**Supplementary document: Intervention cost analysis for five countries**

***ASCENT scenario***

We calculated intervention costs per patient from a provider perspective of two digital adherence technologies for TB treatment: (i) medication labels, and (ii) smart pillbox. The cost analysis was carried out in five countries: Ethiopia, Philippines, South Africa, Tanzania and Ukraine, as part of the ASCENT trial [1]. Medical labels were not trialled in Ukraine, thus only smart pillbox-related costs were calculated for that country. All cost data were sourced from the ASCENT trial expenditures in local currency and converted to 2023 USD [2]. Intervention costs were defined as the sum of three main components: (i) technology costs, (ii) support costs, and (iii) training costs. Patient costs have not been calculated for this analysis.

After estimating the cost of the intervention (all patients total and per patient) incurred during the trial, we also estimated the possible cost of the intervention in a post-ASCENT scenario, assuming the digital adherence technologies were incorporated as part of routine care.

*(i) Technology costs*

Technology costs comprise of purchasing and shipping costs, digital adherence platform costs and phone infrastructure and SMS-related costs, and are reported in Table 1.

Pillboxes were purchased as kits. Each kit included the box itself and also the battery, the electronic remote module with charging chip, a SIM card with six months of data and a charger. When calculating the pillbox cost per patient, we accounted for the cost of purchasing the box ($53.75), the average reuse of the box in the country during the research period (Ethiopia: 2.2, Philippines: 1.5, South Africa: 1.2, Tanzania: 2.0, Ukraine: 1.7) and a 2.5$ cleaning fee per each re-use. Pill boxes were shipped from South Africa, the location where the manufacturer (Wisepill Technologies) is based. Shipping costs per box were 0.78$ in South Africa, 1.66$ in the Philippines, 1.84$ in Ethiopia, 2.81$ in Tanzania, and 1.54$ in Ukraine. Costs specific to procurement and importation fees are not included.

Purchasing and shipping costs for the label intervention only included the cost of printing, as all labels were printed locally in each country. In addition, the label intervention only required an associated phone infrastructure whose costs include a monthly short-code rental line fee (and a yearly toll-free infrastructure in Tanzania only).

The ASCENT adherence online platform (Everwell Hub) was part of both interventions and required a one-off setup and configuration cost of 10,000$ in all countries, plus monthly hosting fees and IT support from the vendor of 4,000$.

SMS costs were calculated accounting for the average number of messages sent by the patients (labels intervention only) and average number of messages sent to each patient (both pillboxes and labels), which included registration confirmation and notifications (such as reminders).

**Table 1**. Technology costs per patient expressed in 2023 USD.

| | Purchasing and shipping ($/patient) | Adherence platform ($/patient) | Phone Infrastructure ($/patient) | SMS ($/patient) | Total per patient ($/patient) | Total ($ per all patients) |
|---|---|---|---|---|---|---|
| Ethiopia | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Label | 0.30 | 29.21 | 1.70 | 2.75 | 33.96 | 43,165 |
| Pillbox | 27.64 | 29.21 | - | 0.18 | 57.03 | 71,967 |
| Philippines | | | | | | |
| Label | 1.70 | 27.52 | 1.02 | 2.55 | 32.79 | 52,102 |
| Pillbox | 38.33 | 27.52 | - | 0.27 | 66.12 | 72,728 |
| South Africa | | | | | | |
| Label | 1.20 | 47.56 | 1.67 | 1.81 | 52.24 | 34,423 |
| Pillbox | 45.99 | 47.56 | - | 0.17 | 93.72 | 84,063 |
| Tanzania | | | | | | |
| Label | 0.50 | 30.35 | 10.45 | 2.48 | 43.79 | 57,053 |
| Pillbox | 30.94 | 30.35 | - | 0.13 | 61.42 | 69,709 |
| Ukraine | | | | | | |
| Pillbox | 34.19 | 104.06 | - | 0.25 | 138.05 | 109,136 |

*(ii) Support costs*

Support costs include costs of all visits and calls/messages made to health care workers in health facilities by ASCENT project staff to solve queries (Table 2). A senior technical officer from the project team was responsible for solving queries during the trial, and we costed 50% of their time spent on implementation activities (i.e. we do not cost research activities). Of this, based on observation, we assumed 40% of their time, irrespective of the specific DAT intervention, was spent on answering calls and messages, and 40% on visiting the health facilities (and the remaining 20% on training). The number of visits performed was recorded and is multiplied by the average cost of travel. We also used local salaries of nurses to cost healthcare staff time during visits in each country.

