

Cost of illness of non-multidrug-resistant tuberculosis in Germany – an update

Online Supplement

Inpatient costs

The InEK (Institute for the Hospital Remuneration System) provides detailed data for tuberculosis patients treated for the first time or retreated after relapse in hospitals on its G-DRG-Browser [Data according to §21 KHEntgG, State 3.10.2019]:

In 2017, 2362 TB patients belonging to the DRG category E76C were treated in hospitals for, on average, for 6.2 days (SD \pm 2.9 days), and 222 TB patients belonging to DRG category E76 B were treated, on average, for 8.3 days (SD \pm 3.3 days). A total of 3,525 TB patients, the majority of TB patients, was assigned to category E76 A, i.e. hospitalized at least 14 days, with an average of 38.9 days (SD \pm 29.2). The mean per-day reimbursement for those patients was €320.77 [DKG 18]. Thus, after subtracting the number of 112 MDR-TB cases for whom a hospital stay had been reported to the Robert Koch Institute [personal evaluation Bonita Brodhun, 7.10.2019], the weighted mean number of days when TB patients were treated in German hospitals can be calculated as follows: $(6.2 \text{ days} \times 2362 \text{ patients [E76C]}) + (8.3 \text{ days} \times 222 \text{ patients [E76B]}) + (38.9 \text{ days} \times 3525 \text{ patients [E76A]})$ divided by the total of 6109 patients $[(14,644.4 + 1,842.6 + 137,122.5): 6,109] = 25.14$ days.

The mean weighted cost due to hospitalization per standard TB patient is accordingly $[(2362 \text{ patients} \times \text{€}3,544.97 \text{ as base rate} \times 0.937) + (222 \text{ patients} \times \text{€}3,544.97 \text{ as base rate} \times 1.097) + (3,525 \text{ patients} \times \text{€}320.77 \text{ as mean reimbursement per day} \times 38.9 \text{ days})]$ divided by the total of 6,109 patients $(\text{€}7,845,706.33 + \text{€}863,320.72 + \text{€}43,984,784.33 = \text{€}52,693,811.38): 6,109 = \text{€}8,625.60$. Legal discounts and surcharges of the hospitals in addition to the DRG reimbursement had not been taken into account for calculation, because they would only marginally affect the final amounts.

Costs of doctor's and laboratory services in the outpatient setting

The resulting costs are charged to the SHI according to the SHI scheme revised in 2019 ("Einheitlicher Bewertungs-Maßstab", EBM) [reference 8_of the publication] and multiplied by the fixed prices for all utilized service types and providers. When adding the single costs as

described in Table 4 of the publication the costs of doctor's and laboratory services, separated by culturally positive or negative TB, are as follows:

1. Pulmonary TB adults

- a) Pulmonary TB, culturally confirmed TB, outpatient treatment only: €1,073,29 (positions 1, 3 to 34 added up)
- a) Pulmonary TB, culturally confirmed TB, outpatient treatment after initial hospitalization: €482,47 (post-hospital positions 1, 3 to 6, 12, 13,16, 23 to 34 added up)
- b) Pulmonary TB, culturally negative TB, outpatient treatment only: €808.26 (positions 1, 3 to 16, 20 to 34 added up; 17 to 19 excluded)
- c) Pulmonary TB, culturally negative TB, outpatient treatment after initial hospitalization: €362.17 (post-hospital positions 1, 3 to 6, 12, 23 to 34 added up; positions 17 to 19 excluded)

2. Non-pulmonary TB adults

- a) Non-pulmonary TB, culturally confirmed TB, outpatient treatment only: €699.52 (positions 1, 3 to 6, 9 to 19 each once, 20 to 34 added up)
- b) Non-pulmonary TB, culturally confirmed TB, outpatient treatment after initial hospitalization: €263.47 (post-hospital positions 1, 3 to 6, 23 to 34 added up)
- c) Non-pulmonary TB, culturally negative TB, outpatient treatment only: €549.59 (positions 1, 3 to 6, 9 to 16 each once, 20 to 34 added up; positions 7, 8, 17 to 19 excluded)
- d) Non-pulmonary TB, culturally negative TB, outpatient treatment after initial hospitalization: €263.47 (post-hospital positions 1, 3 to 6, 23 to 34 added up)

