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Table S1. Summary of the evidence on the determinants of costs and efficiency in economies of scale (n=40)^a.

ECONOMETRIC STUDIES (n=9)

Antiretroviral therapy (n=2)

- *Scale* was found to explain 48.4% of the variability in unit costs per patient in Ethiopia.²³
- *Patient volume* (no. patients receiving treatment) and *maturity* were strong independent significant predictors of per-patient costs in 54 clinical sites in Botswana, Ethiopia, Mozambique, Nigeria, Uganda, and Vietnam.^{93, b} For patient volume, unit costs declined by 43% as patient volume increased from 500 to 5,000 patients, and by 28% from 5,000 to 10,000 patients.^{93, b}

HIV counselling and testing (n=2)

- *Scale* was found to explain between 28% and 83% of variability in unit costs (83% in India, 28% in Russia, 33% in South Africa and 29% in Uganda; Also 20% in Mexico but *p* value of regression was insignificant).^{69, 96}
- The percentage of costs assigned to personnel (*use of fixed resources*) explained 58% of the variability in cost per post-test counselled client.⁶⁹
- Sites with higher service volume tended to have lower unit costs.⁹⁶
- Quality indicators were not found to be significantly associated with unit costs and explained almost none of the variation in observed unit costs.⁹⁶

Key populations (n=6)

- *Scale* was found to explain: 75% of the variability in cost per commercial sex worker (CSW) in a study in southern India assessing 15 programmes that provided service to 33,941 sex workers;⁷⁴ 85% of the variability in cost per CSW in a study in India assessing 17 interventions by non-government organisation (NGO) with a mean of 1,047 CSW reached by each intervention;⁷⁵ and, 25% per person registered in a study in India assessing 107 interventions by NGOs with an estimated number of people registered at 134,391.⁷⁹ Results from the PANCEA project suggest that scale could explain 88%, 84% and 38% of the variability in unit costs in CSWs in India, Russia and South Africa, respectively.⁹⁶
- Results from the PANCEA project illustrates that scale could explain 45% and 96% of the variability in unit costs in needle exchange programs and rehabilitation focused programs (risk reduction programs focusing on Injected Drug Users) in Russia.⁹⁶
- In Russia, a doubling in scale was significantly associated with a \$5 decrease per hour of contact in CSWs.⁹⁶ In India, a doubling in scale was significantly associated with a 42% drop in cost per hour in CSWs.⁹⁶
- Duration of scale-up was significantly related to an increase in average costs ($\beta=0.376$, $p<0.001$).²²
- Efficiency improved with increasing number of truck drivers served and contacted by programmes⁷⁸ and CSW⁷⁷ but statistical significance was only found in the latter case.

Elimination of mother to child transmission (n=1)

- *Scale* was found to explain 42% of the variability in unit cost in a study of 15 sites in India ($p=0.038$).⁹⁶
- An inflection point in eMTCT programs in India was observed beyond which an up-turn in unit costs may be seen. However, this observation was due to one data point and, if excluded, costs level off but do not increase.⁹⁶

^a: Some studies include more than one core service; ^b: This study excluded ARV expenditures.

Table S1. Summary of the evidence on the determinants of costs and efficiency in economies of scale (n=40)^a (Continued).

DESCRIPTIVE STUDIES (n=34)

Antiretroviral therapy (ART) (n=17)

- *Scale of provider* was suggested as a determinant of unit costs in several studies.^{27, 43, 32, 33, 29}
 - A negative association between unit costs and the number of patients receiving ART treatment was observed in one study in India with 4 sites.⁴³
- The *proportion of fixed costs* varied between studies.
 - During expansion of ART it was observed that *fixed costs* may be reduced due to the increasing numbers of patients.^{27, 32, 33}
 - A substantial proportion of cost was also observed to be incurred by human resources/personnel/salaries (15.8%; range: 2.0%-38.1%)^b ^{36, 32, 39, 43, 30, 31, 40, 28, 47, 41} and through laboratory tests and treatment monitoring (25.9%; range: 5.1%-41.2%)^b.^{29, 38, 26, 22, 41}
- It was observed that financial measures to *reduce the costs to patients* may ensure more effective treatment (in terms of adherence). It was noted that this would place higher demands on *fixed resources* and thus increased efficiency.^{36, 38, 40}
- Cost reduction is observed with the *maturation* of sites as scale-up occurs.^{27, 20}
 - A study of 43 sites across five countries reported a 47% drop in per patient ART costs between the first and second 6-month period after the beginning of scale-up, followed by an additional 30% in the following year.²⁰

HIV counselling and testing (n=3)