**Table 2**. Support costs per patient expressed in 2023 USD. Support costs were calculated as the same for both interventions.

| | Technical officer salary ($/patient) | Visits ($/patient) | Healthcare worker salary ($/patient) | Total per patient ($/patient) | Total ($ per all patients) |
|---|---|---|---|---|---|
| Ethiopia | 5.17 | 4.92 | 0.06 | 10.15 | 25,707 |
| Philippines | 4.63 | 3.34 | 0.12 | 8.09 | 21,763 |
| South Africa | 20.26 | 1.13 | 0.20 | 21.59 | 33,595 |
| Tanzania | 6.38 | 2.67 | 0.05 | 9.09 | 22,170 |
| Ukraine | 16.66 | 2.98 | 0.12 | 19.77 | 15,577 |

*(iii) Training costs*

Training on the use of the digital adherence technologies was provided to healthcare workers. All training was carried out between December 2020 and March 2023. Training costs include: cost of venue and refreshments, accommodation and transportation, and salaries of trainers and trainees (Table 3).

Salaries are highly variable across countries due to different healthcare workers being trained or giving the training. In Ethiopia only nurses received training and only doctors provided training,

respectively at an hourly salary of 0.88$ and 3.70$. Similarly in Tanzania, where nurses and doctors have an hourly salary of 1.74$ and 3.79$. In Ukraine a similar number of nurses and medical doctors received training, as well as provided the training. Healthcare workers salaries in Ukraine are highly variable, so we assumed the average base hourly salaries of 12.15$ and 18.00$ for nurses and doctors respectively. In the Philippines mostly nurses received and gave the training, but also a small number of doctors were involved, at an hourly salary of 4.24$ and 11.59$ respectively. In South Africa, nurses provided the training, but a large number of interns were also trained. New interns had to be trained frequently due to the short duration of their work contracts. Nurses and interns in South Africa have an hourly salary of 7.97$ and 1.28$, respectively.

Additionally, a technical officer from the ASCENT team supported the training and we costed 20% of their time for these activities.

**Table 3**. Training costs per patient in 2023 USD. Training costs were calculated as the same for both interventions.

| | Venue and refreshments ($/patient) | Accommodation and transportation ($/patient) | Healthcare staff salaries ($/patient) | Technical officer salary ($/patient) | Total per patient ($/patient) | Total ($ per all patients) |
|---|---|---|---|---|---|---|
| Ethiopia | 0.19 | 0.08 | 0.96 | 0.25 | 1.48 | 3,746 |
| Philippines | 0.03 | - | 1.84 | 0.16 | 2.04 | 5,478 |
| South Africa | 5.27 | 1.59 | 3.90 | 1.72 | 5.27 | 19,432 |
| Tanzania | 2.40 | 1.29 | 0.44 | 0.03 | 4.17 | 10,160 |
| Ukraine | 3.14 | 9.08 | 9.57 | 0.41 | 22.21 | 17,500 |

*Combined results*

Main results are reported in Table 4. The cost per patient for the label arm ranged from $43 (Philippines) to $86 (South Africa) while for the pillbox arm this ranged from $59 (Ethiopia) to $180 (Ukraine).

**Table 4**. Intervention costs (total and total per patient) by intervention arm, expressed in 2023 USD.

| | Total per patient ($/patient) | Total ($ per all patients) |
|---|---|---|
| Ethiopia | | |
| Label | 45.59 | 57,892 |
| Pillbox | 58.65 | 86,693 |
| Philippines | | |
| Label | 42.92 | 65,721 |
| Pillbox | 76.25 | 86,347 |
| South Africa | | |
| Label | 86.31 | 60,936 |
| Pillbox | 127.80 | 110,577 |
| Tanzania | | |
| Label | 57.05 | 73,218 |
| Pillbox | 74.68 | 85,874 |
| Ukraine | | |

| | | |
|---|---|---|
| Pillbox | 180.47 | 142,213 |

Technology costs of the labels were low in all countries due to the labels being printed locally, meanwhile technology costs of the pillboxes were higher and highly dependent on the reuse rate of the box. In fact while shipping costs of the boxes in South Africa were low due to the manufacturer being based in the country, the total cost of the technology ended up being higher than in other countries due to South Africa's low reuse rate.

The ASCENT adherence online platform, after an initial set-up investment of 10,000$, required constant monthly payments, which weighted on the total cost of the interventions as they continued to be run through the 18 months period, totalling 72,000$ in each country.

Similarly, the phone infrastructure for the label intervention required monthly payments to purchase the SMS short code line rental. In Tanzania, these costs required an additional yearly renewal infrastructure fee of 6,000$, which made these costs per patient 10-times higher compared to the other countries.

SMS costs were higher for the label interventions than the pillbox due to the former involving outgoing messages of patients submitting the daily code. Pillboxes in Ukraine were set up to send fewer notification compared to other countries, therefore incurring in lower costs.

The high variability in support costs among countries is due to both the variability of salary of the local technical officer, as well as their different number of visits to healthcare facilities during the trial period: 89 in Ethiopia, 78 in the Philippines, 39 in South Africa, 65 in Tanzania and 8 in Ukraine.

Training costs in the Philippines were lower than in most other countries because the majority of training sessions were run online, and the few that were in-person did not require provision of accommodations or transportation. In South Africa, training had to be provided for interns repeatedly due to the short-term duration of their contracts, suggesting a possible optimisation of training in future post-ASCENT scenarios which would lower costs by training interns at the beginning of their employment period.

