**Online Appendix**

**Maheswaran H, Petrou S et al. Economic cost and health-related quality of life outcomes of hospitalised patients with high HIV-prevalence: A prospective hospital cohort study in Malawi.**

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**S1 File: Direct health provider costing methods**

UNAIDS costing guidelines were used to undertake the primary costing studies to estimate the costs for all medical resource outputs used [1]. Broadly, a list of medical resource outputs (e.g. days of admission; full blood count) was identified from the medical data extracted by the doctors. Secondly, interviews were conducted with medical and administrative personnel to identify and quantify the individual resources required to produce the medical resource outputs. Thirdly, the financial data from hospital administration systems, in combination with National and International resource data, were used to value individual resource inputs. Fourthly, the data was used to estimate the cost of each medical resource output. Finally, the estimated resource output costs were used to estimate the total health provider cost for each study participant. A combination of top-down and bottom-up methods were used to estimate the relevant costs [2].

We undertook interviews with central support services to estimate the total central support service costs for running the hospital. This cost was then allocated to each department (Medical wards, Laboratory, Radiology and Pharmacy). We used the number of staff working in each of these departments divided by the total number of staff at the hospital to estimate the proportion of the total central support costs consumed by each relevant department. Some central support costs (e.g. catering, costs of locum staff) were only allocated to the medical wards, as the other departments do not benefit from them. For this we used the number of clinical staff working on the medical wards and divided by the total number of clinical staff working in the hospital to determine what proportion of the specific form of central support cost should be allocated to each medical ward.

For the medical wards, we estimated the cost per day of hospital care. Interviews were undertaken with the nurse in charge on the wards to determine the staff who worked on the ward and the time they spent on the ward. Information was obtained on the consumables used, and the quantity of each consumable used annually. A list of all the equipment on the wards was also documented. A unit cost was obtained for all consumables and equipment’s. The total average annual cost of running the ward was estimated. This compromised the cost of staff, consumables and equipment. The cost of central support services was added to these total costs. During the study period, we recorded the daily number of patients on each ward, and this was used to estimate the total number of patient days of admission per year. The total average annual cost for each ward was divided by annual patient days to estimate the average cost per patient day of admission.

We repeated the same procedure for the pharmacy department. We estimated the total average annual cost of running the pharmacy. This compromised the costs of staff, consumables and equipment, in addition to an allocated proportion of the central support services. The pharmacy keeps a record of the total drugs supplied per annum, broken down by drug formulation and doses given. The total average annual cost of running the pharmacy was divided by the total number of drug doses supplied to estimate the average cost per dose of drug dispensed by the pharmacy. This cost was added to the cost of the drug to estimate the total cost of providing the drug to the patient. For the cost of the drugs, we used the international market price [3]. The cost of shipping and insurance was excluded from the international market price for the drugs.

Investigations and procedures are performed through the Laboratory and Radiology department at QECH or on the medical wards. For investigations and procedures, we estimated the direct cost of performing the investigation and the indirect cost of the investigation or procedure. The direct cost of the investigation or procedure comprised the attributable cost of personnel, consumables and equipment. We undertook interviews with the medical, laboratory and radiology staff to quantify each of these items. For equipment and personnel, we recorded the approximate time spent in performing the investigation. A unit cost of each item was obtained and the total direct cost of the investigation or procedure was estimated. The indirect cost of the investigation comprised the cost per test of the department and the cost of the central support services. For this we estimated total cost, including the cost of central support services, and divided this by the total outputs of the department. For investigations and procedures performed in the Laboratory and Radiology department, we used the total number of tests performed as the denominator. For the Laboratory and Radiology department, we undertook interviews to estimate the numbers and grades of staff working in the department, and the consumables and equipment used. For all these items we quantified the proportion of the time spent on performing investigations or procedures, and the proportion of time spent on general duties or activities. For the indirect costs, we summed total costs based on resources used for activities other than performing a specific investigation or procedure. We used the estimated direct cost of performing investigations and procedures performed on the ward. Some investigations are performed outside QECH. For these we used the cost charged to QECH as the total cost of the investigation.