- *Staff mix*³⁷ and more efficient use of *human resource* were suggested to be determinants of cost in two studies covering 12 and 6 sites in Zambia and Rwanda, respectively.⁹⁴
- *Staff workload* (the ratio of staff to service volume) rather than scale as service volume may explain cost variation.⁶⁴

Condom promotion and distribution (n=3)

- A study of 18 parishes in Masaka, Uganda found that a strong increase in the uptake (74%) of interventions was accompanied by a significant drop in unit costs (34%).⁵⁴
- One study from Tanzania found that, during scale-up, *programme maturity* was accompanied by almost 40% reduction in annual costs.⁵⁵
- In condom social marketing programmes, costs appeared to decline significantly as the projects progressed, and began to level out after 3-5 years.⁵³

Key populations (n=8)

- Mass media time⁹⁶ and personnel costs^{79, 75, 78, 73, 76, 82} (36.1%; range 14.3%-50.1%) were observed to be substantial components of costs.
- *Age* of the intervention and *maturity* of the programme was related to a 43-55% decrease in average annual costs (from the first to the third year).⁷³
- Increase in *scale of services* at some stage may result in less *efficiency* as more effort has to be spent in order to get to the resistant hard to reach sub-groups.⁵⁶

Voluntary medical male circumcision (VMMC) (n=1)

- Cost breakdowns identified human resources/personnel to be the key cost drivers.⁸⁶

Elimination of mother to child transmission (n=2)

- Costs of drugs and laboratory tests were identified as the main cost drivers but it was observed that scale up of activities may also result in reduction of these expenses.⁸⁹
- Lower unit costs were observed in high HIV prevalence settings as *overheads and start up costs* are spread over a greater number of women.⁹⁰

^a: Some studies include more than one core service.

^b: Estimates derived from studies that provided all salaries, non-salaries and capital costs.

Table S2. Summary of the evidence on the determinants of costs and efficiency in economies of scope (n=23^a).

Antiretroviral therapy (ART) (n=3)

- *Integrating* HIV and TB programmes through synergies in resource-limited settings increases their effectiveness and optimise the use of limited resources and clinical staff time.^{10, 46}
- *Integrated* HIV treatment and care services were found to be feasible and cost-effective.⁹

Behaviour Change Communication (BCC) (n=1)

- The major cost driver of BCC interventions that included peer education, radio broadcasts, magazines, public outreach events and billboards was personnel (63.9%) followed by recurrent contracted services (8.2%) and supplies (7.0%).⁵²

HIV counselling and testing (HCT) (n=18^b)

- *Integration* of voluntary HCT (VCT) with other health services improved quality,⁶¹ increased the utilisation of services and reduced the cost per visit by up to 33%^{70, 57} but was found to be more costly in other studies.^{20, 95}
- Costs savings of integrated vs stand-alone HCT services ranged from 17% to 47%,^{64, 63, 95} with a previous review summarizing the results from five studies^{67, 59, 61, 70, 57} identifying cost savings between 31% and 79%.⁹
- Provider-initiated testing and counselling was found to identify HIV-positive patients at about 40% of the cost of client-initiated VCT.⁶⁴
- A strong and functioning *referral system* was found to be important for creating demand with integrating services.^{9, 69, 63, 45, 33, 31, 29, 67, 35, 24, 70, 25}

Voluntary medical male circumcision (VMMC) (n=1)

- *Type of provider* may influence units costs as provision of VMMC services in an existing family clinic was related to lower unit cost per VMMC procedure compared to provision in a standalone clinic solely dedicated to VMMC (\$65.85 vs \$100.88).⁸⁸

Elimination of mother to child transmission (eMTCT) (n=1)

- High unit costs were found in relatively smaller hospitals in areas with relatively low HIV prevalence, *integration* of VCT and eMTCT services could increase efficiency.⁹¹

^a: Twenty three studies (twelve^{69, 91, 64, 20, 63, 95, 46, 33, 31, 24, 52, 88} of which not included in Sweeney et al. (2012) review⁹)

^b: Eighteen studies (nine^{69, 64, 20, 63, 95, 33, 31, 24, 52} of which not included in Sweeney et al. (2012) review⁹).

TB: Tuberculosis.

Table S3. Summary of the evidence on other determinants of costs and efficiency (n=48)^a.