***Best-case post-ASCENT scenario***

To estimate the possible costs the interventions would have outside of a research environment, we re-calculated technology, support and training costs in a best-case scenario, assuming each technology was incorporated as part of routine care. We imagine a best-case extreme scenario where the patients using the technology correspond to the totality of notified TB cases in the country. We do this in order to calculate the possible minimum cost per patient the healthcare providers would have to pay if they decided to implement the technology as part of their routine care. Thus, we calculated the cost per patient by considering the totality of adult (15+ years of age) patients treated for TB in 2022 as reported in the WHO Global TB report 2023 (Table 5). Lower DAT coverage was achieved during the trial [1], but for the purpose of this analysis, in order to estimate the absolute minimum cost per patient, we consider all adult TB patients. Full breakdown of results is reported in Table 6.

**Table 5**. Number of TB notified cases in adult individuals in 2022 as reported in the WHO Global TB report 2023 [3].

| | |
|---|---|
| Ethiopia | 102,274 |
| Philippines | 405,378 |
| South Africa | 199,294 |
| Tanzania | 83,083 |
| Ukraine | 18,196 |

For the label intervention, printing costs would not change. For the pillboxes however, in a best-case scenario we assume that all countries have a box reuse rate of 3 (meaning each box purchased can be used up to 4 times that year), which substantially lowers the cost of the box per patient. Additionally, adherence platform costs would not require new set-up. While monthly payments of 4,000$ for hosting and support of the adherence platform would still have to be paid in South Africa and Ukraine, this would not be the case in Ethiopia, Philippines and Tanzania. In Ethiopia servers were purchased for a cost of 35,000$, meaning that after this initial expense, no additional costs to host the platform by a private vendor would have to be paid. Similarly in the Philippines and Tanzania, plans for integration of the pillbox technology into the current infrastructure mean that after an initial investment of 25,000$ no additional monthly expenses would be incurred, making the ongoing adherence platform costs in these countries virtually zero in the long-run.

To recalculate the support costs, we used the same technical officer salaries as in the previous analysis, however in future scenarios, where digital adherence technologies are incorporated as part of routine care, a staff member from the Ministry of Health could potentially be responsible for this support, with implications for the associated salary costs. We estimated the possible number of visits by assuming 40% of the technical officer work-days spent on visits, and two visits per day. However, in the long-run, as the technology becomes an integral part of the routine care, less support would probably be needed.

A similar logic is extended to the training, as it is probably unrealistic that stand-alone face-to-face training sessions would be offered in the long-run if the DAT interventions became part of routine care. It is possible that other, less costly and time-consuming forms of training would be implemented instead. For the purpose of this exercise, we assumed that one online training session would be organised per year.

**Table 6**. Intervention costs (total and total per patient) by intervention arm in a best-case scenario post-trial, expressed in 2023 USD.

| | Technology ($/patient) | | | | Support ($/patient) | Training ($/patient) | Total per patient ($/patient) | Total ($ per all patients) |
|---|---|---|---|---|---|---|---|---|
| | Purchase + Shipping | Adherence platform | Phone infrastructure | SMS | | | | |
| **Ethiopia** | | | | | | | | |
| Label | 0.30 | 0.47 | 0.013 | 2.75 | 0.47 | 0.12 | 4.12 | 421,014 |
| Pillbox | 15.77 | 0.03 | - | 0.18 | | | 16.56 | 1,725,451 |
| **Philippines** | | | | | | | | |
| Label | 1.70 | 0.12 | 0.002 | 2.55 | 0.11 | 0.13 | 4.60 | 1,865,774 |
| Pillbox | 15.72 | 0.01 | - | 0.27 | | | 16.23 | 6,601,842 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **South Africa** | | | | | | | | |
| Label | 1.20 | 0.24 | 0.003 | 1.81 | 0.36 | 0.52 | 4.13 | 822,947 |
| Pillbox | 15.50 | 0.24 | - | 0.17 | | | 16.79 | 3,345,581 |
| **Tanzania** | | | | | | | | |
| Label | 0.50 | 0.58 | 0.071 | 2.48 | 0.56 | 0.17 | 4.37 | 362,947 |
| Pillbox | 16.01 | 0.03 | - | 0.13 | | | 16.90 | 1,426,239 |
| **Ukraine** | | | | | | | | |
| Pillbox | 15.69 | 2.64 | - | 0.25 | 4.64 | 2.31 | 25.53 | 464,519 |


1. Jerene, D., et al., *Effectiveness of digital adherence technologies in improving tuberculosis treatment outcomes in four countries: a pragmatic cluster randomised trial protocol.* BMJ open, 2023. **13**(3): p. e068685.
2. *XE Currency Converter*. Available from: https://www.xe.com/.
3. World Health Organisation. *Global Tuberculosis Programme*. 2022; Available from: https://www.who.int/teams/global-tuberculosis-programme/data.