assets, drawing down savings, and borrowing money.

Cost information was collected across three periods; **pre-diagnosis, health-seeking phase** (from when the patient initially sought health care due to symptoms related to TB to TB diagnosis), **drug-susceptible TB treatment phase** (from the start of treatment for DS-TB to confirmation of multi-drug resistance), and **MDR-TB treatment phase** (from the start of treatment for MDR-TB to treatment completion). Cost incurred during the two-year treatment follow-up was not included. Catastrophic costs were defined as total TB-related costs (direct and indirect) exceeding 20% of annual pre-TB household income, in accordance with WHO's End TB Strategy indicator (15). All costs are presented in JPY. USD equivalents were calculated using a fixed exchange rate of JPY 150 per USD 1, reflecting the approximate prevailing rate during the study period.

Analysis

Considering the small number of expected sample size, no statistical analysis was conducted. The results were presented descriptively with numbers and proportions. The costs were compared among phases of the treatment, by type, and by different subgroups.

Results

Participant characteristics

A total of 27 participants were enrolled across seven facilities. The mean age was 45.2 years (SD 20.4; range 20 - 83), and 48.1% were male. Eighteen participants (66.7%) were foreign-born. Japan-born participants were older on average than foreign-born participants (mean 65.8 vs. 34.9 years). Participant characteristics are summarized in Table 1.

Table 1. Characteristics of MDR-TB patients enrolled in the catastrophic cost survey, Japan (n = 27)

Characteristics	n (%)
Age (years)	
Mean ± SD	45.2 ± 20.4
<65	23 (85.2)
≥65	4 (14.8)
Sex	
Male	13 (48.1)
Female	14 (51.9)
Place of birth	
Japan-born	9 (33.3)
Foreign-born	18 (66.7)
Mode of detection	
Contact investigation	4 (14.8)
TB screening (school, workplace, etc.)	11 (40.7)
Symptomatic visit	11 (40.7)
Other	1 (3.7)
Treatment history	
New case	21 (77.8)
Previously treated	5 (18.5)
Unknown	1 (3.7)
HIV status	
Negative	14 (51.9)
Unknown	13 (48.1)
Comorbidities	
None	15 (55.6)
Present	10 (37.0)
Unknown	2 (7.4)
Use of delamanid and/or bedaquiline	
Yes	26 (96.3)

No	1 (3.7)
Use of linezolid and/or clofazimine	
Yes	17 (63.0)
No	10 (37.0)
Planned treatment duration	
≤18 months	18 (66.7)
>18 months	7 (25.9)
Unknown	2 (7.4)
Hospitalization during TB treatment	
Yes	17 (63.0)
No	10 (37.0)
National health insurance	
Insured	22 (81.5)
Other/unknown	5 (18.5)
Living alone	
Yes	7 (25.9)
No	20 (74.1)

 Excluding diagnostic admissions.

Abbreviations: MDR-TB, multidrug-resistant tuberculosis; SD, standard deviation; TB, tuberculosis.

Eleven participants (40.7%) were detected through symptomatic presentation, 11 (40.7%) through routine screening, and four (14.8%) through contact investigation. Five participants (18.5%) had a history of prior TB treatment. No participant tested positive for HIV, although HIV status was unknown for 13 (48.1%). Comorbidities were present in 10 participants (37.0%). Twenty-six participants (96.3%) were receiving delamanid and/or bedaquiline, and 17 (63.0%) were receiving linezolid and/or clofazimine. Seventeen participants (63.0%) were hospitalized at some point during TB treatment (excluding diagnostic admissions).

Catastrophic cost

Four participants were excluded from the cost analysis: two were foreign-born who had been hospitalized at the time of the interview, however were later reported to the investigators that they had

returned to their country of origin immediately upon discharge. One was missing direct cost and the other was missing household income data.