3. Pulmonary TB children

- a) Pulmonary TB, culturally confirmed TB, outpatient treatment only: €759.83 (positions 2, 3, 9 to 12, 14 to 34 added up)
- b) Pulmonary TB, culturally confirmed TB, outpatient treatment after initial hospitalization: €349.15 (post-hospital positions 2, 3, 12, 14,16, 23 to 34 added up)
- c) Pulmonary TB, culturally negative TB, outpatient treatment only: €494.80 (positions 2, 3, 9 to 12, 14 to 16, 20 to 34 added up)
- d) Pulmonary TB, culturally negative TB, outpatient treatment after initial hospitalization: €228.85 (post-hospital positions 2, 3, 12, 23 to 34 added up)

4. Non-pulmonary TB children:

a) Non-pulmonary TB, culturally confirmed TB, outpatient treatment only: €519.18 (positions 2, 3, 9 to 12 and 14 to 19 once each, 20 to 34 added up)

b) Non-pulmonary TB, culturally confirmed TB, outpatient treatment after initial hospitalization: €130.15 (post-hospital positions 2, 3, 23 to 34 added up)

c) Non-pulmonary TB, culturally negative TB, outpatient treatment only: €369.25 (positions 2, 3, 9 to 12 and 14 to 16 each once, 20 to 34 added up)

d) Non-pulmonary TB, culturally negative TB, outpatient treatment after initial hospitalization: €130.15 (post-hospital positions 2, 3, 23 to 34 added up)

Purely outpatient costs (medication included)

a) Adults with pulmonary TB

The weighted outpatient non-medical costs (for microbiology, laboratory and doctor's services) of TB in adults with pulmonary TB monitored by pneumonologists with reference to the basic presumptions (culturally confirmed TB in 79.4% of the cases) are ($€1,073.29 \times 0.794$ [proportion of culturally confirmed TB patients]) + ($€808.26 \times 0.206$ [proportion of culturally negative TB patients]) = $€852.19 + €166.50 = €1,018.69$. By adding the costs of medication of €714 for a 6 month short course (as described in Table 2 of the publication) the costs amount to *€1732.69*.

b) Adults with non-pulmonary TB

The weighted outpatient costs for non-pulmonary TB in adults (cultural confirmation in 64% of cases) are ($€699.52 \times 0.64$ [proportion of culturally confirmed TB patients]) + ($€549.59 \times 0.36$ [proportion of culturally negative TB patients]) = $€447.69 + €197.85 = €645.54$. By adding the costs of medication of €714 (as described in Table 2 of the publication) the costs amount to *€1,359.54*.

c) Weighted outpatient costs between adults with pulmonary and non-pulmonary TB

As 72.0% of patients suffered from pulmonary TB, the weighted outpatient costs for adult TB patients with TB are ($€1,732.69 \times 0.72$) + ($€1,359.54 \times 0.28$) = *€1,628.21*.

d) Children with pulmonary TB

For children treated as outpatients with just a triple combination (no therapy with E), costs due to pulmonary TB are amount to €1,362.23 for culturally confirmed TB patients (€759.83 plus

€602.4 medication) and €1,097.2 for culturally negative TB patients (€494.8 plus €602.4 medication). With reference to the basic assumptions (cultural confirmation in pulmonary TB in 48.5% of all TB cases) the weighted outpatient costs for children with pulmonary TB are $(€1,362.23 \times 0.485) + (€1,097.2 \times 0.515) = €660.68 + €565.06 = €1,225.74$.

e) Children with non-pulmonary TB

For children treated as outpatients with a triple combination, costs due to non-pulmonary TB amount to €1,121.58 for culturally confirmed TB patients (€519.18 plus €602.4 medication) and €971.65 for culturally negative TB patients (€369.25 plus €602.4 medication). As 40.8% of all non-pulmonary TB patients in children are culture positive, the weighted costs are accordingly $(€1,121.58 \times 0.408) + (€971.65 \times 0.592) = €457.60 + €575.22 = €1,033.82$.

f) Weighted outpatient costs between children with pulmonary and non-pulmonary TB

As in total 75.8% of the children suffer from pulmonary TB the weighted costs of children with TB as outpatients are $(€1,225.74 \times 0.758) + (€1,033.82 \times 0.242) = €929.11 + €249.94 = €1,179.05$.