Programme level determinants of costs beyond the control of lower level service providers (n=43)

Location (n=4)

- No clear pattern in costs was suggested in relation to the *location* of sites (urban vs rural areas) more generally, independent of scale.^{37, 29, 26} (ART)
- Assessing the costs in 12 sites in Zambia, lower unit costs were found in *urban* compared to *rural* areas due to larger catchment populations and numbers of clients served.³⁷ (HCT)
- Costs for ART were 11% higher in *urban* compared to *rural* sites (\$229.6 vs \$203.3).⁴²
- Costs for HCT were 40% higher in *rural* compared to *urban* sites (\$9.75 vs \$5.86) due to higher costs of providing technical support as a result of greater distances from administrative offices resulting in higher staff travel expenses.⁴²
- Lower unit costs in *urban* compared to *rural* areas were found for eMTCT.³⁷

Time^{ART, CD, eMTCT, HCT} (n=7)

- In an econometric study costs dropped 41% between months 0–12 and 25% between months 12–24.⁹³ (ART)
- Cost reductions over time may be attributed to
 - differences in initial start-up and administration costs.^{43, 53, 90} (ART, eMTCT, CD)
 - reductions in the price of ARV drugs over time.⁴³ (ART)
 - increases in human resource costs occurring at a much slower rate than the number of patients receiving treatment.³⁸ (ART)
 - provider maturity and expertise.³² (ART)
 - task shifting to less expensive cadres of health care personnel.^{32, 66, 72} (ART, HCT, KP)

Input prices^{ART, CD, eMTCT} (n=11)

- Higher drug prices,⁴² especially of second-line regimens compared to first-line regimens,^{48, 46, 33} may increase treatment costs significantly.⁴⁵ (ART)
- Price levels (represented by per capita GDP) between countries were found to be significant predictors of per patient costs, with costs increasing by 22% for each doubling in per-capita GDP.⁹³ (ART)
- Shift in drug recommendations for eMTCT may result in higher costs for drugs.^{89, 100, 98, 97} (eMTCT)
- Condom-source model used (eg. Importation of condoms by a private partner, use of donor funds, initial donation of condoms, with a switch to commercial purchase over three to five years), may be an important driver for condom social marketing costs.⁵³ (CD)

Ownership and models of delivery^{ART, BCC, HCT, VMMC} (n=17)

- For ART
 - Costs of facility-based care in Uganda were much lower than home-based care in one study (\$337 vs \$738)³⁵ but did not differ in another (\$879 vs \$832).³⁶
 - Costs were not different between hospital and health centres in Zambia (\$362 vs \$358)³⁷ but hospitals had much lower costs than primary care clinics in South Africa (\$843 vs \$1,255).²⁹
 - Costs in the private sector were considerably higher than the public sector in Nigeria (\$2,680 vs \$1,081).⁴¹
 - Costs of provision of ART at health centres was at 74% of cost at hospital level.^{37, 47}
 - Costs for HCT and ART were higher in tertiary facilities compared to secondary ones (\$18.65 vs \$6.37 in HCT and \$341.16 vs \$206.46 in ART, respectively).⁴² (HCT, ART)
 - Secondary and tertiary sites might be more expensive than primary sites due to a more expensive care model that may offset, at least to some degree, the benefits of economies of scale enjoyed by those sites.⁹³
- For CT, costs are higher in health centres compared to hospitals (\$22.29 vs \$15.35)³⁷ and costs of stand-alone sites were higher than costs of
 - Facility-based sites (\$41 vs \$32)⁹⁵
 - Mobile clinics (\$28.88 vs \$15.32)⁶³
 - Hospitals (\$20.79 vs \$12.61)⁶⁷
 - home-based door-to-door care (\$20.79 vs \$8.95)⁶⁷
 - integrated STI and HIV/AIDS facilities (\$17.74 vs \$12.3)⁵⁷
 - Cost per HCT client was higher in private clinics compared to public facilities in provider-initiated testing and counselling services (\$6.27 vs \$5.52 and \$13.87 vs \$10.92 in Kenya and Swaziland, respectively), and lower in client-initiated VCT services (\$7.53 vs \$13.55 and \$12.01 vs \$12.97, respectively).⁶⁴
 - Private clinics were substantially less efficient than public facilities at identifying HIV-positive cases.⁶⁴
- For KP,
 - Costs were higher in the hospital clinic compared to an HIV community clinic and an STI community clinic and lower in a prison clinic (\$77.61 vs \$68.17 vs \$40.90 vs \$24.12).⁸⁰
- In VMMC,
 - Costs were lower in static sites compared to outreach sites in two studies in Kenya (\$32.3 vs \$40.21)^{83, b} and Zimbabwe (\$60.19 vs \$72.17).⁹⁸
 - Higher unit costs for outreach VMMC services compared to static sites due to higher operational costs which included costs for the running and maintenance of vehicles and cost of staff per diems.^{83, b}
- For BCC interventions,
 - Costs per person reporting systematic condom use were 13.6 (public outreach events), 5.6 (radio broadcasts) and 1.2 (magazines) times higher compared to the costs per person reached.⁵²

Referral system^{ART, HCT, eMTCT} (n=3)

- Suboptimal functioning may result in inability to detect and refer patients at earlier stages of disease, which may lead to higher pre-ART and first year costs.^{31, 24} (HCT, eMTCT)
- Down-referred patients may produce savings of up to 50% per visit, in high volume, well-resourced urban sites.³⁴ (ART)
- Fixed costs were also much lower at a down-referral site compared to the treatment-initiation site.³⁴ (ART)

Table S3. Summary of the evidence on other determinants of costs and efficiency (n=48)^a (Continued).