Among the remaining 23 participants, the mean total cost was 1,164,856 JPY (7,766 USD), with a median of 733,770 JPY (4,892 USD). Indirect costs accounted for 53.4% of total costs (mean 622,174 JPY; median 0 JPY). MDR-TB treatment medical costs constituted the largest direct cost component (27.1%, mean 315,766 JPY; median 341,000 JPY), followed by DS-TB medical costs (10.0%, mean 116,559 JPY; median 3,240 JPY), MDR-TB non-medical costs (4.5%, mean 52,458 JPY; median 31,200 JPY), DS-TB non-medical costs (3.3%, mean 38,509 JPY; median 15,360 JPY), and pre-diagnostic costs (1.7%, mean 19,391 JPY; median 3,536 JPY) (Figure 1). Mean pre-TB annual household income was 3,421,565 JPY (22,811 USD). Twelve of 23 participants (52.2%) experienced catastrophic costs (Table 2, Figure 1).

<Figure 1. Components of total TB-related economic burden (n=23)>

Legend: DS-TB: drug susceptible TB, MDR-TB: multi-drug resistant TB**>**

Sub-group analysis

Five participants receiving either social welfare assistance or additional subsidy from the local government had substantially lower mean direct costs (142,540 JPY) compared with the overall mean (542,682 JPY). One participant treated without delamanid or bedaquiline also had a lower direct cost (165,610 JPY). To examine whether these low-cost outliers influenced overall findings, sensitivity analyses were conducted. Excluding the five participants receiving social welfare or subsidies increased the mean total cost from 1,164,856 JPY to 1,258,832 JPY; excluding the one participant not using bedaquiline or delamanid yielded a similar increase to 1,210,276 JPY. Neither exclusion materially changed the overall pattern (Table 2, Figure 2).

Table 2. Economic burden for all, and by status of subsidy and treatment regimen

	All (n = 23)	Excluding those receiving welfare or subsidy (n=18)	Excluding one patient not receiving BDQ/DLM (n=22)
Mean pre-TB household income, JPY	3,421,565	3,885,333	3,331,636
Mean total cost, JPY (median)	1,164,855 (733,770)	1,258,852 (742,745)	1,210,276 (742,745)
Mean direct cost, JPY	542,682	653,832	559,822
Mean indirect cost, JPY	622,174	605,000	650,455
Catastrophic costs (≥20% of income)	12/23 (52%)	10/18 (56%)	12/22 (55%)

<Figure 2. Total economic burden by all and by subgroups>

Legend: BDQ: bedaquiline, DLM: delamanid)

Economic burden also differed by country of birth and age group (Table 3). Foreign-born participants had lower pre-TB household income (mean 2,488,286 JPY) than Japan-born participants (mean 4,873,333 JPY). Hence, although Japan-born participants had higher mean total costs, the proportion of those experiencing catastrophic cost was higher among foreign-born participants (57% vs. 44%). Participants aged ≥60 years had lower pre-TB household income. However, because of absence of indirect cost, the total cost was lower, leading to a lower proportion of those experiencing catastrophic cost, compared with those aged ≤59 years old (20% vs 61%).

Table 3. Economic burden by country of birth and age group

	Japan-born (n = 9)	Foreign-born (n = 14)	Age ≥60 (n = 5)	Age ≤59 (n = 18)
Mean pre-TB household income, JPY	4,873,333	2,488,286	2,880,000	3,572,000
Mean total cost, JPY (median)	1,369,227 (751,720)	1,033,474 (434,490)	407,129 (365,736)	1,375,335 (842,262)
Mean direct cost, JPY	749,227	409,903	407,129	580,335
Mean indirect cost, JPY	620,000	623,571	0	795,000
Catastrophic costs (≥20% of income)	4/9 (44%)	8/14 (57%)	1/5 (20%)	11/18 (61%)

Impact on employment, study and coping strategies

Employment data were available for 22 participants. Prior to diagnosis, 16 were employed, four were students, two were retirees, and one was a homemaker. Among the 16 who were employed, after starting their MDR-TB treatment, nine remained employed, five became unemployed, and two were on medical leave (Figure 3). Among students, one discontinued part-time work and one took academic leave due to their treatment.

Participants reported multiple coping strategies. The most common were reducing non-food expenditure (48%), followed by reducing food expenditure (30%), and drawing down savings (26%). Five participants (22%), four of whom were foreign-born, received financial support or loans from family or acquaintances. Borrowed amounts ranged from 320,000 to 2,000,000 JPY (2,100 - 13,300 USD), with a median of 400,000 JPY (2,700 USD).

