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Inter-facility transfers for emergency obstetrical and neonatal care in rural Madagascar: a cost-effectiveness analysis

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ABSTRACT

Context There is a substantial lack of inter-facility referral systems for emergency obstetrical and neonatal care in rural areas of sub-Saharan Africa. Data on the costs and cost-effectiveness of such systems that reduce preventable maternal and neonatal deaths are scarce.

Setting We aimed to determine the cost-effectiveness of a non-governmental organisation (NGO)-run inter-facility referral system for emergency obstetrical and neonatal care in rural Southern Madagascar by analysing the characteristics of cases referred through the intervention as well as its costs.

Design We used secondary NGO data, drawn from an NGO's monitoring and financial administration database, including medical and financial records.

Outcome measures We performed a descriptive and a cost-effectiveness analysis, including a one-way deterministic sensitivity analysis.

Results 1172 cases were referred over a period of 4 years. The most common referral reasons were obstructed labour, ineffective labour and eclampsia. In total, 48 neonates were referred through the referral system over the study period. Estimated cost per referral was US$336 and the incremental cost-effectiveness ratio (ICER) was US$70 per additional life-year saved (undiscounted, discounted US$137). The sensitivity analysis showed that the intervention was cost-effective for all scenarios with the lowest ICER at US$99 and the highest ICER at US$205 per additional life-year saved. When extrapolated to the population living in the study area, the investment costs of the programme were US$0.13 per person and annual running costs US$0.06 per person.

Conclusions In our study, the inter-facility referral system was a very cost-effective intervention. Our findings may inform policies, decision-making and implementation strategies for emergency obstetrical and neonatal care referral systems in similar resource-constrained settings.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Large study sample from a widely understudied population in remote Southern Madagascar.
⇒ Programmatic data and reliance on expert panel process for defining survival rates.
⇒ No long-term follow-up data of patients is available due to the cross-sectional nature of the study.
⇒ Robust cost-effectiveness analysis methodology, including detailed and comprehensive costing data.

BACKGROUND

Reducing the global maternal mortality ratio to less than 70 per 100 000 live births by 2030 is a key target of the Sustainable Development Goals.[1] Haemorrhage, sepsis, unsafe abortion and other complications of delivery account for more than 50% of maternal deaths in sub-Saharan Africa (SSA).[2] Most neonatal deaths in SSA are attributable to either intrapartum complications or complications linked to preterm delivery.[3] Many of these fatalities are preventable through access to timely and high-quality emergency obstetrical care (EmOC).

However, mothers and neonates in SSA often experience significant delays in accessing EmOC services, (ie, when deciding to seek, reach and receive adequate care[4]). Access to and availability of adequate means of transportation, including ambulance referral services to EmOC centres, reduces these delays,[5 6] which, in turn, reduces maternal and neonatal mortality.[7 8]

The implementation of ambulance referral systems for EmOC services in SSA has been described for several, mostly rural contexts, including in Uganda,[9 10] Burundi[11] and Ethiopia.[12] They mostly differed in the type of referral service provided (ie, from home to health facility vs inter-facility referral) and the level of medical support provided to patients during referrals. Only a minority of these programmes have been evaluated through a cost-effectiveness analysis.[9 12]

Africa's health financing gap is estimated at US$66 billion annually and the financing need for maternal and child health services is particularly acute.[13 14] Thus, reliable data on cost and cost-effectiveness of ambulance programmes are essential for designing and prioritising maternal health interventions in SSA.

We aimed to describe case and service characteristics as well as analyse the costs and cost-effectiveness of an EmOC inter-facility referral system established by a non-governmental organisation (NGO) in rural Madagascar. Our findings may inform policies, decision-making and implementation strategies for EmOC referral systems in resource-constrained settings.

METHODS

Study design

This is a retrospective study using secondary data, routinely collected as part of an NGO intervention. A data-sharing agreement with the NGO was in place.