Outpatient costs following hospitalisation

a) Adults with pulmonary TB

After treatment in hospital, TB therapy must continue on an outpatient basis without interruption. Compared with the purely outpatient therapy of adults, monitoring and the period of medication is reduced by 25 days (see section "Inpatients costs"), Thus, the weighted costs for adults suffering from pulmonary TB after initial hospitalisation amount to $(€482.47 \times 0.794) + (€362.17 \times 0.206) = €383.08 + €74.61 = €457.69 + €563 \text{ medication} = €1,020.69$.

b) Adults with non-pulmonary TB

The costs for adults suffering from non-pulmonary TB with further treatment outside the hospital are $€263.47 + €563 \text{ medication} = €826.47$.

c) Weighted outpatient costs following hospitalisation between adults with pulmonary and non-pulmonary TB

Thus, the weighted treatment costs for adults with TB following the hospital stay are $(€1,020.69 \times 0.72) + (€826.47 \times 0.28) = €734.90 + €231.41 = €966.31$.

d) Children with pulmonary TB

The treatment costs for children (without medication) after the initial hospital stay suffering from pulmonary TB with further treatment outside the hospital are $(€349.15 \times 0.485$ [proportion of culturally confirmed TB patients]) + $(€228.85 \times 0.515$ [proportion of culturally negative TB patients]) = $€169.34 + €117.86 = €287.20 + €497.9$ medication = $€785.1$

e) Children with non-pulmonary TB

The treatment costs for children (without medication) after the initial hospital stay suffering from non-pulmonary TB with further treatment outside the hospital are $€130.15 + €497.9$ medication = $€628.05$

f) Weighted outpatient costs following hospitalization between children with pulmonary and non-pulmonary TB

Thus the weighted treatment costs (without medication) for children with TB following the hospital stay are $(€785.1 \times 0.758) + (€628.05 \times 0.242) = €595.11 + €151.99 = €747.10$

Combined inpatient/outpatient TB costs

Hospital treatment occurred in 89.5% of all adult TB cases, so in adults the weighted costs for a standard TB case are $[(€8,625.60 + €966.31) \times 0.895] + (€1,628.21 \times 0.105$ [outpatients only]) = $(€9,591.91 \times 0.895) + €170.96 = €8,584.76 + €170.96 = €8,755.72$.

For children, the combined costs can be calculated as follows: $[(€8,625.60 + €747.10) \times 0.895] + (€1,179.05 \times 0.105) = (9,372.7 \times 0.895) + 123.80 = €8,388.57 + €123.80 = €8,512.37$.

As 96% of all Tb cases were adults the average costs in Germany in 2018 per patient were $(€8,755.72 \times 0.96) + (€8,512.37 \times 0.04) = €8,745.99$

Calculation of Public Health costs

a) Personnel and material costs of the public health service

At the central location for combating TB in Hamburg, where all radiographic examinations and screening tests for LTBI are performed, the Central Hamburg Public Health Department employed 4 medical technical assistants in 2019, with resultant total salary costs of €225,287 (TVL E8 Positions, Level 4), including additional administrative costs of 15% and a lump office workplace fee. On the basis of a mean of 211 workdays per year and a workday of 7.7 hour (462 minutes), the resulting personnel expenses for one medical technical assistant is $€0.58$ per minute.

The tasks of the medical technical assistants (MTA) comprise the performance of all QuantiFERON (QFT) tests, the least expensive IGRA, in contact subjects (centrifugal contact investigation), to look for potential source cases of reported TB index cases (centripetal contact investigation), to provide the first (and the second) CXR to exclude an active TB in potential source cases and in QFT positive contact persons. The costs of performing a QFT at the expense of the Public Health Department in a Hamburg laboratory are currently €35.

In addition, MTA have to perform the CXR examinations to exclude active TB cases according to §36 IfSG before they start living in shared accommodations.

For QFT positive contacts who have decided to start a preventive therapy of latent TB infection (LTBI) a CD documenting the unremarkable CXR result has to be burned and to be sent to the settled pneumonologist or pediatricist together with a copy of the QFT result. In those QFT positive contact persons who do not start or finish a PT an invitation for a second CXR examination within 1 year will be sent according to the German contact tracing guidelines as in the 1st year after MTB infection the probability of developing an active TB is highest.

