# **BMJ Open** Direct patient costs of maternal care and birth-related complications at faithbased hospitals in Madagascar: a secondary analysis of programme data using patient invoices

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# ABSTRACT

**Objectives** We aimed to determine the rate of catastrophic health expenditure incurred by women using maternal healthcare services at faith-based hospitals in Madagascar.

**Design** This was a secondary analysis of programmatic data obtained from a non-governmental organisation. **Setting** Two faith-based, secondary-level hospitals located in rural communities in southern Madagascar. **Participants** All women using maternal healthcare services at the study hospitals between 1 March 2019 and 7 September 2020 were included (n=957 women). **Measures** We collected patient invoices and medical records of all participants. We then calculated the rate of

catastrophic health expenditure relative to 10% and 25% of average annual household consumption in the study region.

**Results** Overall, we found a high rate of catastrophic health expenditure (10% threshold: 486/890, 54.6%; 25% threshold: 366/890, 41.1%). Almost all women who required surgical care, most commonly a caesarean section, incurred catastrophic health expenditure (10% threshold: 279/280, 99.6%; 25% threshold: 279/280, 99.6%). The rate of catastrophic health expenditure among women delivering spontaneously was 5.7% (14/247; 10% threshold).

**Conclusions** Our findings suggest that direct patient costs of managing pregnancy and birth-related complications at faith-based hospitals are likely to cause catastrophic health expenditure. Financial risk protection strategies for reducing out-of-pocket payments for maternal healthcare should include faith-based hospitals to improve health-seeking behaviour and ultimately achieve universal health coverage in Madagascar.

## INTRODUCTION

Reducing maternal and neonatal mortality is a key element of the United Nations Sustainable Development Goals. In 2017, approximately 295000 women died from obstetric complications worldwide.<sup>1</sup> Women living in

# Strengths and limitations of this study

- This study is the first to describe the rate of catastrophic health expenditure incurred by women using maternal healthcare services at faith-based hospitals in Madagascar.
- To eliminate recall bias and increase data quality, we based study outcomes on patient invoices and medical records and not on self-reported costs or conditions.
- We did not look at healthcare expenditure at the household level.
- Our study was limited to two faith-based referral hospitals in rural regions of Madagascar.

sub-Saharan Africa (SSA) are over 300 times more likely to die from obstetric complications than women in the European Union.<sup>1</sup> While there has been substantial progress in reducing all-cause maternal mortality in SSA by 39% between 2000 and 2017, this is insufficient to reach the goal of less than 70 maternal deaths per 100 000 live births by 2030.<sup>1</sup> The main causes of maternal deaths in SSA are postpartum haemorrhage, infections, hypertensive disorders during pregnancy and abortion.<sup>2</sup> Together, these conditions account for more than 50% of all maternal deaths in the region.<sup>2</sup>

Among the multitude of individual and health system level obstacles in accessing quality maternal healthcare services, out-of-pocket (OOP) payments are a major reason for not seeking skilled care during pregnancy or delaying the decision of seeking care.<sup>3</sup> <sup>4</sup> Catastrophic health expenditure (CHE), commonly defined as OOP payments for healthcare exceeding 10% or 25% of a household's annual income or consumption,<sup>5</sup>

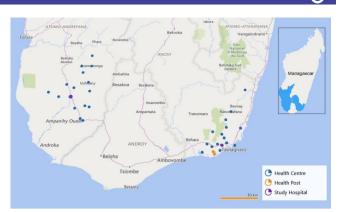
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can have long-term socioeconomic consequences for affected households. Poorer households are more vulnerable to financial hardship after experiencing CHE and face a high risk of being driven deeper into poverty.<sup>67</sup> Poverty in turn can limit a household's capacity to pay for future episodes of illness and the negative long-term consequences of poverty on health are widely recognised.<sup>8</sup> Despite the widespread introduction of cost-exemption policies and the abolishment of direct patient costs for maternal healthcare in many countries in SSA, expectant mothers still face OOP payments for maternal care and birth-related complications.<sup>9-11</sup> Diagnostic procedures, medicines and delivery supplies are the main drivers of OOP payments.9 10 In Ghana, Kenya, Tanzania and Burkina Faso, 30%–90% of women pay at least a fraction of treatment costs OOP, even after the implementation of cost-exemption schemes or the abolishment of direct patient costs for maternal care in these countries.<sup>9 12 13</sup>