Study area and context

The study took place in Atsimo-Andrefana, Androy and Anosy, rural regions in the South of Madagascar. Poverty rates in the study region are high with over 80% of the population living on less than US$1.90 per day.[15] Nationally, neonatal and maternal mortality ratios remain high with a maternal mortality ratio of 335 per 100 000 and a neonatal mortality ratio of 20 per 1000 live births, respectively.[16]

The Malagasy health system is organised into three tiers of care. While some public emergency referral services exist at the district and national level, they fall short of covering a significant amount of the population, especially in rural areas of the country.

Intervention

Setting

To improve access to EmOC, the German-Malagasy NGO Doctors for Madagascar established an inter-facility referral system for obstetrical and neonatal care in Atsimo-Andrefana (Ampanihy, Betioky-sud and Benenitra districts), Androy (Bekily district) and Anosy region (Fort-Dauphin district). The intervention covered a catchment population of around 1 million people (Malagasy Ministry of Health, 'Sectorisation', 2020). The intervention was rolled out sequentially, starting in Atsimo-Andrefana and Androy in 2016 and in Anosy in 2018. A four-wheel drive ambulance was stationed at each of three secondary referral hospitals: Hopitaly Zoara Fotadrevo, Hopitaly SALFA Manambaro and Hopitaly SALFA Ejeda, which served 18, 23 and 13 participating primary health centres, respectively Secondary referral hospitals offer inpatient care surgical care, obstetrical care, including emergency C-sections and basic neonatal care.

Participating primary health centres (locally known as Centres de Santé de Base (CSB); n=54) could call the ambulance 24 hours per day without charge. If a referral was deemed necessary by a trained medical dispatcher, the ambulance was sent to the CSB to transfer the patient to a higher-level care facility. The referral was free for patients and participating health centres, all costs were covered by the NGO.

Vehicles and equipment

All ambulances were Toyota four-wheel drive vehicles, equipped with a stretcher, oxygen, emergency medical equipment and drugs. (online supplemental file 1) summarises the medical equipment and drugs, which were available on board an ambulance vehicle.

To improve pre-transport emergency care, the NGO equipped participating CSBs with emergency kits containing alcohol, compresses, cotton swabs, isotonic glucose solution, isotonic saline, intravenous catheters, intravenous lines, scissors, sterile and non-sterile gloves and urinary catheters. These kits were checked and refilled by NGO staff after each referral.

Emergency medical teams

All calls from CSBs requesting a referral were processed by a medical emergency dispatcher, usually a medical doctor trained in EmOC and familiar with the local setting. If the dispatcher deemed a referral to be necessary, a vehicle was sent to retrieve the patient from the CSB.

The medical team aboard each vehicle always consisted of a trained midwife and a driver who had received basic life support training. If necessary, a medical doctor accompanied critical referrals. The medical doctor was an employee of the implementing NGO and accompanied approximately 5% of referrals. This decision was made on a case-by-case basis by the dispatcher.

Performance-based bonus payments

The referring healthcare worker received a cash bonus of US$2.5 for each case referred through the intervention, paid at the end of the month.

Participants

All women who presented at one of the participating CSBs during the intervention period with an acute complication during pregnancy, childbirth, or post partum and whose emergency referral was deemed necessary by the medical dispatcher were eligible to participate. Similarly, all neonates born or treated at participating CSBs within the neonatal period of 28 days and whose emergency referral was deemed necessary by the medical dispatcher were eligible to participate.

All obstetrical and neonatal patients using the ambulance referral system between 5 January 2016 and 31 September 2020, were included in the descriptive analysis.

Mothers and neonates presenting at CSBs not participating in the intervention were not eligible for ambulance referral.

Patients could refuse referral services at any point in time.

Data collection and data entry

Medical records

The data source for patient and referral characteristics were case data sheets filled by the ambulance staff. These data sheets included details on patient characteristics (eg, gestational age) and the referral indication.

All data were digitised into summary Excel tables by NGO personnel. Healthcare staff, who were not otherwise involved in this study, replaced patient identifying information with numerical pseudonyms before forwarding the Excel sheets to the research team for analysis. Codes linking pseudonyms and identifying information were not accessible to the research team.