<Figure 3. Changes in the status of employment among participants who were working prior to diagnosis (n=16)>

Discussion

This study provides the first systematic assessment of catastrophic costs among MDR-TB patients in Japan and adds to emerging evidence from other low-burden, high-income settings such as Taiwan (16). Despite the small sample size, the demographic profile of participants closely reflected the national MDR-TB population in Japan, where the average age of newly notified MDR-TB patients in 2024 was 50.5 years and 48.9% (n=22) were foreign-born (17).

Our findings demonstrate that catastrophic costs remain common among MDR-TB patients in Japan, despite the long-standing universal health insurance and TB-specific public subsidy framework. More than half of affected households (52.2%) experienced catastrophic costs – while the proportion was certainly lower than the pooled WHO estimate of approximately 82% among predominantly low- and middle-income countries (1,18), it remained well above the End TB Strategy's goal of eliminating such cases entirely. Notably, the proportion was nearly identical to that reported in Taiwan (52%, 95% CI: 39–64%) (16), despite differences in health system structure, subsidy design, and patient demographics. Together, these findings challenge the assumption that high-income settings with extensive financial protection mechanisms can reliably prevent catastrophic economic burden among MDR-TB patients (19).

A distinctive feature of the Japanese context was the composition of direct costs. Direct medical costs accounted for 37% of total TB-related costs - substantially higher than the 4% reported in Taiwan and consistently lower proportions reported in LMICs (20–22). This burden was driven primarily by MDR-TB treatment-phase drug expenditures. Although mean DS-TB medical costs appeared elevated (116,559

JPY), the very low median (3,240 JPY) indicated that these costs were inflated by a small number of patients who chose to pay for private hospital rooms; thus, drug costs during DS-TB treatment were negligible for most participants. In contrast, MDR-TB medical costs showed both high mean (315,766 JPY) and median (341,000 JPY) values, indicating a broad and consistent burden across participants.

Two structural mechanisms likely explain these findings. First, bedaquiline and delamanid, although covered under the TB-specific public subsidy, require a 5% patient co-payment. Even with the high-cost medical expense benefit cap, this co-payment accumulates over prolonged treatment. Second, linezolid and clofazimine, which were used by more than 60% of participants, are not registered as anti-TB drugs in Japan and therefore fall outside the TB-specific subsidy, subjecting patients to standard national insurance co-payments of 10 to 30%. Local subsidy schemes, such as Tokyo's programme for residents exempt from residence tax, effectively eliminate these co-payments, however, such support is unevenly distributed across the country.

Indirect costs, reflecting income loss, constituted the largest share of total costs (53.4%), a finding which was consistent with previous cost surveys (16)(23). Despite known socioeconomic differences between Japan-born and foreign-born residents (24), indirect costs were nearly identical in absolute terms (mean 620,000 JPY versus 623,571 JPY). This suggests that the degree to which prolonged MDR-TB treatment disrupts employment and earnings did not differ greatly by country of birth in our study. However, because foreign-born participants had significantly lower pre-TB household income, the same absolute income loss translated into a higher proportion of annual income, contributing to higher proportion of patients experiencing catastrophic cost (57% vs. 44%). Foreign-born participants were also more likely to borrow money, indicating greater financial distress. A further important caveat is that the most economically vulnerable foreign-born patients, particularly students and technical intern trainees whose visa status depends on continued employment (25,26), often return to their home countries in the midst of their treatment (27), and are therefore not captured in this study. Hence, the true burden among foreign-born MDR-TB patients in Japan is likely underestimated by our findings.

Although the small sample size limits definitive policy conclusions, several implications emerge. First, indirect costs cannot be mitigated through disease-specific subsidies alone. Addressing income loss will require multisectoral approaches spanning labour policy, social protection, and migrant support, particularly for foreign-born patients in precarious employment arrangements (28, 29). Second, reducing direct medical costs will require structural reforms. Accelerating regulatory approval and uptake of shorter MDR-TB regimens could reduce cumulative drug expenditure by shortening treatment duration. Incorporating linezolid and clofazimine into the TB-specific subsidy framework would substantially reduce patient co-payments, but this requires pharmaceutical companies to pursue indication extension. However, commercial barriers to pursuing indication extensions in small disease markets are well recognized (30,31), and this may therefore pose a similar challenge for MDR-TB in Japan. Government-facilitated or publicly funded regulatory pathways, similar to those used for rare diseases, may be necessary. Third, expanding income-tiered local subsidy schemes, such as Tokyo's programme,

could provide targeted protection for economically vulnerable patients without requiring national-level regulatory reform.