For all the costings, we obtained staff salaries from the QECH Human Resources departments and included employer contributions and fringe benefits. The costs of consumables and equipment were obtained from the Malawi Ministry of Health price catalogue. For costs that were not available in the catalogue, we used the international market prices. We first contacted local suppliers to obtain costs, and if these were not available, we contacted international suppliers and manufacturers. Equipment costs were annuitized over their useful life with an annual discount rate of 3%. For large laboratory and imaging equipment, we assumed the useful lifetime to be 5 years. This assumption was based on discussions with laboratory and radiology staff on time before equipment should be replaced. For all other equipment, including general office equipment, we assumed the useful lifetime to be 3 years.

The *total direct health provider cost* comprised the cost of the stay on the hospital ward, the cost of all investigations and procedures and the cost of all drugs given. The cost of stay on the hospital ward was estimated by multiplying the average cost per day of admission by the total number of days stayed on each ward. The total cost of investigations and procedures per participant was estimated by multiplying the relevant unit costs by the number of times the investigations and procedures were performed. The total cost of drugs per participant was estimated by multiplying the cost of each drug given by the number of doses administered. The cost of each drug included the cost of dispensing the drug through the pharmacy department.

**S2 File: Direct non-medical and indirect costing methods**

Two interviewer-administered questionnaires were developed to record direct non-medical and indirect costs incurred by participants and their main family member or carer who remained with them at hospital during the admission. The direct non-medical costs included the cost of transportation, food, drinks, toiletries, clothing and other items bought during the hospital admission. For indirect costs, we recorded whether participants or their carers had taken time off work, and if so, the amount of time, and multiplied this by their self-reported income [4]. The first questionnaire was administered on the first working day after hospital admission, and asked about all direct non-medical and indirect costs incurred on the day of their hospital admission. Follow-up questionnaires were administered to participants every three to seven days thereafter, and captured direct non-medical and indirect costs for the preceding day they were in hospital.

The *total direct non-medical and indirect cost* per participant was estimated for the duration of the hospital admission. This included costs incurred by the participant and their main family member/carer who stayed with them during their hospital admission. For participants who died during their hospital admission, these costs were estimated for the period from admission till death. The total direct non-medical and indirect cost was estimated by adding the costs on the day of admission, to the average daily cost for each subsequent period between interviews multiplied by the duration of each subsequent period.

The questionnaires were forward translated into Chichewa, the local language of the study population, and back translated by two independent bilingual Malawians. The questionnaires were then pilot tested, and discussions were held with senior Malawian staff working at the Malawi-Liverpool Wellcome Trust Clinical Research Programme before the final version was agreed upon.

**S3 File: Health-related quality of life assessment methods**

All study participants were asked about their health-related quality of life (HRQoL) on the first day after their admission or on the first day on which they were able to respond to the questions. HRQoL was assessed every three to seven days thereafter, however, we examined the earliest recorded assessment in order to reflect the pre-treatment health state.

Participants completed both the descriptive EQ-5D-3L system and the visual analogue scale (VAS). The responses to the descriptive component were converted to an EQ-5D utility score by using a tariff set. The tariff sets have been derived from national surveys of the general population, with a subset of the 243 health states being valued, most commonly using the time trade-off method [5]. The remainder of the EQ-5D health states were subsequently valued through the estimation of a multivariate model. As there is no Malawian EQ-5D tariff, the Zimbabwean EQ-5D tariff set [6] was used. The visual analogue scale is similar to a thermometer, and ranges from 100 (best imaginable health state) to 0 (worst imaginable health state). Participants recorded how good or bad their health was on the day of completion by drawing a line on the scale.

The tables below provide the estimates for the unit costs for healthcare resources obtained from the primary costing study.