We collected the original data in French and translated it into English. Data were cleaned by three independent researchers with regular check-ups to assure consistency in data cleaning. Data were additionally cross-checked and screened for double entries, out-of-range values and overall consistency. In case multiple referral indications were given, an expert panel of three Malagasy physicians determined the main referral indication, which was grouped following the approach by Abegunde *et al*.[17] All data were stored in a password-protected database to which only the research team had access.

Financial records

The data source for the costs of the intervention was NGO financial records from 2016 to 2019. A researcher extracted data from the original records and categorised them into investment and running costs and corresponding subcategories (medical equipment, administration, transport, communication, consumables, pre-transport care, performance-based bonus payments and training activities). Costs were classified as investment costs if they were one-time costs paid for the initial set-up of the intervention (eg, costs for the ambulance vehicles). Conversely, costs were defined as running costs if they were recurring costs necessary to continue programmatic activities (eg, fuel costs).

Investment costs were annualised based on lifetime estimates or records of items based on expert estimates from NGO staff active in the study region.

We included all costs associated with the initial establishment of the referral systems, for example, acquisition of equipment and ambulances, as well as running costs for the three project sites in the cost-effectiveness analysis (CEA). Costs for treatments at CSBs and referral hospitals were not included, as those were not supported through the programme. Data were collected in Malagasy ariary or Japanese Yen (one invoice) and converted to US dollars for analysis (exchange rate: US$1=3867.09 Malagasy ariary (as of 22 September 2020) and US$1=105.671 Japanese Yen (as of 30 September 2020).

Data analysis

Descriptive statistics

We performed a descriptive analysis, including frequency distributions, for medical records using Stata V.16.

Cost-effectiveness analysis

We used a CEA to quantify the costs per life year saved, as well as the incremental cost-effectiveness ratio of the intervention. As this was not a randomised control trial, we did not develop a health economic analysis plan. We also assessed the sensitivity of the analysis to a variation of parameters. We adhere to the Consolidated Health Economic Evaluation Reporting Standards guideline for economic evaluations of healthcare interventions in structuring this manuscript.[18]

The main outcomes of the model were incremental cost-effectiveness ratios (ICER) per life year saved through the intervention overall, and separately by cohort, where one cohort was defined as all cases referred due to the same referral indication. To calculate the costs for each cohort, we multiplied the average costs per referral by the number of patients per cohort. For each cohort, we calculated the following ICER: (costs of ambulance referral system − costs of no referral system)/((life years saved neonates referred + life years saved mothers referred) − (life years saved neonates not referred + life years saved mothers not referred)). To obtain the overall ICER of the intervention, we added the ICERs for individual cohorts, weighted by the frequency of their occurrence.

Study population and model

This economic evaluation followed a CEA, with a healthcare provider's perspective. For each medical condition that constituted a referral indication, we developed one decision analytical model (if the condition affected only mother or neonate, n=8 models) or two (if the condition affected both mother and neonate, n=9 models) intervention cohorts, as well as the corresponding number of control cohorts (n=17 models). The starting age for mothers in the models was 24 years and 0 years for neonates. Individuals from the intervention cohorts were referred to secondary hospitals, while individuals from comparison cohorts were not referred and received only primary care. For all models, a time horizon of 100 years was chosen to anticipate a lifetime.

Online supplemental files 2 and 3 outline the non-reversible patient journey for referred and non-referred mothers and referred and non-referred neonates, respectively. For the intervention cohort, the patient journey consisted of the following stages: (1) initial presentation at the health centre with a certain pathology, (2) likelihood of referral to a higher level of care, (3) likelihood of survival on reaching the referral hospital and (4) follow-up period after the referral for which all-cause mortality was applied. For the control group, the patient journey differed in that it lacked the stage of referral. It consisted of the following stages: (1) initial presentation at the health centre with a certain pathology, (2) likelihood of survival with a given pathology at the primary care level.

For all cohorts, all-cause mortality was calculated on an annual basis, whereas the first two stages for the comparison groups and the first three stages for the intervention groups were treated as one-time stamp.