Strengths and limitations

This study has several strengths. It provides the first systematic assessment of catastrophic costs among MDR-TB patients in Japan and one of the first from any low-burden, high-income country. Participating institutions collectively managed approximately half of all MDR-TB patients nationally, supporting the representativeness of the studied population. Direct medical costs were estimated using medical receipts brought by participants, improving accuracy and strengthening the validity of cost estimates, while majority of previous studies have relied on patients' self-report.

Limitations include the small analytical sample, which precluded formal statistical comparisons and limits precision. Recruitment through participating facilities may have introduced selection bias, potentially underrepresenting patients with limited engagement in care or those who discontinued treatment. Although receipt-based verification improved accuracy for medical costs, self-reported income and indirect cost data remain subject to recall bias. Finally, extrapolation of costs for patients interviewed early in treatment introduces uncertainty, although this approach aligns with the WHO methodology.

Conclusion

This study demonstrated that catastrophic costs remain prevalent among MDR-TB patients in Japan, affecting more than half of households despite universal health insurance and a TB-specific public subsidy framework. The burden was driven by direct medical costs for MDR-TB treatment and by substantial income loss during prolonged treatment. Foreign-born patients and those of working age faced disproportionately higher risk. These findings challenge the assumption that high-income settings with universal coverage can reliably prevent catastrophic economic burden among MDR-TB patients. Targeted reforms are needed, including extension of the TB-specific subsidy to encompass all core MDR-TB drugs, accelerated adoption of shorter regimens, and strengthened income protection for economically vulnerable patients, to close remaining gaps and advance End TB Strategy targets.

Abbreviations

BDQ: bedaquiline

DS-TB: drug-susceptible tuberculosis

DLM: delamanid

GDF: Global Drug Facility

JPY: Japanese Yen

MDR-TB: multi-drug resistant tuberculosis

SD: standard deviation

TB: tuberculosis

USD: US Dollar

WHO: World Health Organization

Declarations

Ethics approval and consent to participate: The study was conducted in accordance with the Declaration of Helsinki. The protocol was reviewed and approved by the Institutional Review Board of Nagoya City University (reference number: 24033-3). The study objectives and procedures were explained to each patient verbally and in writing, and patients were asked to provide their written consent before participating in the interview. Each patient was given 3,000 JPY for their time.

Consent for publication: NA

Availability of data and materials: The datasets used for this current study are available from the corresponding author upon reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Author contributions: LK, KU, KS, AS, and TY conceptualized the study LK, KU and KS collected data, and LK and KU led the analysis. LK led the manuscript development, including data analysis. LK, KU, KS, AS, and TY contributed to the discussion, read and approved the final manuscript.

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Figures

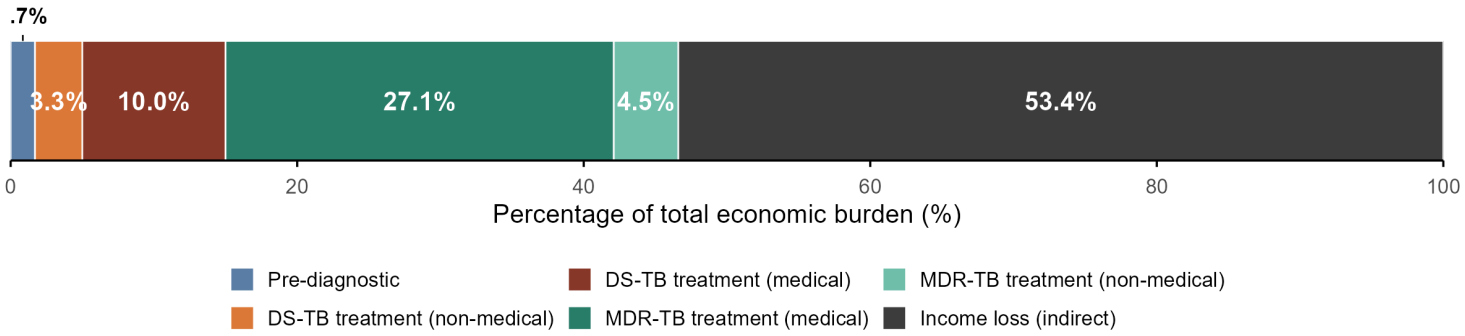


Figure 1

Components of total TB-related economic burden (n=23)