S4 Table: Mean health provider unit cost - Ward stay and drug dispensing costs

S5 Table: Mean health provider unit cost - Radiological and imaging investigations

S6 Table: Mean health provider unit cost - Laboratory investigations

S7 Table: Mean health provider unit cost - Ward-based investigations and procedures

**S4 Table: Mean health provider unit cost - Ward stay and drug dispensing costs**

|  |  |  |
| --- | --- | --- |
| Cost category | Mean direct health provider cost | |
| 2014 US Dollars | 2014 INT Dollars |
| Cost per day of admission  TB Ward  Male medical  Female medical | 14.48  15.35  16.17 | 40.17  42.58  44.80 |
| Pharmacy dispensing cost  Mean cost per table, vial, ampoule dispensed | 0.0058 | 0.0162 |

**S5 Table: Mean health provider unit cost - Radiological and imaging investigations**

|  |  |  |
| --- | --- | --- |
| Investigation | Mean Total Cost | |
| 2014 US Dollars | 2014 INT Dollars |
| Chest X-Ray | 10.73 | 27.56 |
| Abdominal X-Ray | 10.73 | 27.56 |
| Cervical Spine X-Ray | 7.85 | 21.78 |
| Thoracic Spine X-Ray | 7.85 | 21.78 |
| Lumbar Spine X-Ray | 7.85 | 21.78 |
| Other plain X-Ray | 10.73 | 27.56 |
| Abdominal/Renal Ultrasound | 16.81 | 46.67 |
| Pelvic Ultrasound | 16.81 | 46.67 |
| Neck Ultrasound | 16.81 | 46.67 |
| Doppler Ultrasound | 19.25 | 53.45 |
| Chest Ultrasound | 16.81 | 46.67 |
| \*MRI Head | 50.89 | 68.55 |
| \*MRI Spine | 50.89 | 68.55 |
| \*CT Head | 22.08 | 61.33 |
| \*CT Thorax | 22.08 | 61.33 |
| \*CT Abdomen | 22.08 | 61.33 |

\*Service out-sourced to external provider

MRI: Magnetic resonance imaging

CT: Computed Tomography

**S6 Table: Mean health provider unit cost - Laboratory investigations**

|  |  |  |
| --- | --- | --- |
| Investigation +/- Procedure | Mean Total Cost | |
| 2014 US Dollars | 2014 INT Dollars |
| Malaria Film | 2.56 | 7.11 |
| Peripheral blood film | 4.93 | 13.43 |
| Group and X match | 13.22 | 36.86 |
| Full Blood Count (FBC) | 5.35 | 14.28 |
| Erythrocyte sedimentation rate (ESR) | 1.47 | 4.08 |
| \*Prothrombin Time | 12.24 | 34.00 |
| Urea + Electrolytes (U+Es) | 11.33 | 31.56 |
| Creatinine | 3.94 | 11.04 |
| Liver Function Tests (LFTs) | 8.76 | 24.44 |
| Lipid Profile | 10.44 | 29.09 |
| Cardiac enzymes | 8.19 | 22.83 |
| Random / Fasting glucose | 3.69 | 10.36 |
| CD4 count | 15.48 | 42.99 |
| HIV Viral Load | 27.63 | 31.04 |
| Hepatitis B surface antigen (Hep B sAg) | 3.32 | 9.22 |
| Hepatitis C antibody (Hep C Ab) | 5.88 | 9.51 |
| VDRL | 3.35 | 9.31 |
| Malaria rapid diagnostic test | 2.16 | 6.00 |
| Blood Culture | 33.77 | 82.18 |
| Urine microscopy | 2.40 | 6.70 |
| Stool microscopy | 2.10 | 5.85 |
| CSF/LP | 41.63 | 114.27 |
| Sputum smear (Microscopy and AFB) | 5.86 | 15.01 |
| Sputum for GeneXpert (rapid TB test) | 25.51 | 60.69 |
| \*Sputum culture for Tuberculosis | 17.42 | 48.39 |
| Lymph node aspirate for Micro (AFB, cell count) | 7.76 | 20.21 |
| \*Lymph node aspirate for Cytology | 29.87 | 82.98 |
| Lymph node biopsy for Micro (AFB) | 6.77 | 17.57 |
| Lymph node biopsy for Histology | 49.53 | 136.63 |
| Cytology | 27.66 | 76.84 |
| Pregnancy Test | 3.93 | 10.94 |
| \*\*Diagnostic Pleural Tap | 17.60 | 47.73 |
| \*\*Diagnostic Ascitic Tap | 17.60 | 47.73 |
| \*\*Therapeutic and Diagnostic Ascitic Tap | 23.60 | 64.40 |
| \*\*Diagnostic Knee Aspirate | 16.06 | 43.45 |
| \*\*Therapeutic and Diagnostic Pleural Tap | 23.60 | 64.40 |