The personnel costs for the IGRA testing were calculated as follows: The necessary time costs were multiplied by the number of QFT tests. In 2016 and 2017 on average 1,470 QFT were performed in contact persons of culture confirmed index cases with pulmonary TB aged 5 years or older. A mean time cost of 8 min was measured for the preparation and performance of the test, further 11 minutes for documenting the type of contact, the test result and assigning the screened contact person to the respective index person in a table. This results in personnel costs of €11.02 per tested contact, i.e., in total €16,199.40 for 1,470 QFT tests.

QFT positive contacts are encouraged to make an appointment with a pulmonologist or podiatrist in private praxis nearby the contact's residence in order to discuss a potential PT. For this purpose the report of the QFT result will be copied and the unremarkable CXR result burned to a CD and sent to that pulmonologist. In 2016 and 2017 on average 16.5% of the IGRA were positive, i.e., 243 contacts (1,470 QFT tests x 0.165) per year in the group of contacts aged at least 5 years. On average 8 active TB cases were found by testing and subsequent chest X-ray. Copying, burning and preparation for sending takes in total 14 minutes (14 x €0.58). However, only 77 (32.8%) of those 235 started a PT (and only 39, equivalent to 50.6% of all who had started or 16.6% of all persons with LTBI, respectively), finished it. Accordingly, the additional time required for fulfilling that task can nearly be considered negligible; it amounts on average only to €0.43 per contact patient: $(14 \text{ minutes} \times €0.58 \times 235) / 1,470 \times 0.328 = €0.43$.

Counselling IGRA positive contact persons on the benefits and risks of a subsequent PT is the duty of a doctor whose personell costs amount to €1.07 per minute [specialist, E14 position]. According to internal measurements of working times it takes on average 25 minutes which incurs doctor´s expenses of €26.75 (€1.07 x 25).

b) Costs of chest X-ray (CXR) examinations

The remaining medical technical assistants costs can be attributed solely to radiological examinations and their associated administrative costs, referred to “radiological procedure”, which amounts to €208,455.41 (€225,287 minus €16,831.59 (€16,199.40 for QFT testing and €632.1 [€0.43 x 1470]) for informing the chosen pulmonologists).

In 2017 and 2018 on average 3419 radiological examinations were conducted on average. This amounts to personnel expenses of €60.97 (€208,455.41:3,419) per radiological procedure (which will also be utilized not only for contact investigations but predominantly for investigations according to § 36 IfSG). The radiological procedure also includes organizing an appointment for QFT-positive contacts to attend the first CXR examination and to invite those contacts for a second one within 1 year if they did not start or finish a PT). Upon failing to reply, these contact individuals again receive up to two further summonses, and, if necessary, are informed by telephone either personally or by their lodging providers (e.g. shelters for the homeless and other residences).

Moreover, this work involves maintaining a registration site, explaining the steps of CXR examination and filling in radiographic certificate cards.

Additional to these costs are the costs for the evaluation of the radiological images by a specialist, Such a physician needs on average 4 minutes to assess one image and documenting the result, resulting in personnel expenses of €4.28 (€1.07 x 4).

Further material costs are incurred utilizing a digital radiography apparatus. The acquisition costs of the radiograph system used in Hamburg AGFA DR 600 (CE 0413) amount to €256,000 including value added tax (VAT). Assuming a linear depreciation of the instrument over a period of 10 years, costs of €25,600 per year incur plus average annual maintenance costs of €1,140, i.e. in total €26,740 per year. By dividing this by the number of 3419 examinations, each CXR examination creates expenses only for radiographic equipment of €7.82 (€26,740/3,419). Consequently, the total costs per contact for the performance of a radiological investigation within the scope of a contact investigation (sum of the personnel costs for medical

technical assistants and a physician plus equipment costs) amount to €73.07 (€60.97 + €7.82 + €4.28)

c) Expenses for contact investigations in children aged below 5 years

For children below 5 years who were contact persons a chest X-ray examination has to be performed immediately in addition to the TST (or IGRA test) and a INH chemoprophylaxis has to be started. Furthermore, a second TST has to be performed 8-12 weeks after the initial one – if the initial TST was negative. Children who have been scored TST positive have to be sent to the CXR examination for a second time. In Hamburg children aged below 5 years are sent to a pediatric hospital with special care for tuberculosis (ASV according to §116 b of SGB V) or to a settled pediatrics. There, if the child has no LTBI the following costs at the expense of the Public Health office will arise:

Pediatric flat rate €25.54 (GOP 4000), two times under the assumption the second visit up to 3 months later falls into a second quarter and thus a new flat rate can be charged, adding to €51.08, furthermore a CXR €16.34 (GOP 34241) and two Mantoux testings €1.94 (2 x €0.97 GOP 2200), in total €69.36.