Legend: DS-TB: drug susceptible TB, MDR-TB: multi-drug resistant TB

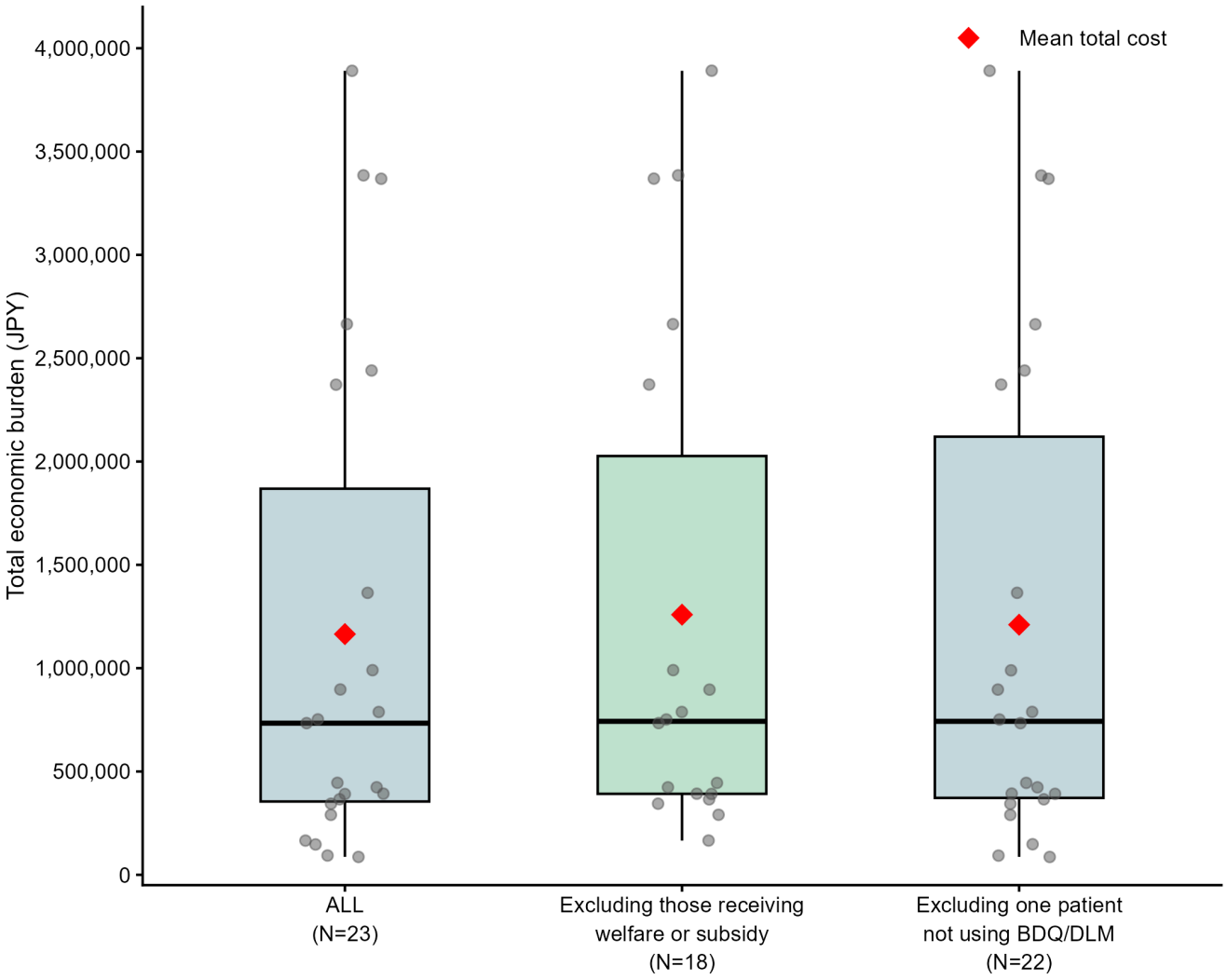


Figure 2

Total economic burden by all and by subgroups

Legend: BDQ: bedaquiline, DLM: delamanid)