\*Service out-sourced to external provider

\*\*Includes cost of procedure

Urea + Electrolytes (U+Es): Urea, Sodium and Potassium

Liver Function Tests (LFTs): Total protein, Albumin, Bilirubin, Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) Gamma-glutamyl transpeptidase (GGT) and Lactate dehydrogenase (LDH)

Lipid Profile: Total Cholesterol (TC), Triglyceride (TG), Low-density lipoprotein (LDL), high-density lipoprotein (HDL)

Cardiac enzymes: Creatine Kinase (CK & CKMD), Lactate dehydrogenase (LD)

VDRL: Venereal Disease Research Laboratory test for Syphilis

CSF/LP: Lumbar puncture to obtain cerebrospinal fluid

AFB: Acid-fast bacilli test for Tuberculosis

**S7 Table: Mean health provider unit cost - Ward-based investigations and procedures**

|  |  |  |
| --- | --- | --- |
| Investigation or Procedure | Mean Total Cost | |
| 2014 US Dollars | 2014 INT Dollars |
| Urine Dipstick | 0.82 | 2.27 |
| HIV Test | 3.87 | 10.74 |
| Electrocardiography (ECG) | 2.61 | 7.24 |
| Echocardiogram | 15.05 | 41.82 |
| Therapeutic Pleural Tap | 12.88 | 35.78 |
| Therapeutic Ascitic Tap | 4.55 | 12.63 |
| Lymph node aspirate | 2.21 | 6.14 |
| Insertion of Naso-Gastric tube | 3.87 | 10.74 |
| Insertion urinary catheter | 11.65 | 32.37 |
| Incision and drainage | 3.40 | 9.44 |
| Chest Drain | 32.71 | 88.63 |
| Therapeutic Lumbar Puncture | 8.55 | 22.13 |
| \*Gastroscopy/Endoscopy/Laryngoscopy | 470.70 | 1307.51 |
| \*Colonoscopy | 470.70 | 1307.51 |
| \*Bronchoscopy | 470.70 | 1307.51 |
| \*Endoscopy +/- Banding | 470.70 | 1307.51 |
| Laparoscopic Surgery | Not costed | |
| Laparotomy | Not costed | |

\*Not costed, cost obtained from private health provider

The tables below show the EQ-5D utility scores derived using the UK York A1 tariff [5].