In Madagascar, 78.8% of the population of 26 million live on less than US\$1.90 a day (2011 PPP).<sup>14</sup> Poverty rates are especially high among rural communities.<sup>15</sup> Maternal mortality remains high (335 deaths per 100 000 live births).<sup>1</sup> Eighty-three per cent of Malagasy women report obstacles to access healthcare and women living in rural areas are particularly affected.<sup>16</sup> The most common obstacle is a lack of financial resources and women from the poorest wealth quintile are more likely to face obstacles to seeking care (78%) than those from the richest wealth quintile (58%).<sup>16</sup> But even in urban regions of Madagascar, 85% of households resort to coping mechanisms such as borrowing money or selling assets to cover treatment costs for maternal care.<sup>17</sup>

The healthcare system in Madagascar is organised by different levels of specialisation. Community health workers and health centres provide primary care at the community level and refer more complicated cases to specialised district and regional centres. In 2015, the Malagasy Ministry of Health created a national pooled funding mechanism to reduce user-fees at the point of care and to increase overall healthcare utilisation.<sup>18</sup> Maternal healthcare services including antenatal care and caesarean sections (C-sections) should be free of charge at public health facilities.<sup>19</sup> Apart from public health facilities, faith-based hospitals play a major role in Madagascar's healthcare system,<sup>20</sup> including health facilities run by the Catholic and Lutheran churches. The health department of the Lutheran Church of Madagascar (SALFA) is the largest non-public healthcare provider in the country, running over 50 healthcare facilities and treating around 250 000 patients a year, mainly in rural regions.

However, despite severe financial obstacles to accessing maternal healthcare services, data on direct treatment costs from Madagascar are extremely rare. To date, only one study reported costs for maternal care and birth-related complications obtained from a public urban tertiary hospital.<sup>17</sup> No data are available from faith-based hospitals, even though they play an important role for providing maternal healthcare services. Thus, the extent



**Figure 1** Study region. Map of the administrative regions Atsimo-Andrefana (left) and Anosy (right, marked on inset). Dots show study hospitals at Ejeda and Manambaro and health centres and health posts which referred women to study hospitals during the duration of the study.

to which direct patient costs result in CHE at faith-based hospitals is unknown. Therefore, we aimed to estimate the rate of CHE caused by direct patient costs for maternal care and birth-related complications at faith-based hospitals in two communities in the rural south of Madagascar. We expect the results of this study to guide policy development related to financial risk protection and to promote efforts towards reducing OOP payments and promoting universal health coverage in Madagascar.

# METHODS

## Study area and context

The study area was located in the rural regions of Atsimo-Andrefana and Anosy in southern Madagascar (figure 1). Atsimo-Andrefana (1.8 million inhabitants) and Anosy (833000 inhabitants) are among the most remote regions of the island.<sup>21</sup> The majority of the population in Atsimo-Andrefana (82%) and Anosy (84%) live below the national poverty line of US\$129.56 total annual per capita consumption<sup>21</sup> and 78.8% of the national population live below the International Poverty Line of US\$1.90 per day (2011 PPP).<sup>14</sup> The region of Atsimo-Andrefana is divided into nine health districts, served by nine public hospitals, 116 public health centres and 68 public health posts.<sup>22</sup> The Lutheran church of Madagascar runs two districtlevel hospitals and three health centres in the region. Anosy region is divided into nine health districts, served by three public hospitals, 65 health centres and 14 health posts.<sup>22</sup> The Lutheran church runs one district-level hospital and three health centres in the region. The study hospitals located in Ejeda (54 beds) and Manambaro (50 beds), run by the Lutheran church of Madagascar, offer non-surgical and surgical maternal healthcare services. Women could either directly seek care at the study hospitals or be referred from a health post or centre for further treatment. There was no public emergency referral system and women usually had to arrange their own transportation. Doctors for Madagascar, a German-Malagasy nongovernmental organisation (NGO) offered direct cash support for maternal healthcare services and a referral service from selected health centres and health posts to the study hospitals free of charge.