We applied these exclusion criteria for the CEA: date of referral not during the study period; referral indication unknown or unrelated to emergency obstetrical and neonatal care; referral indications with less than 10 cases.

Pathway probabilities

Medical records were used to determine the number of mothers and neonates treated at participating CSBs for each referral indication.

Given that there was no previously published data for this context, survival rates for both referred and non-referred mothers and neonates were estimated through a two-stage expert panel process. Three Malagasy physicians, otherwise not involved in this study formed the expert panel. They were chosen as a convenience sample, as they were familiar with the NGO's intervention and had long-term experience in maternal health in the intervention area.

The research team reviewed existing literature from low-income and middle-income countries on maternal survival rates for all referral indications. Both Google Scholar and PubMed were searched to identify relevant studies. From these, we extracted data on survival rates for individual referral indications at primary and secondary facilities as well as information on study design, context, strengths and limitations. We presented these data to the expert panel.

The panel then defined survival rates for each referral indication. Results of this expert panel process are summarised in tables 1 and 2 below. For each condition, the expert panel defined a maximum and minimum survival rate for mothers and neonates at both primary and secondary facilities, as well as an average survival rate agreed on by all experts. This rate formed the baseline estimate for our CEA models.

Life years

Health outcomes were estimated based on local life expectancy tables.[19] Costs and life-years saved were discounted at a 3% discount rate. This rate reflects the average annual growth of the Malagasy economy during the study period[20] and aligns with the approach for discounting in economic evaluation suggested by Haacker *et al*.[21]

Sensitivity analysis

Given that no probabilistic data was available in the literature, we performed a one-way deterministic sensitivity analysis for the survival rates for referred and non-referred mothers and neonates to assess the impact of individual model parameters and assumptions on the model outputs.

Table 1 Survival estimates for mothers

Referral indications mothers (n)	Survival rates when referred to secondary care			Survival rates when not-referred (primary care only)			References
	Min	Max	Baseline	Min	Max	Baseline	
Obstructed labour (251)	95%	99%	98%	80%	99%	90%	27–29
Ineffective labour (137)	98%	99%	99%	85%	99%	95%	30–32
Extrauterine gravidity (50)	99%	95%	99%	0%	0%	0%	33–35
Post-partum haemorrhage (46)	70%	90%	80%	20%	80%	30%	36
Intrauterine fetal death (45)	90%	99%	95%	85%	95%	93%	37
Eclampsia (39)	65%	96%	75%	30%	90%	50%	38–40
Placenta previa (34)	85%	98%	87%	50%	95%	70%	41–44
Abortion (30)	90%	99%	95%	85%	95%	90%	45
Risk of premature delivery (26)	99%	99%	99%	98%	98%	99%	36
Placenta retention (25)	99%	99%	99%	50%	99%	91%	46 47
Delivery (22)	98%	99%	98.5%	95%	99%	96.5%	36
Infection post partum (19)	90%	98%	95%	70%	95%	80%	48 49
Risk of uterus rupture (17)	90%	95%	92.5%	5%	40%	35%	50–53
Fetal distress (12)	98%	99%	98.5%	70%	99%	96.5%	54–56
Malaria (12)	98%	99%	99%	95%	98%	97.5%	57

Minimum, maximum and baseline survival estimates for referred and non-referred mothers grouped by referral indication. Survival estimates were obtained by expert panel consensus.

Table 2 Survival estimates for neonates

Referral indications neonates (n)	Survival rates when referred to secondary care			Survival rates when not-referred (primary care only)			References
	Min	Max	Baseline	Min	Max	Baseline	
Obstructed labour (251)	60%	90%	70%	25%	80%	35%	27–29
Ineffective labour (137)	45%	95%	55%	30%	88%	35%	30–32
Eclampsia (39)	30%	80%	50%	15%	50%	25%	38–40
Placenta previa (34)	50%	95%	60%	20%	90%	30%	41–44
Risk of premature delivery (26)	15%	98%	70%	15%	97%	25%	58 59
Delivery (22)	85%	98%	92%	75%	95%	85%	36
Risk of uterus rupture (17)	20%	93%	90%	3%	40%	10%	50–53
Fetal distress (12)	70%	99%	95%	30%	98%	55%	54–56
Respiratory distress (12)	5%	90%	20%	1%	50%	5%	60 61
Malaria (12)	90%	98%	95%	90%	94%	91%	50
Neonatal infection (10)	5%	85%	70%	5%	80%	50%	58 62

Minimum, maximum and baseline survival estimates for referred and non-referred neonates grouped by referral indication. Survival estimates were obtained by expert panel consensus.