**S8 Table: EQ-5D utility scores (UK tariff) by discharge medical diagnosis**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Discharge medical diagnosis | N | EQ-5D utility scores (UK tariff) | | |
| **On admission** | **Last recorded** | **Change** |
| Mean (SE) | Mean (SE) | Mean (SE) |
| All | **640** | **0.267 (0.02)** | **0.382 (0.02)** | **+0.116 (0.02)** |
| Pulmonary tuberculosis | 54 | 0.207 (0.05) | 0.391 (0.05) | +0.184 (0.05) |
| Tuberculosis of meninges and central nervous system | 16 | 0.062 (0.10) | 0.192 (0.07) | +0.130 (0.14) |
| Tuberculosis of intestines, peritoneum | 9 | 0.384 (0.14) | 0.332 (0.10) | -0.053 (0.09) |
| Tuberculosis of bones and joint | 4 | 0.073 (0.15) | 0.125 (0.07) | +0.052 (0.11) |
| Tuberculosis of other organs | 15 | 0.324 (0.10) | 0.309 (0.10) | -0.015 (0.09) |
| Miliary tuberculosis | 17 | 0.156 (0.10) | 0.074 (0.06) | -0.082 (0.09) |
| Tuberculosis - retreatment | 6 | 0.412 (0.22) | 0.551 (0.18) | +0.139 (0.10) |
| Septicaemia\* | 58 | 0.303 (0.05) | 0.474 (0.05) | +0.171 (0.05) |
| Candidiasis | 6 | 0.073 (0.07) | 0.207 (0.11) | +0.134 (0.15) |
| Cryptococcal meningitis | 36 | 0.236 (0.07) | 0.348 (0.07) | +0.112 (0.08) |
| Viral infection | 8 | 0.449 (0.10) | 0.361 (0.15) | -0.088 (0.09) |
| Pneumocystis Jivorecii pneumonia | 8 | 0.382 (0.13) | 0.392 (0.17) | +0.010 (0.21) |
| Malaria | 13 | 0.338 (0.09) | 0.326 (0.11) | -0.011 (0.03) |
| Kaposi’s sarcoma | 20 | 0.145 (0.07) | 0.228 (0.07) | +0.083 (0.05) |
| Neoplasms - excluding Kaposi's | 7 | 0.424 (0.14) | 0.149 (0.20) | -0.276 (0.18) |
| Diabetes mellitus without complications | 5 | 0.610 (0.09) | 0.791 (0.06) | +0.181 (0.12) |
| Diabetes mellitus with complications | 9 | 0.148 (0.14) | 0.186 (0.14) | +0.038 (0.09) |
| Anaemia | 35 | 0.355 (0.07) | 0.492 (0.07) | +0.137 (0.06) |
| Mental health disorders | 9 | 0.426 (0.12) | 0.564 (0.12) | +0.137 (0.15) |
| Meningitis\*\* | 36 | 0.294 (0.06) | 0.518 (0.07) | +0.225 (0.07) |
| Epilepsy; Convulsions | 10 | 0.381 (0.18) | 0.437 (0.20) | +0.056 (0.09) |
| Other neurological problems | 15 | 0.308 (0.10) | 0.368 (0.10) | +0.060 (0.09) |
| Cerebrovascular disease | 23 | 0.087 (0.08) | 0.224 (0.10) | +0.138 (0.06) |
| Hypertension | 7 | 0.132 (0.19) | 0.245 (0.15) | +0.114 (0.13) |
| Congestive heart failure; non-hypertensive | 15 | 0.371 (0.10) | 0.416 (0.10) | +0.045 (0.10) |
| Other cardiovascular problems | 12 | 0.308 (0.12) | 0.536 (0.10) | +0.228 (0.13) |
| Pneumonia\*\* | 91 | 0.295 (0.04) | 0.434 (0.04) | +0.139 (0.04) |
| Other respiratory problems | 11 | 0.236 (0.12) | 0.609 (0.11) | +0.373 (0.13) |
| Acute - Intestinal infection | 10 | 0.292 (0.15) | 0.332 (0.11) | +0.039 (0.14) |
| Chronic - Intestinal infection | 14 | 0.170 (0.12) | 0.274 (0.11) | +0.104 (0.11) |
| Upper gastrointestinal disorders | 11 | 0.286 (0.10) | 0.331 (0.12) | +0.045 (0.13) |
| Liver disease | 14 | 0.229 (0.11) | 0.306 (0.10) | +0.077 (0.09) |
| Diseases of the genitourinary system | 18 | 0.307 (0.08) | 0.491 (0.10) | +0.184 (0.11) |
| Diseases of the musculoskeletal system | 6 | 0.131 (0.10) | 0.031 (0.13) | -0.100 (0.14) |
| Other problems (<5 cases) | 12 | 0.170 (0.10) | 0.370 (0.11) | +0.200 (0.10) |

\*Except in Labour

\*\*Except that caused by TB or Cryptococcal

The tables below show the findings from the model diagnostics for the multivariate analysis of EQ-5D utility scores.