## **Data collection**

We collected data on direct patient costs which women incurred for maternal care and birth-related complications between 1 March 2019<sup>10</sup> and 7 September 2020 at the study hospitals. Our primary data sources were patient invoices and patient records containing information on patient age, diagnosis at admission, type of referral, name of the referring healthcare centre and treatment details. We obtained primary data from an NGO, which implemented a maternal health programme at the study hospitals. Healthcare staff, who were not otherwise involved in this study, replaced patient identifying information with numerical pseudonyms before forwarding digitised patient invoices and records to the research team for analysis. We collected the original data in French and translated it to English. All data were stored in a protected database.

## Exclusion and inclusion criteria

All women receiving maternal care or care for birthrelated complications at the two study hospitals during the study period were included. Women presenting with more than one admission diagnosis or seeking care for themselves and their newborns were excluded from analysis.

## **Data analysis**

We coded admission diagnoses and treatment details obtained from patient invoices and medical records according to the International Classification of Diseases (ICD) V.10.<sup>23</sup> Procedures were coded according to the Systematised Nomenclature of Medicine (SNOMED, V.2020-07-31).<sup>24</sup> In case of uncertainty (ie, ambiguity of language), we sought clarification from two Malagasy physicians who were unfamiliar with the aim of this study. ICD and SNOMED codes of diagnoses and procedures extracted from patient invoices and medical records are summarised in online supplemental tables 1 and 2. Diagnoses not related to 'pregnancy, childbirth and the puerperium' (ICD Codes O00-O99) were classified as 'other'. Direct treatment costs were collected and analysed in Malagasy Ariary and converted to USD for reporting (average annual exchange rate 2019, US\$1=Ar3618.32).

We calculated average treatment costs for each diagnosis and procedure defined by ICD and SNOMED codes, respectively. Only primary diagnosis and one procedure per woman were considered for analysis. We then calculated the proportion of women who incurred CHE per diagnosis and per procedure. In addition, we analysed the prevalence of individual diagnoses and procedures among all women incurring CHE. All analyses were performed in STATA (V.14.2, StataCorp). The results were considered statistically significant for p $\leq$ 0.05. We used violin plots to show summary statistics as well as probability densities of the data as some treatment cost distributions had multiple peaks (ie, multimodal distribution).<sup>25</sup> Probability densities were smoothed by a Gaussian kernel density estimator, plots were prepared using GraphPad Prism V.9.

## **Definition of CHE**

To assess the prevalence of CHE households incurred for maternal care and birth-related complications in the study region, we defined CHE using total direct patient costs and annual household consumption. We used total direct patient costs as the numerator. We adopted a common convention and used total household consumption as the denominator, which better captures the effect of health expenditures on disposable income. We calculated annual household consumption for each study region by multiplying individual annual per capita consumption with the average number of household members according to most recent household survey data.<sup>26</sup> For our purposes, a household was defined as having incurred CHEs if the direct patient costs exceeded 10% or 25% of the annual household consumption in the study region.<sup>5</sup>

## RESULTS

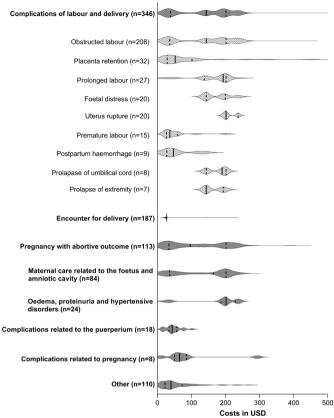
Data were available for 957 women who received maternal healthcare services at the study hospitals during the study period. There were no missing data.