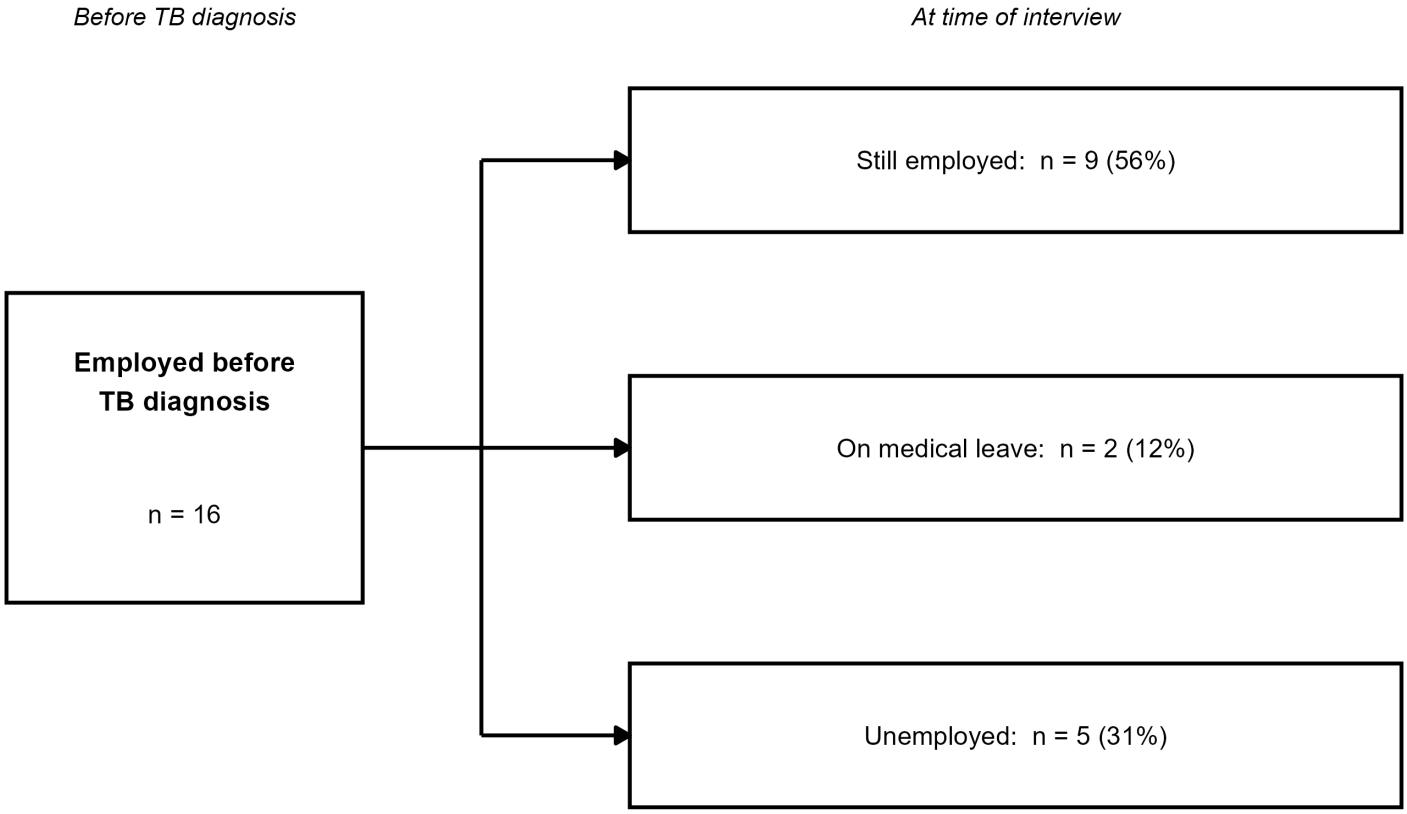


Figure 3

Changes in the status of employment among participants who were working prior to diagnosis (n=16)

Supplementary Files

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- Supplementaryfilequestionnaire.docx