Patient and public involvement statement

This study did not involve patients in the research process. However, we did involve three independent Malagasy clinicians in the research process as key informants for the expert panel process to define survival probabilities for the different patient pathways. This greatly enhanced the applicability and relevance of our research in the context of Southern Madagascar.

RESULTS

Referral characteristics

In total, 1172 patients (48 neonates and 1124 women, respectively) were referred through the intervention. Most referrals took place in the Atsimo-Andrefana region (54%), followed by Anosy (45%) and Androy regions (1%). The average distance per referral was 52.8 km.

Demographic and clinical characteristics

The mean age of women was 23.6 years (n=1118; IQR=12). Most neonates (78%, 36/46) were in their first week of life. 80% of calls were made for direct obstetrical causes above all for obstructed/prolonged labour (40%, 445/1,124) (table 3). For neonates, the most common referral indications were respiratory distress (29%, 14/48) or infection (21%, 10/48) (table 4).

Complications during pregnancy, childbirth and post partum, which triggered the referral of mothers (n=1124) from participating CSBs to secondary referral hospitals. CSB, Centre de Santé de Base (public primary care facility).

Complications during the neonatal period, which triggered the referral of neonates (n=48) from participating CSBs to secondary referral hospitals.

Not all calls resulted in a completed referral. In 97 cases the ambulance was dispatched but the referral was not completed. Most commonly (65%, 63/97) the complication had been resolved at the CSB either with (25%, 24/97) or without (40%, 39/97) support from the ambulance staff. In eight cases (8.2%) the woman or neonate had passed away before the ambulance reached the CSB

Table 3 Referral reasons for mothers

Obstetrical complication	Women (n=1124)	(%)
Direct causes	906	80.6
Abortion and its complications, including intra-uterine fetal death	89	7.9
Ectopic pregnancy	52	4.6
Embolism	1	0.1
Hypertensive disorders	61	5.4
Prepartum/postpartum haemorrhage	114	10.1
Obstetrical trauma	18	1.6
Obstructed/prolonged labour	445	39.6
Other direct causes	141	12.5
Indirect causes	123	10.9
Anaemia	7	0.6
Malaria	12	1.1
Tuberculosis	1	0.1
Other indirect causes	88	7.9
Other cases*	37	3.3
No obstetrical complication specified	58	5.2

*Such as: no medical staff present at CSB, insufficient equipment for delivery at CSB.
CSB, Centres de Santé de Base.

Table 4 Referral reasons for neonates

Complication	Neonates (n=48)	%
Abdominal bloating	3	6.3
Birth defect	9	18.8
Dehydration	4	8.3
Hypothermia	1	2.1
Icterus	1	2.1
Unspecified infection*	10	20.8
Premature birth	4	8.3
Respiratory distress	14	29.2
Syphilis	1	2.1
Other (=vomiting)	1	2.1

*Unspecified infection included neonates showing signs of infection such as fever, altered cardiorespiratory status or marmorated skin.

and in four cases (4.1%) the patient or patient's relatives refused the referral.

Costs

The total intervention costs over the study period were US$394 197.

Online supplemental files 4 and 5 show the detailed distribution of cost of operating one vehicle over the intervention time frame (January 2016 to September 2020).

The average cost per referral was US$367 (n=1075). If the costs of the project were shared among all people living in the project area, initial investment costs would be US$0.13 per person and annual running costs US$0.06 per person.

Around 20% of the population in the study region are women of reproductive age. Assuming that each of these women could be a potential beneficiary of the project, the costs per potential beneficiary amount to US$0.57 per person in investment and US$0.26 in annual running costs.