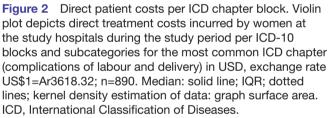
## Study population

The mean age of women was 24.3 years (SD: 7.2). The duration of hospitalisation was 5.1 days (SD 5.2) and 75.1% of women received surgical care. 35.6% were referred by ambulance. The mean distance travelled was 23.2 km (SD 18.7 km), whereas the distance was higher for women referred by ambulance (24.3 km, SD: 18.8) than for those who arranged their own means of transport (15.5 km, SD: 17 km; p=0.001). Neither age (p=0.23) nor distance travelled to the hospital were associated with direct patient costs. Sixty-two women (62/957, 6.5%) presented with more than one diagnosis; on five occasions (5/957, 0.5%) both mothers and new-borns required medical care. These cases were excluded from subsequent analysis.

#### **Diagnoses**

The most common ICD-10 blocks at admission were complications of labour and delivery (346/890, 38.9), followed by encounter for delivery (186/890, 21%), pregnancies with abortive outcomes (113/890, 12.7%) and maternal care related to the fetus and amniotic cavity and possible delivery problems (84/890, 9.4%, figure 2). Only a minority presented with diagnoses related to oedema, proteinuria and hypertensive disorders in pregnancy, childbirth and the puerperium (24/890, 2.7%), complications predominantly related to the puerperium (18/890, 2.0%) and other disorders predominantly related to





pregnancy (8/890, 0.9%). A total of 110/890 (12.4%) of women presented with diagnoses not included in the ICD chapter pregnancy, childbirth and the puerperium. Frequency and percentages of ICD chapter blocks and pertaining diagnoses are summarised in online supplemental table 3.

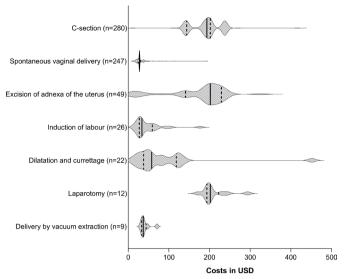
#### **Direct treatment costs**

### Direct treatment costs per diagnostic category

On average, women spent US\$100.39 (SD: 83.23) per case on maternal healthcare services. Direct treatment costs for encounter for delivery ranged from US\$9.92 to US\$237.46. Direct treatment costs for abortion and eclampsia ranged between US\$8.48 and US\$389.63 and US\$15.70 to US\$237.46, respectively. Overall, we observed a high variation of direct treatment costs among individual categories. The highest variation occurred in the category 'molar pregnancy' (SD 120.14) and the lowest in the category' "spontaneous vaginal delivery' (SD 8.63, figure 2).

## Direct treatment costs per procedure

The most common procedures were C-section (n=280) and spontaneous vaginal delivery (n=247). The mean



**Figure 3** Direct patient costs per procedure. Violin plot depicts direct treatment costs incurred by women at the study hospitals during the study period per procedure in United States Dollars (USD), exchange rate US\$1=Ar3618.32; n=645. procedures were assigned according to the Systematised Nomenclature of medicine clinical terms (SNOMED CT, V.2020-07-31). median: solid line; IQR: dotted lines; kernel density estimation of data: graph surface area. procedures are shown if n>5.

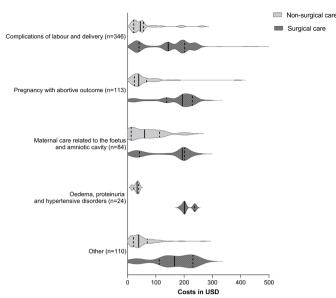
costs of a C-section and spontaneous vaginal delivery were US\$191.29 (SD: 38.47) and US\$30.40 (SD: 18.29), respectively. The most expensive procedures were hysterectomy (n=3; US\$249.98, SD: 26.89) and laparotomy (n=12) performed due to extrauterine gravidity, uterus rupture or haemorrhage (US\$209.84, SD: 32.11, figure 3).