Upstream costs and systems^{ART, HCT, KP, VMMC, eMTCT} (n=10)

- Costs above the service delivery level have been reported to account for 35% to 46% of the cost of providing ART in India.⁴³
- Costs of external supervision and support comprised
 - 5.9%, 4.3%, 3%, 5.3% and 8.7% of the costs of services in hospitals and 9.8%, 7.3%, 6.1%, 14% and 14% of the costs in health centres in Zambia for ART initiation, ART follow-up, eMTCT prenatal care and postnatal care, and HCT, respectively.³⁷ (ART, HCT, eMTCT)
 - 6.7% and 1.7% of all programmatic costs for pre-ART and ART (including training) in Botswana, Ethiopia, Nigeria, Uganda and Vietnam.²⁰ (ART)
 - 6% and 11% in dispensaries and hospitals, respectively, in HCT in Kenya.⁶¹ (HCT)
 - 0.5% of total costs of MC in Lesotho.⁸⁵ (VMMC)
 - 43.5% of total costs per patient per year, in an integrated model of PHWs and mHealth support intervention in Uganda.⁷² (KP)
- In one study in Uganda, transport and supervision (including overheads) accounted for 9.7% and 7.8% of costs in home-based and facility based care, respectively.³⁶ (ART)
- Transportation and storage of drugs and medication accounted for 7% of total indirect and overhead costs per patient on 1st year ART in Haiti⁴⁶ and 1.2% of total ART costs in the public sector in Nigeria.⁴¹ (ART)
- NGO overheads may be considerable in order to ensure continuity of quality ART care.³⁸ (ART)

Impact on health systems costs^{VMMC} (n=5)

Infant MC can lower *health (upstream) system costs* because of moderate implementation costs, high and durable protective effects, and the averted HIV-care costs.^{87, 84, 88, b, c}

Targeting efficiency^{HCT} (n=1)

- Costs per infection averted were found to be lower when voluntary HCT, integrated within eMTCT services, *targeted* couples rather than individuals, and couple counselling would be more cost-effective in regions with higher prevalence of HIV.⁶⁰

Organisation and other environmental factors^{KP} (n=1)

Number of NGOs per district was negatively associated to unit costs in India.⁷⁹

Determinants of costs at the provider level (n=15)

Case mix/ severity^{ART} (n=7)

- Significant predictors of increased treatment costs and affordability of ART care include
 - Individual level characteristics including age,^{46, 47} being male,²⁸ increased body weight⁴⁶ and socio-economic position.⁴⁴
 - Severity of disease^{46, 47, 21, 49} particularly in the first year of treatment²⁸ and last year of patient's life (in middle-income settings).^{49, 50}

Service quality improvement^{ART} (n=4)

- Loss to follow-up/ lack of adherence may be a key source of inefficiency resulting in a cost mark-up of between 15% and 55%.^{46, 33, 29}
- Frequency of clinical follow-up, laboratory monitoring of established patients and optimization of the care package accompanying ART were significant independent predictors of per-patient costs.⁹³

Task shifting^{ART, KP, VMMC} (n=6)

- Task shifting, expressed as the ratio of doctors to other clinical staff, did not appear to be significantly related to per patient costs.⁹³
- Cost reductions in ART care may be achieved by task shifting to less expensive cadres of health care personnel.^{32, 42} (ART)
- Task shifting from surgeons to medical officers to provide MC resulted in a reduction in a 24% reduction in personnel costs.⁸⁷ (VMMC)
- Peer health workers may be a valuable resource to assist with task shifting and cost savings (eg by shifting caregiver tasks and costs onto themselves and the care program).⁷² (KP)
- Financial cost savings of 11% for patient eligible for down-referral who remain in care and respond to ART treatment were reported with down-referral of stable ART patients from doctor-managed, hospital based ART clinic to a nurse-managed primary health care facility, without compromising patient outcomes.³⁴ (ART)

^a: Some studies include more than one core service; ^b: Kioko, personal communication, 2010; ^c: Chiwevu, personal communication, 2010.

ART: Antiretroviral therapy; BCC: Behaviour Change Communication; CD: Condom promotion and distribution; HCT: HIV Counselling and Testing; KP: Key Populations; VMMC: Voluntary Medical Male Circumcision; eMTCT: Elimination of Mother To Child Transmission.