Cost-effectiveness analysis

Incremental life-years saved through the programme were 37 882 (rounded to the full year) undiscounted and 4872 when discounted at 3%.

The overall ICER of the ambulance system was US$70 per additional life-year saved undiscounted and US$137 per additional life-year saved when discounted at 3%.

The ambulance intervention proved particularly cost-effective for cases of extrauterine gravidity, risk of uterus rupture and postpartum haemorrhages with ICERs of less than 30 (discounted at 3%). The programme proved least effective for cases of malaria in pregnancy and post-partum infection. Table 5 below lists the costs per life year saved as well as the ICER per diagnosis.

Sensitivity analysis

The sensitivity analysis showed the intervention to remain cost-effective for most scenarios tested. However in the following cases either the survival rate estimates at the participating CSB exceeded the baseline estimate at the referral hospital or the worst case estimate at the

Table 5 Results of cost-effectiveness analysis

Referral indication (n)	Cost per life year saved discounted/ undiscounted (USD)	ICER discounted/undiscounted
Obstructed labour (251)	11.2/5.9	62.9/30.1
Ineffective labour (137)	11.7/6.2	115.1/54.7
Extrauterine gravidity (50)	14.4/8.0	14.4/8.0
Postpartum haemorrhage (46)	17.1/9.5	26.4/14.6
Intrauterine fetal death (45)	15.0/8.3	710.9/394.0
Eclampsia (39)	14.8/7.8	40.1/20.7
Placenta previa (34)	12.3/6.5	57.8/28.3
Abortion (30)	15.0/8.3	284.3/157.6
Risk of premature delivery (26)	11.0/5.8	72.9/32.7
Placenta retention (25)	14.3/7.9	171.3/94.9
Delivery (22)	10.4/5.4	288.5/138.9
Infection post partum (19)	59.9/33.2	379.1/210.1
Risk of uterus rupture (17)	10.9/5.7	15.6/8.0
Fetal distress (12)	10.3/5.3	76./34.5
Malaria (12)	10.3/5.3	447.8/217.8
Respiratory distress neonate (12)	170.2/75.8	227.0/101.0
Neonatal infection (10)	48.6/21.7	107.2/75.6

Costs per life-year saved (in USD) and ICER per diagnosis, undiscounted and discounted at 3%.
ICER, incremental cost-effectiveness ratios.

hospital was lower than the baseline estimate at the CSB, rendering the scenario not cost-effective: Mothers survival for eclampsia, neonates survival for ineffective labour, neonate survival for neonatal infection, neonates survival for respiratory distress and neonates survival for risk of premature delivery tested.

DISCUSSION

The aim of this study was to evaluate the characteristics, costs and cost-effectiveness of an NGO-run inter-facility referral system for EmOC in rural Madagascar.

This study revealed three main findings: First, the most common referral indication for mothers was obstructed/prolonged labour and unspecified infection or respiratory distress for neonates. Second, the largest drivers of costs for the intervention were initial investment costs for the vehicles and running costs including staff wages. Consequently, ambulance lifespan is a particularly important determinator of the intervention's cost-effectiveness. Lastly, the CEA demonstrated the intervention to be very cost-effective, with an ICER of US$137 per additional life year saved (discounted at 3%). The intervention was particularly cost-effective for the following conditions: extrauterine gravidity, risk of uterus rupture and post-partum haemorrhage. The sensitivity analysis conducted showed the intervention to remain cost-effective in most scenarios tested. While there are no other studies evaluating similar interventions in Madagascar, our intervention shows itself to be more cost-effective than other CEAs conducted in Madagascar, which reported ICERs of US$1023 per quality-adjusted life year (QALY) gained for an intervention expanding access to antibiotics for plague care and prevention,[22] US$177 per disability-adjusted life year (DALY) averted for a drone-supported community treatment programme for tuberculosis[23] and US$531.2 per DALY averted[24] for the indoor-residual spraying activities of the national tuberculosis control programme, showing our intervention to have a much lower ICER.