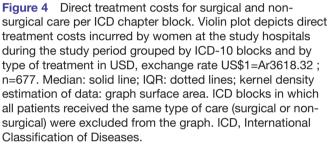
#### Direct treatment costs for non-surgical care

Two-hundred and twenty-six women received non-surgical care. The most common diagnostic block in this group were pregnancies with abortive outcomes (n=52), 30 of which were uncomplicated abortions. Complications of labour and delivery (n=28) including placenta retention and postpartum haemorrhage were the second most common diagnostic block. All women receiving non-surgical care for complications related to the puerperium (n=18) had a postpartum infection. The most common non-surgical treatments were antibiotics (n=199, 88.1%) and analgesia (n=131, 58%). Among the same diagnostic block direct patient costs were significantly higher for women requiring surgery than for those receiving non-surgical treatment (p<0.005). Figure 4 illustrates these findings.

### **Catastrophic health expenditure**

The average annual consumption per household was Ar1575840 (US\$435.52) and Ar1613280 (US\$445.86) in Anosy and Atsimo-Andrefana, respectively.<sup>26</sup> Patient expenditures were assumed to be catastrophic when exceeding Ar157584 (US\$43.55) and Ar161328 (US\$44.59) using the 10% threshold and Ar393960





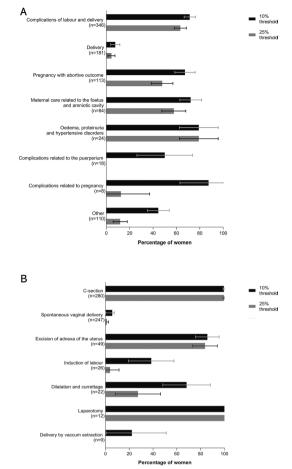
(US\$108.88) and Ar403320 (US\$111.47) using the 25% threshold in Anosy and Atsimo-Andrefana, respectively.

Overall, 486 of 890 women (54.6%) faced CHE at 10% and 366 of 890 (41.1%) at 25% threshold. Four procedures did not cause CHE at 10% or 25% threshold: blood transfusion, vaginal breech delivery, vaginal twin delivery and drainage of pleural cavity. Women who delivered spontaneously faced CHE at 10% in 5.7% (14/247) and at the 25% threshold in 1.2% (3/247) of cases. The most common cause of CHE was C-section at 10% threshold (279/280, 99.6%) and 25% threshold (279/280, 99.6%). The second most likely cause was excision of the adnexa of the uterus at 10% threshold (42/49, 85.7%) and 25% threshold (41/49, 83.7%). The percentages of CHE at 10% and 25% thresholds by ICD-10 blocks and surgical procedures are shown in figure 5.

#### DISCUSSION

This study analysed direct patient costs of maternal healthcare services and estimated the rate of CHE incurred at two district-level faith-based hospitals in rural Madagascar using patient invoices and medical records as the data source. Our study revealed two main findings. First, the rate of CHE was high. Second, we found considerable variation in costs per diagnosis and treatment.

The overall rate of CHE (10% threshold: n=486/890, 54.6%; 25% threshold: n=366/890, 41.1%) was higher than in most other studies from SSA, which range from 33% in Ghana (relative to 5% of annual household



**Figure 5** Catastrophic health expenditure by ICD chapter block and by procedure. (A) Percentage of women incurring catastrophic health expenditure for each ICD-10 chapter block and (B) by procedure (classified according to the systematised nomenclature of medicine clinical terms SNOMED CT (V.2020-07-31)), relative to 10% and 25% of annual household consumption during the study period; n=890. Error bars depict 95% CI of the mean. ICD, International Classification of Diseases.