On the basis of the simplified assumption that the child is scored TST positive already initially and, thus, a second TST is no longer required, the costs amount to €84.73 (two times pediatric flat rate GOP [€25.54 x 2] plus two CXR examinations [€16.34 x 2] plus Mantoux testing €0.97) = €84.73

In 2017 and 2018 on average each 128 children aged below 5 years were contact persons. Fourteen out of the total of 128 children, or 10.9%, were TST positive, received a PT and a second CXR according to the guidelines.

The weighted costs of screening children below 5 years in Hamburg to be paid by the Public Health department are accordingly €71.03 [(€69.36 x 0.891) + (€84.73 x 0.109)].

In 2017 and 2018 on average each 128 children aged below 5 years were contact persons. High logistic expenses result from the planning of contact investigations in those young children. This is regularly performed by social workers who in general belong to higher pay-scale classes than MTA. Nevertheless, for purpose of simplifications we used the same costs per minutes as for MTA. To arrange the contact investigation in the hospital and to control a necessary second visit of those little children according to the contact tracing guidelines (costs for interpreters not included) clearly more time is necessary and can be estimated to be 55 minutes on average (including on a case-by-case basis attending the families at their homes or in common housing

quarters). Thus €31.90, the costs of 55 minutes ($€0.58 \times 55 = €31.90$) per contact person aged lower than 5 years has to be added.

d) Type of contact patients of infectious TB cases

The 1598 contacts could be assigned to a total of 213 index cases with culture confirmed pulmonary TB patients, i.e. 7.5 contacts per infectious TB case. 254 (17.3%) out of the 1,470 contact aged at least 5 years were investigated to root out the source case and therefore immediately received a CXR for excluding active TB in addition to the other screening procedures described above.

e) Weighted costs arising per infectious TB case due to contact investigations

The weighted costs arising per TB case due to contact investigations from the Public Health perspective can be calculated as follows:

Thus, the costs for the first CXR per contact aged at least 5 years were on average €12.08 ($€73.07 \times 0.165$ QFT positives [243/1,470 contacts]). According to the German guidelines a second CXR examination is required within in a year after the first CXR, in case of preventive therapy preferably after 9 months of isoniazid. As only 39 (16.6%) of all positive 235 contacts who had no active TB finished an PT performed by a pneumonologist or pediatrician in praxis, a second CXR was required in 83.4% of all QFT positive contacts. Thus the costs of the second CXR in the fraction of IGRA positive contacts are €10.09 per contact [$(235-32)/1,470$ multiplied by €73.07].

254 (17.3%) of the 1,470 contacts aged at least 5 year received a CXR examination due to source case searching, amounting to additional costs of $€73.07 \times 0.173$ contacts = €12.64. The laboratory costs of €35 per QFT, €11.02 as average personell costs of performing the QFT, €4.44 for doctor's counselling following a positive QFT [$€26.75 \times 0.166$ contacts], €0.43 for informing settled doctor's on a contact's interest in starting a PT have to be added.

The costs of €85.70 ($€12.08 + €10.09 + €12.64 + €35 + €11.02 + €4.44 + 0.43$) per contact out of 1470 contact persons aged at least 5 years have to be weighted with the costs for contacts aged below 5 years. The screening costs for these children are €71.03 per person, the administrative expenses €31.90, resulting in costs of €102.93.

8.0% of all contact persons were children below 5 years [128/1,598 contacts] the weighted cost of contact investigating per person in Hamburg are €87.08 ($€85.70 \times 0.92 + €102.93 \times 0.08$). As one culture confirmed pulmonary TB case has on average 7.5 contact persons the total average cost per infectious TB case at the expense of the Public Health sector is €653.10.

In Germany, however, the proportion of pulmonary TB cases is only 72.1%, of those 78.2% are culture positive. Accordingly, referring to the costs of TB per case – irrespective of pulmonary infectivity – the figure of € 653.10 has to be multiplied by the factors 0.721×0.782 , ending up in Public Health costs of €368.23 per TB case.