S9 Table: Estimated predicted values compared to actual utility scores

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Model** | **Obs** | **Mean** | **Min** | **Max** | **MSE** | **MAE** | **r2** |
| Observed | 605 | 0.503 | -0.145 | 1.000 |  |  |  |
| Model | OLS | 605 | 0.503 | 0.242 | 0.772 | 0.000 | 0.199 | 0.119 |
| TOBIT | 605 | 0.502 | 0.241 | 0.771 | 0.001 | 0.200 | 0.118 |
| CLAD | 605 | 0.519 | 0.095 | 0.985 | 0.017 | 0.206 | 0.046 |
|  | Flogit | 605 | 0.503 | 0.242 | 0.772 | 0.000 | 0.199 | 0.119 |

OLS: Ordinary Least Squares MSE: Mean Squared Error

Flogit: Fractional logit MAE: Mean Absolute Error

CLAD: Censored least absolute deviations r2: Coefficient of determination

S10 Table: MSE, MAE and R-squared statistics for regression models by utility score range

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | |  | |  | |  | |  | | **Observed EQ-5D utility score** | | | | | | | | | | | | | | | |  |
|  | <0 | | | | | | 0 to <0·2 | | | | | | 0·2 to <0·4 | | | 0·4 to <0·6 | | | 0·6 to <0·8 | | | 0·8 to <1 | | | 1 | | | |
| **Obs** | 29 | | | | | | 45 | | | | | | 139 | | | 155 | | | 180 | | | 56 | | | 14 | | | |
|  | MSE | | MAE | | r2 | | MSE | | MAE | | r2 | | MSE | MAE | r2 | MSE | MAE | r2 | MSE | MAE | r2 | MSE | MAE | r2 | MSE | MAE | r2 | |
| **OLS** | 0.495 | | 0.495 | | 0.018 | | 0.355 | | 0.355 | | 0.012 | | 0.180 | 0.180 | 0.043 | 0.003 | 0.079 | 0.008 | 0.178 | 0.179 | 0.014 | 0.305 | 0.305 | 0.008 | 0.433 | 0.433 | n/a | |
| **TOBIT** | 0.495 | | 0.495 | | 0.016 | | 0.354 | | 0.354 | | 0.010 | | 0.179 | 0.180 | 0.040 | 0.004 | 0.078 | 0.009 | 0.179 | 0.180 | 0.014 | 0.308 | 0.308 | 0.010 | 0.426 | 0.426 | n/a | |
| **CLAD** | 0.502 | | 0.502 | | 0.021 | | 0.407 | | 0.407 | | 0.005 | | 0.176 | 0.193 | 0.015 | 0.008 | 0.104 | 0.002 | 0.157 | 0.168 | 0.024 | 0.261 | 0.268 | 0.001 | 0.421 | 0.421 | n/a | |
| **Flogit** | 0.495 | | 0.495 | | 0.018 | | 0.355 | | 0.355 | | 0.012 | | 0.180 | 0.180 | 0.043 | 0.003 | 0.079 | 0.008 | 0.178 | 0.179 | 0.014 | 0.305 | 0.305 | 0.008 | 0.433 | 0.433 | n/a | |

OLS: Ordinary Least Squares Flogit: Fractional logit CLAD: Censored least absolute deviations

MSE: Mean Squared Error MAE: Mean Absolute Error r2: Coefficient of determination

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