expenditure) to 47% in Cameroon (relative to 20% of total household income).<sup>13 27</sup> However, differences in study methodology may limit comparability. Women who delivered spontaneously rarely faced CHE (14/247, 5.7% at 10% threshold; 3/247, 1.2% at 25% threshold). This is in line with findings from a recent review, which reported CHE being caused by vaginal deliveries in only one out of 12 countries in SSA.<sup>28</sup> In contrast, 71.4% (247/346) and 63.3% (219/346) of women who were treated for birth-related complications including obstructed labour (208/346), placental retention (32/346), and foetal distress (20/346) faced CHE at 10% and 25% threshold, respectively. In addition, women who required surgical care (n=664) were at high risk of CHE (10% threshold: n=383/664, 57.7%; 25% threshold: n=347/664, 52.3%). Emergency obstetric care is likely to cause CHE in SSA, with C-sections being a particularly expensive component of care.<sup>28–30</sup> However, the rate of CHE as a result of emergency obstetric care including surgical care was higher in our study compared with other countries. In Uganda and Mali, only 25% and 21% of households face CHE (relative to 10% of annal household expenditure and 15% of annual household income, respectively) due to a C-section or emergency obstetric care.<sup>6 31</sup> In Ghana, 33% of households face CHE because of obstetric complications (relative to 5% of annual household expenditure).<sup>13</sup> The high rate of CHE in our study was most likely due to the composition of the patient sample. We used data from two faith-based hospitals serving as reference hospitals, where the majority of women were treated for birth-related complications. These cases often required surgical care, which is usually more expensive. Costs of a C-section in our study were also higher than those reported from an urban public healthcare provider in Madagascar (US\$191 vs US\$161 (corrected for inflation).<sup>17</sup> This is in line with the finding that treatment provided by faith-based hospitals compared with public hospitals may generally be more expensive in SSA.<sup>32</sup> The high proportion of people living below the international poverty line of US\$1.90 per day in Madagascar (78.8%) compared with Ghana (13%), Uganda (41.5%) and Mali (50.3%) may as well have contributed to this finding.<sup>14</sup>

The overall direct patient costs for maternal healthcare services including spontaneous vaginal delivery, C-section, abortion, eclampsia and maternal haemorrhage were similar to other reports from countries in SSA, such as Ghana, Tanzania and Uganda.<sup>28</sup> The direct patient costs were lowest for spontaneous vaginal delivery, as it requires few drugs and consumables and brief hospitalisation. Direct patient costs were highest for birth-related complications, which were likely to require a C-section. Direct patient costs for a C-section were more than six times higher than those for a spontaneous vaginal delivery. This ratio was similar to data from a public urban hospital in the DRC<sup>33</sup> but lower compared with data from rural and urban primary and secondary health facilities in Burkina Faso where costs for a C-section are up to 27 times higher than those for a spontaneous vaginal delivery.<sup>10</sup> More generally, OOP payments for emergency obstetric care-including surgical and non-surgical treatment-are two to six times higher than for spontaneous vaginal delivery in Burkina Faso, Ghana and Benin.<sup>10 34</sup>

OOP payments for birth-related complications may pose a significant hindrance for women seeking life-saving care, especially for those from poor socioeconomic backgrounds.<sup>35</sup> Two-thirds of Malagasy women report direct patient costs as an obstacle to seeking care.<sup>16</sup> Similar findings have been reported from various other settings across SSA.<sup>4</sup> Antenatal care visits increased by 25% in a rural district in Madagascar when user fees were abolished, further supporting the notion that pregnant women forgo seeking qualified care due to direct patient costs.<sup>18</sup> Interestingly, the treatment costs of some birth-related complications for which women received a surgical intervention were capped at US\$237.46 and US\$201.75 at Manambaro and Ejeda hospital, respectively. This likely indicates that direct patient costs were capped by faith-based hospitals to lower financial obstacles to accessing care.