In accordance with our findings, other systems for EmOC referral in SSA have found direct obstetrical complications, especially abortion and obstructed labour to be the main referral indications for mothers to secondary health facilities in resource-constrained settings.[11 12]

Compared with other ambulance referral systems in Uganda,[9] Burundi[11] and Ethiopia,[12] costs for our intervention were high. This finding is however not surprising considering that referrals in other interventions were not accompanied by trained medical personnel receiving salaries. Neither ambulance carried medical equipment and neither publication included overhead costs such as administrative costs in their CEA. In addition, our intervention covered a large rural area in the remote south of Madagascar; there were no paved roads and conditions deteriorated during the rainy season when parts of the intervention became inaccessible. This increased costs for vehicle maintenance and fuel. These differences in the design of the interventions, as well as their contexts of implementation, likely explain the higher ICER of US$137 per additional life-year saved (discounted) when compared with ICERs of US$16[9] and US$25 per additional life-year saved[12] in Uganda and Ethiopia, respectively. Further, these studies only included referrals in their analysis which were deemed 'undoubtedly effective',[9 12] that is, cases in which the referral was likely to have a large impact on life-years saved. Our model on the other hand included all cases in the calculation of the overall ICER.

Consequently, costs per referral were higher for our setting than in other studies. Tayler-Smith *et al* reported costs of US$61 per referral, with 1478 ambulance referrals per year,[11] compared with 1075 completed referrals over 4 years, with an average cost per referral of US$367 in our setting.

Regarding the per capita costs, our intervention compares preferably, with investment costs of US$0.13 per person and annual running costs of US$0.06 per person, when extrapolated to the entire population serviced. This is lower than what has been reported in other rural settings, for example, in Burundi (€0.43/capita/year),[11] suggesting that the intervention described here served a larger population at comparable costs and suggesting that the intervention could be sustainable, even in a setting where most of the population lives in extreme poverty.[25] The fact that the referral system has such low per capita costs and a lower ICER than components already incorporated into the national malaria control programme in Madagascar,[24] suggests that the referral system described herein could be feasibly adapted into the national care system in Madagascar.

Our study has three main strengths: First, we used secondary NGO data as the basis for all analyses. This reduced the potential for erroneous data as there was no need to rely on estimations. Further, our data provide insights into a particularly vulnerable and resource-constrained setting for which data is otherwise hard to obtain. Second, we included all costs for the running of the ambulance system in the CEA, including overhead costs such as administrative costs, rendering more realistic cost estimates than other studies. Third, we obtained survival estimates using a multistep expert consensus process, when these data were not available from the literature.

Our study has several limitations. First, we were constrained by the availability of programmatic data and had to rely on expert opinions to estimate equipment lifespans as well as survival rates for the economic model. For the latter, to mitigate potential bias we established an expert panel consensus process to estimate survival rates. This may have led to an overestimation or underestimation of survival rates for the different conditions included in the model, as expert opinion builds on subjective experience, not representative data. Despite these limitations of expert opinion, however, they are commonly used in cost-effectiveness analyses in the absence of stronger data to estimate model parameters, as was the case in our setting.[26] Additionally, we drew on the available literature from similar settings in SSA to put the estimates obtained from the expert panel process into context and verify for any outliers or implausible values. Second, data were not available on mothers' post-delivery complications or their previous patient history to allow for more nuanced calculations for life years saved and our model only accounted for mothers and neonates, for whom referral was successful. However, we do not expect either factor to have a large impact on the model's cost-effectiveness and are confident that the approach of constructing separate models per cohort can robustly identify the most cost-effective applications of inter-facility EmOC referrals. Last, we did not assess whether the intervention met the referral needs of the population in the study area.

CONCLUSION

Our study is the first to report the cost-effectiveness of an EmOC inter-facility referral system in Madagascar. We find the intervention to have been very cost-effective, especially for cases requiring surgical care. Our findings highlight the need for a comprehensive approach to providing rural EmOC services and may provide guidance on public health resource allocation in Madagascar.

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