Direct patient costs varied greatly among individual diagnoses and procedures. The costs for spontaneous vaginal delivery in our study ranged from US\$9.92 to US\$193.46 which was higher than variations reported from Uganda (US\$2.7-US\$33.90), Malawi (US\$10.20 -US\$24.00) or Ghana (US\$7.70–US\$14.60).<sup>36</sup> The costs for a C-section varied between US\$111.05 and US\$415.86, which was similar to those at an urban public healthcare provider in Madagascar where costs for a C-section range from US\$5 to US\$351.<sup>17</sup> The variation of costs could be caused by multiple factors. First, differences in treatment protocols or surgical practice between the study hospitals may have influenced the services provided and the length of hospital stay. Second, the availability of resources including drugs and consumables may have affected direct patient costs. This may be aggravated by drug shortages and rising drug prices during the COVID-19 pandemic, which have been reported in other countries in SSA<sup>37</sup> and were empirically observed in Madagascar. Third, identical procedures were performed for a wide range of pathologies, indicating that differences in resource requirements may have contributed to cost variation. Last, the average inflation rate of 5.3% over the study period could additionally influence the variation of costs across cases.<sup>38</sup> The low predictability of costs is further compounded by informal payments at health facilities<sup>39</sup> or stock-outs at hospital pharmacies.<sup>40</sup>

Our study has limitations. First, we used two different data sets to obtain information on household consumption and health expenditure, which may lead to an inaccurate estimate of CHE. This is because we conducted a secondary analysis of programme data, which did not contain information on an individual household's income or consumption. Instead, we used consumption data from the most recent DHS survey. As the study hospitals were the only secondarylevel hospitals providing maternal and newborn healthcare in the study region, DHS data likely reflect the sociodemographic characteristics of patients' households. Second, we calculated the prevalence of CHE using one-time health expenditure incurred by a single household member. This likely results in an underestimation of the true prevalence of CHE. Third, our analysis did not consider indirect costs of maternal healthcare, such as for transport, food or clothing. However, transport costs play a major role in causing CHE and deter patients from seeking care.<sup>13 16 35</sup> Fourth, we obtained our data from patient invoices which were issued by the hospitals, not directly from patients. While healthcare personnel are likely to have a great interest in accurately invoicing expensive treatments, they might not have done so for low-cost treatments as they might have been deterred by the efforts of reporting. Thus, the rate of CHE might be higher than estimated. Fifth, coding of diagnoses was done retrospectively from free text patient invoices and medical records by the data analyst. Therefore, even though we sought clarification with healthcare personnel when necessary, this may have introduced coding errors. Last, data were only available from faith-based hospitals in rural regions and limited to the south of Madagascar. However, faith-based hospitals are an important pillar of the Malagasy healthcare system and no other study has previously reported data on direct patient costs for maternal healthcare from faith-based hospitals in Madagascar.

# CONCLUSIONS

Overall, our findings suggest that direct patient costs of managing maternal care and birth-related complications at faith-based hospitals in rural Madagascar are very commonly catastrophic relative to annual household consumption. OOP payments for maternal healthcare are likely to contribute to high poverty levels in Madagascar and may deter women from seeking care. Effective policies to reduce OOP payments may, in turn, alleviate poverty, promote health-seeking behaviour and ultimately contribute to reducing maternal mortality in Madagascar.

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**Contributors** MAF, SK and JVE developed the study design in collaboration with RMR, MR, SR and TB. RMR, MR and MAF collected the data. MAF, SK and JVE contributed to the analysis. MAF wrote the first draft of the manuscript. All authors contributed to the manuscript. All authors read and approved the final manuscript. JVE is responsible for the overall content as the guarantor.

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#### Competing interests None declared.

Patient and public involvement Neither patients nor the public were involved in study development, choice of outcome measures and patient recruitment or any other aspect of this study.

Patient consent for publication Not applicable.

**Ethics approval** Ethical approval for this study was obtained from the Ethics Committee of the Medical Faculty of Heidelberg University (S-713/2020). In addition, we obtained formal approval to conduct this secondary analysis of de-identified NGO data from the district health office (a regional subdivision of the Malagasy Ministry of Health) in Atsimo-Andrefana.

Provenance and peer review Not commissioned; externally peer reviewed.

**Data availability statement** Data are available on reasonable request. The raw data that support the findings of this study are available from the corresponding author, JVE, on request.

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